Ministry of Higher Education
& Scientific Research
University of Kerbala
College of Applied Medical Sciences
Department of Clinical Laboratories

Study Effect of Bacterial Infections on Some Physiological and Biochemical Parameters in Heart Failure Patients, in Karbala

A thesis
Submitted to the council of the
College of Applied Medical Sciences – University of Kerbala
In Partial of Fulfillment of the Requirements for the Degree of Master in Clinical Laboratories

Submitted by

(Zainab Nasee Arif)

B. Sc. Applied Medical Sciences/University of Kerbala, 2018

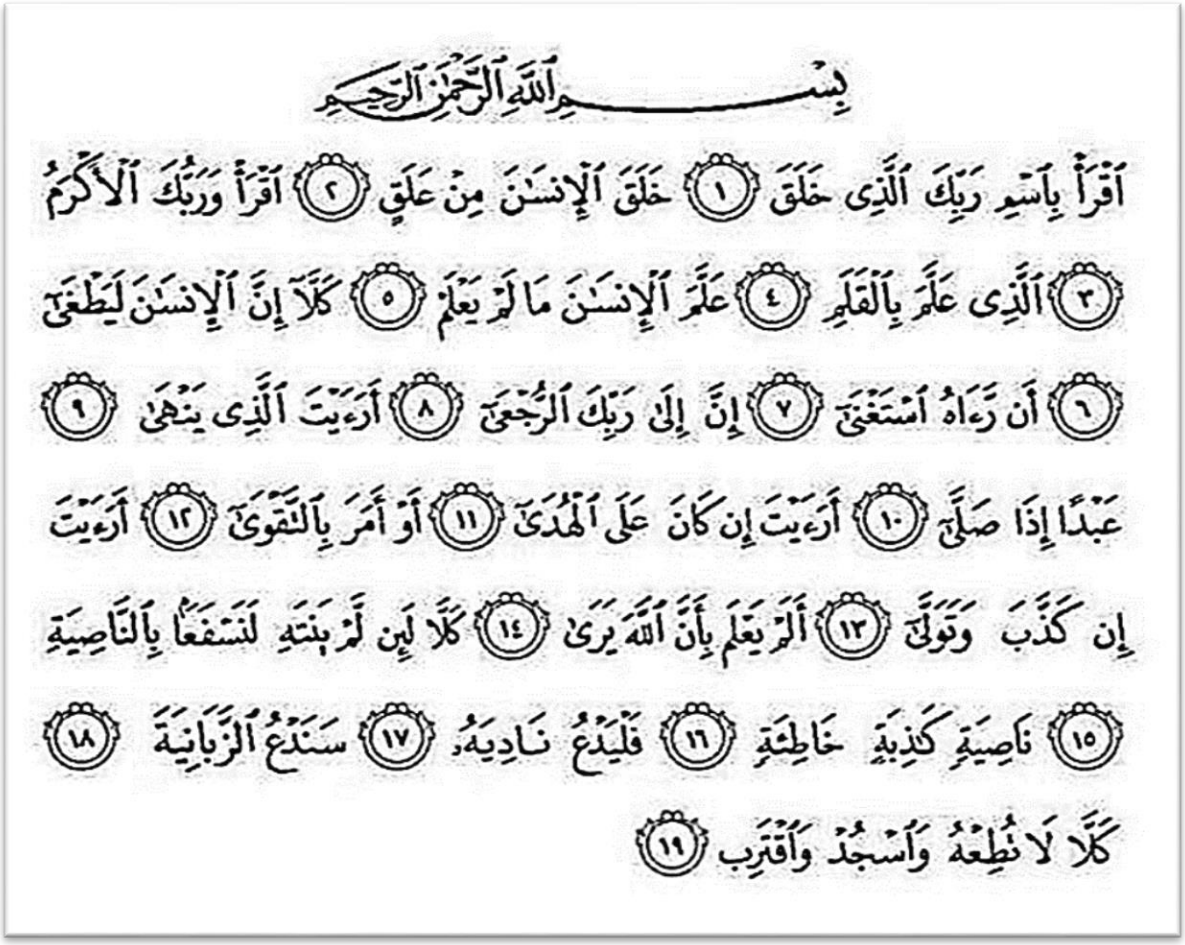
Supervised by

Assist. Prof.
Dr. Alaa Abdul Hussein Al-Daamy

Specialist Doctor
Dr. Ahmed Qasim Al-haideri

August (2021)

Muharam (1443)



صدق الله العلي العظيم

سورة العلق عدد آياتها (١٩)

Dedication

I would like to dedicate this thesis to

every holy drop of blood that fell on this earth

My supervisor Dr. Alaa, who was a role model for me in this life and taught me how to follow his steps to be as diligent and successful as him.

My family, who were tired with me and supported me a lot at this stage. They provided me with all possibilities, despite all circumstances.

My second family friends and acquaintances who supported me a lot at all times.

My dearest person, who implanted in me faith and hope and believed in my abilities until I reached this stage.

Everyone, who gets benefit of this work.

Acknowledgments

Praise be to God for making things easier to complete this stage.

All thanks, appreciation and gratitude to the supervisors, Dr. Alaa Al-Damay, who hold my hand from the first step in this journey until the end of the completion of the thesis.

Thanks and appreciation to the supervisor, Dr. Ahmed Al-Haidari, who made it easy for me to accomplish the task in the best way.

Thanks and appreciation to Dr. Zaid in the college Science, Chemical Department, who helped me in the thesis.

Thanks and appreciation to Dr.Ahmed Jamil Al-Hantawi for helping me as much he could in the thesis.

Thanks and appreciation to Assist. Prof. Karem in the college of Applied Medical Sciences for helping me as much he could in the thesis.

Thanks and appreciation to the Deanship and Head of the Department of Clinical Laboratories.

Thanks and appreciation to the Ministry of Health, and in particular the Department of the Karbala Center for Heart Diseases and Surgery.

I would like to thank everyone who helped me in any way and I forget to mention his name.

Summary

The aim of the study is to identify the most common bacterial species that are responsible for sepsis in heart failure patients, study their relationship with risk factors for heart failure and determine their antibiotic susceptibility pattern.

The study was done from October-2020 to May-2021 in the Heart Center in Hospital of Imam Hussain Medical City in Karbala. Ten ml of venous blood sample where taken from 71 heart failure patients after admission to the CCU and the same number for control. There are important procedure of blood culturing we have to fallow it, after that many analyses had been conducted such as CRP, BNP, Troponin, Lipid profile (TC, HDL, LDL and TG), Renal function tests (Urea Creatinine), General parameters (Age, Weight, Gender), Physiological Parameters (ABO, CBC, Systolic Blood Pressure, Diastolic Blood Pressure and Glucose), Microbiological tests (Bacterial Identification and Antibiotics Susceptibility Tests**)** and Nanotechnology study (XRD, FTIR, AFM, SEM and the inhibitory efficacy of Free-Meropenem and Nano-Meropenem.

The results were CRP (46.013) mg/l, BNP(218.84) ng/dl, Troponin (Heart Failure Without Bacterial Infection (924.526) ng/ml and Heart Failure With Bacterial Infection (383.97) ng/ml, TG (138.61) mg/dl, HDL (44.323) mg/dl , LDL (113.249) mg/dl, TC (160.423) mg/dl, Creatinine (1.343) mg/dl, Urea (62.658) mg/dl, RDW SD (49.253) fl, RDW CV (49.253) %, NEUT (70.129) %, LYM (20.329) %, MCHC in patient of heart failure with bacterial infection (31.393) g/dl, HgB (12.804) g/dl, WBC (12.670) 10^3/ µl, Glucose (202.336) mg/dl. And the common blood group in heart failure with bacterial infection was O. The most common bacterial causes infection for heart failure patients

was *Staphylococcus hominis ssp hominis* and the common antibiotic resistance to the most it was meropenem. In heart failure there were some correlation between some parameters like RBC with both HGB and HCT, as it was positive correlation (0.728 and 0.792), respectively. Also there were correlation in HGB with HCT and between MCV with MCH as it was positive correlation too (0.893 and 0.890), respectively. Significances correlation at (0.01) can also be seen between PDW and both MPV and P-LCR as it was positive correlation (0.733 and 0.737), respectively too. In the same time there was Significances correlation at (0.05) between MPV and P-LCR, as it was positively (0.503). Correlation also seen between TC and both HDL and LDL, as it was positive correlation (0.661 and 0.937), respectively. And between LDL and HDL, as it was positive correlation (0.534). There was correlation between Urea and Creatinine, as it was positive correlation (0.548). Lastly there was correlation between DBP and SBP, as it was positive correlation (0.709). In heart failure with bacterial infection there were some difference correlation parameters like in MCHC with MCH, as it was positive correlation (0.733). And between PLT with RBC, HGB and HCT, as it was positive correlation (0.625, 0.574 and 0.575), respectively. Also there were correlation in NEUT with both WBC and LYM, as it were positive and inverse correlation (0.969 and -0.555), respectively. There was correlation between PDW and RDW, as it was positive correlation (0.622). There was correlation at between PCT with RBC, HGB with HCT, as it was positive correlation (0.654, 0591 and 0.574), respectively. Correlation also had been seen between Age and BNP, as there was inverse correlation (- 0.527). Also there were correlation between CRP and both TG, and creatinine, as there was positive correlation (0.731, 0.894). While there was correlation between CRP with HDL, LDL, and Urea, as there were inverses and positive correlation (- 0.505, -0.505 and

0.664), respectively. There was correlation between Creatinine with TG and correlation between Glucose with Weight, as there was positive correlation (0.763, 0.593), respectively.

The conclusions of the study were the most common bacterial species that causes infection to heart failure was *Staphylococcus hominis ssp hominis*, and meropenem had resistance to the most bacterial present.

List of Contents

List of Tables

List of Figures

List of Appendix

List of Abbreviations

Abbreviations	Items
5KG	5-KETO-D-GLUCONATE
AHF	Acute heart failure
ADO	ADONITOL
AES	Advanced expert system
AlaA	Alanine ARYLAMIDASE
APPA	Ala-Phe-Pro ARYLAMIDASE
AGAL	ALPHA-GALACTOSIDASE
AGLU	ALPHA-GLUCOSIDASE
AMAN	ALPHA-MANNOSIDASE
ACC/AHA	American College of Cardiology/American Heart Association
ABR	Antibiotic resistance
AST	Antibiotic susceptibility testing
ARGs	Antimicrobial resistance genes
ADH2s	ARGININE DIHYDROLASE
ADH1	ARGININE DIHYDROLASE 1
ARVC	Arrhythmogenic right ventricular cardiomyopathy
AFM	Atomic Force Microscope
AF	Atrial fibrillation
BACI	BACITRACIN RESISTANCE
BGAR	BETA GALACTOPYRANOSIDASE
BGURr	BETA GLUCURONIDASE
BaLAP	BETA-ALANINEARYLAMIDASE pNA
BGAL	BETA-GALACTOSIDASE
BGAL	BETA-GALACTOSIDASE
BGUR	BETA-GLUCORONIDASE
BGLU	BETA-GLUCOSIDASE
BGUR	BETA-GLUCURONIDASE \
NAGA	Beta-N-ACETYL-GALACTOSAMINIDASE
BNAG	BETA-N-ACETYL-GLUCOSAMINIDASE
Bxyl	BETA-XYLOSIDASE
BUN	Both blood urea nitrogen
BNP	B-type natriuretic peptide
CaO	Calcium oxide
CMR	Cardiac magnetic resonance
CO	Cardiac output
CVD	Cardio vesicular disease
CMP	Cardiomyopathies
CV	Cardiovascular

TC	Cholesterol
CHF	Chronic heart failure
CKD	Chronic kidney disease
COPD	Chronic obstructive pulmonary disease
CIT	CITRATE (SODIUM)
CALIBER	Clinical Research Using Linked Bespoke Studies and Electronic Health Records
CBC	Complete blood count
CT	Computed tomography
Cu	Copper
CuO	Copper oxide
CAD	Coronary artery disease
CCU	Coronary care unit
CMT	COUMARATE
CRP	C-reactive protein
Cr	Creatinine
CDEX	CYCLODEXTRIN
AMY	D-AMYGDALIN
dCEL	D-CELLOBIOSE
ODEC	DECARBOXYLASE bASE
dGAL	D-GALACTOSE
dGLU	D-Glucose
DM	Diabetes mellitus
DBP	Diastolic blood pressure
DCM	Dilated cardiomyopathy
Dmal	D-MALTOSE
dMAL	D-MALTOSE
Dman	D-MANNITOL
dMAN	D-MANNITOL
Dmne	D-MANNOSE
dMNE	D-MANNOSE
dRAF	D-RAFFINOSE
dRIB	D-RIBOSE dRIB
dSOR	D-SORBITOL
Dtag	d-TAGATOSE
Dtre	D-TREHALOSE
E dTRE	D-TREHALOSE
D-XYLOE dXYL	D-XYLOSE
EF	Ejection fraction
ECG	Electrocardiogram
ELLM	ELLMAN

ESR	Erythrocyte sedimentation rate
EUCAST	European Committee on Antimicrobial Susceptibility Testing
OFF	FERMENTATION?GLUCOSE
FT-IR	Fourier transform infrared spectroscopy
FFAs	Free fatty acids
GGT	GAMMA-GLUTAMYL-TRANSFERASE
GGAA	Glu-Gly-Arg-ARYLAMIDASE
AGLTp	GlutamylArylamidase pNA
GlyA	Glycine Arylamidase
HbA1c	Glycosylated hemoglobin
Au	Gold
NC6.5	GROWTH IN 6.5%
H2S	H2S PRODUCTION
HACEK	Haemophilus, Aggregatibacter, Cardiobacterium, Eikenella, Kingella
HF	Heart failure
HFrEF	Heart failure with a reduced ejection fraction
HFpEF	Heart failure with preserved EF
HFmrEF	Heart loss with mid-range EF
HCT	Hematocrit
HgB	Hemoglobin
HBP	High blood pressure
HDL	High density lipoprotein
HIV	Human immune virus
HCM	Hypertrophic cardiomyopathy
IE	Infective endocarditis
IVC	Inferior vena cava
ICU	Intensive care unit
I	Intermediate
INLV	Isolated noncompaction of the left ventricle
JVP	Jugular venous pressure
LAC	LACTOSE LAC 0.96 mg
IARL	L-Arabitol
AspA	L-Aspartate ARYLAMIDASE
LA	Left atrial
LV	Left ventricular
LVEF	Left ventricular ejection fraction
LVH	Left ventricular hypertrophy
LeuA	Leucine ARYLAMIDASE
IHISa	L-HISTIDINE assimilation
LIP	LIPASE
ILATk	L-LACTATE alkalinisation
LDL	Low Density Lipoprotein

ProA	L-Proline ARYLAMIDASE
PyrA	L-Pyrrolydonyl-ARILAMIDASE
LYM	Lymphocyte
LDC	LYSINE DECARBOXYLASE
MgO	Magnesium oxide
MNT	MALONATE
MCH	Mean Corpuscular Hemoglobin
MCHC	Mean Corpuscular Hemoglobin Concentration
MCV	Mean Corpuscular Volume
MPV	Mean platelet volume
MBdG	METHYL-B-D-GLUCOPYRANOSIDE
MIC	Minimum inhibitory concentration
MODS	Multiple organ dysfunction syndrome
MI	Myocardial infarction
MC	Myocarditis
NAG	N-ACETYL-D-GLUCOSAMINE
NPs	Nanoparticles
NEUT	Neutrophil
NYHA	New York Heart Association
NVs	Novel
NOVO	NOVOBIOCIN RESISTANCE
O129R	O/129 RESISTANCE
OPTO	OPTOCHIN RESISTANCE
ODC	ORNITHINE DECARBOXYLASE
OTC	Over-the-counter
PLE	PALATINOSE
PED	Pediatric emergency department
PHOS	PHOSPHATASE
PIPLC	PHOSPHATIDYLINOSITOL PHOSPHOLIPASE C
PLT	Platelet
PDW	Platelet Distribution Width
P-LCR	Platelet Large Cell Ratio
PCT	Plateletcrit
POLYB	POLYMIXIN B RESISTANCE
KBr	Potassium bromide
POMs	Prescription-Only Medications
PCT	Procalcitonin
PUL	PULLULAN
RBC	Red Blood Cell
RDW-CV	Red cell Distribution Width-Coefficient of Variation
RDW-SD	Red cell Distribution Width-Standard Deviation
RCI	Red cell indices

RAAS	Renin-angiotensin-aldosterone system
R	Resistance
RCM	Restrictive cardiomyopathy
SAC	SACCHAROSE/SUCRALOSE
S	Sensitive
Si	Silicon
Ag	Silver
Ag2O	Silver oxide
SUCT	SUCCINATE alkalinisation
SIRS	Systemic inflammatory response syndrome
SBP	Systolic blood pressure
SPRINT	Systolic Blood Pressure Intervention Trial
PLT/MPV	The platelet to mean platelet volume ratio
Ti	Titanium
TiO2	Titanium dioxide
TC	Totaled Cholesterol
TOE	Transesophageal echocardiography
TTE	Transthoracic echocardiography
TG	Triglyceride
TG	Triglycerides
T2D	Type-2 diabetes
TyrA	Tyrosine ARYLAMIDASE
URE	UREASE
WBC	white blood cell
WHO	World Health Organization
XRD	X-ray diffraction
Zn	Zinc
ZnO	Zinc oxide

1.1. Introduction

Heart failure (HF) is a complex clinical syndrome that results from any functional or structural heart disorder, impairing ventricular filling or ejection of blood to the systemic circulation to meet the systemic needs. Heart failure can be caused by diseases of the endocardium, myocardium, pericardium, heart valves and vessels or metabolic disorders. Most patients with HF have symptoms due to impaired left ventricular myocardial function. Patients usually present with symptoms of dyspnea, decreased exercise tolerance and fluid retention, characterized by pulmonary and peripheral edema (Malik *et al*., 2020). More than 6.2 million people in the United States and more than 23 million worldwide suffer from the HF (Virani *et al*., 2020), while this number of HF is expected to increase to1.5 million annually by 2040 (Ruppar *et al*., 2016). Currently, the most common terminology for describing HF is based on left ventricular ejection fraction (LVEF). HF with normal LVEF (≥ 50%) is defined as HF with preserved ejection fraction (HFpEF), and HF with decreased LVEF (< 40%) as HF with reduced ejection fraction (HFrEF). HF patients with LVEF in the range of 40 to 49% are defined as HF with mid-range ejection fraction (HFmrEF) (Choi *et al*., 2019). The risk factors associated with the pathogenesis of cardio vascular disease (CVD) (e.g. diabetes, hypertension, hyperlipidemia and smoking), several lines of evidence have shown that bacterial pathogens may play a main role (Khademi *et al*., 2019). Bacterial infections can contribute to CVD mainly through interaction with inflammatory and immunological pathways, either directly or indirectly (Hogas *et al*., 2017). Infection has been found to directly impair endothelial function by circulating endotoxins, induce proliferation of smooth muscle cells and local inflammation, and activate the innate immune response (Banach *et al*., 2004). On the other hand, indirect damaging effects of bacterial

infections include induction of proinflammatory, hypercoagulability and atherogenic responses, oxidation of low-density lipoprotein, antigen mimicry between bacterial and host cells, induction of nutrient/vitamin malabsorption, and metabolic disruptions such as excess production of ammonia (Khademi *et al*., 2019). Infections represent an important emerging clinical problem that cause decompensation of HF, and in many cases, life-threatening acute systemic disorder (sepsis) and septic shock. Cardiovascular system plays an important role in the development of multiorgan dysfunction in sepsis and refractory septic shock. Cardiovascular dysfunction significantly increases mortality rates in sepsis as compared with sepsis without cardiac dysfunction (Kakihana *et al*., 2016). Infections are an important cause of decompensation of HF that should be early detected and treated using specific protocols and in the presence of sepsis and/or septic shock (Mesquita, 2018). Discovery of antimicrobials in the past century represented one of the most important advances in public health. Antibiotics are natural products produced by microorganisms or their semisynthetic derivatives. These compounds have been a feature of the environment for a long time, so that bacteria have needed to evolve some forms of antibiotic resistance (AR) to survive (Pérez *et al*., 2020). For instance, bacteria inactivate antibiotics by producing enzymes that modify them, but they can also alter their target of action, or prevent the antibiotics from accumulating, either because they are expelled using efflux pumps or by altering the permeability of the membrane (Crofts *et al*., 2017). Unfortunately, the massive use of these compounds in medicine and other human activities has promoted the selection of pathogens that are resistant to one or several antibiotics (Pérez *et al*., 2020). The application of nanoparticles provides a potential strategy to manage infections caused by multi drug resistance organisms (MDROs) (Baptista *et al*., 2018). Nanoparticles can

penetrate the cell membrane of pathogenic microorganisms and interfere with important molecular pathways, formulating unique antimicrobial mechanisms. In combination with optimal antibiotics, nanoparticles have demonstrated synergy and may aid in limiting the global crisis of emerging bacterial resistance (Lee *et al*., 2019).

Aim of The Study

To identify the most common bacterial species that are responsible for sepsis in heart failure patients, study their relationship with risk factors for heart failure and determine their antibiotic susceptibility pattern through the following axes:

1. Blood samples will be collected from the patient and control groups to test the following:
   A. BNP Level to confirm heart failure cases after preliminary identification of the patients by physician using ECG and Echo.
   B. Measure some parameters like Lipid Profile, Troponin, CBC, C-reactive protein and Procalcitonin.
   C. Culturing of blood samples for bacterial isolation.
2. Identification of the isolated bacteria and determination of antibiotic susceptibility pattern using Vitek system. Comparison of the tested parameters between patients and control groups using statistical analysis.

1.2. Literatures Review

1. 2.1. Heart Failure

1.2.1.1. An Overview of Heart Failure Disease

Heart failure (HF) is a multisystem clinical syndrome caused by a decrease in ventricular contractility and/or relaxation (Yancy *et al*., 2013). HF is characterized by ventricular dilatation and/or hypertrophy, venous obstruction, and poor oxygen supply and is caused by cardiac muscle dysfunction (Lindenfeld *et al*., 2010). HF can be classified into many subtypes depending on the left ventricular ejection fraction (LVEF) (Yancy *et al*., 2013). The four functional classes are defined by the New York Heart Association (NYHA) as follows:

Class I: Physical exercise is not limited by HF and ordinary physical activity does not cause symptoms.

Class II: Physical exercise is limited by HF; patients are relaxed at rest but ordinary physical activity induces HF symptoms.

Class III: HF limits physical exercise significantly; patients are relaxed at rest, but less than normal activity causes HF symptoms.

Class IV: Patients with HF cannot perform in any physical activity without having HF symptoms, and they experience symptoms even though they are resting (Inamdar and Inamdar, 2016).

The four stages of the American College of Cardiology/American Heart Association (ACC/AHA) staging system are as follows:

Stage A: While the risk of heart failure is high, there are no signs or symptoms of structural heart disease or heart failure.

Stage B: Heart failure symptoms but no structural heart disease.

Stage C: Heart failure symptoms and structural heart disease.

Stage D: Specialized interventions are needed for refractory heart failure (Inamdar and Inamdar, 2016).

The left ventricle ejection fraction (EF) was determined using this method, there are three major phenotypes that characterize HF and the distinction between these groups is significant due to differences in demographics, co-morbidities, and therapeutic reaction:

1. Heart failure with a reduced ejection fraction (HFrEF) is described as an EF of greater than or equal to 40%.
2. Heart failure with preserved EF (HFpEF): EF is equal to or greater than 50%.
3. Heart loss with mid-range EF (HFmrEF) (other names: HFpEF-borderline and HFpEF-improved as EF in HFrEF increases to greater than 40%): EF is 41 to 49 percent per European guidelines and 40 to 49 percent per US guidelines. This class was formerly known as the gray region between HFpEF and HFrEF, but it has now been given its own name, HFmrEF (Hajouli and Ludhwani, 2020).

Diastolic dysfunction is present in all patients with HFrEF; however, diastolic dysfunction can occur even though systolic dysfunction is absent (Hajouli and Ludhwani, 2020).

1.2.2. Epidemiology

HF affects about 40.0 million people around the world (Vos *et al*., 2016). In 2011, there were approximately 5.7 million patients with HF in the United States, with approximately 870,000 patients newly diagnosed with HF (Mozaffarian *et al*., 2016). According to reports, HF affects 1% to 2% of the population, with the incidence increasing with age (Ponikowski *et al*., 2014). Individuals under the age of 40 have a prevalence rate of 1%, but people above the age of 80 have a prevalence rate of >10% and the rate doubles per decade

of life (Mozaffarian *et al*., 2016). As a result, as the population ages, the number of patients with HF is expected to rise. Furthermore, reduced mortality as a result of recent cardiovascular disease therapeutic advancements may paradoxically increase the number of patients at risk of developing HF.

Furthermore, patients with HF have a high risk of re-hospitalization (44% within one year of discharge) (Maggioni *et al*., 2013) and mortality (20% after one year and 50% after five years) (Ziaeian and Fonarow, 2016). HF has a higher death rate than the majority of cancers (Mamas *et al*., 2017). As a result, managing patients with HF is critical for reducing social, economic, and medical burdens (Kim and Kim, 2018).

1.2.3. Risk Factors of Heart Failure

- Covariates of interest included baseline demography (age, race/ethnicity, height, weight).
- Time-updated assessment of both clinical risk factors (diabetes mellitus, systolic blood pressure, anti-hypertensive medication use, hyperlipidemia, lipid-lowering medication use, use of hormone replacement therapy).
- Some medications for the treatment of cancer.
- People with a genetic predisposition for less common heart diseases, like some types of heart muscle disease, are also at greater risk of developing heart failure.
- Lifestyle habits (smoking status [never, former, current], physical activity [metabolic equivalents per week], alcohol consumption [number of drinks per day]) (Chatterjee *et al*., 2017).

1.2.4. Symptoms of Heart Failure

All patients with suspected HF should have a thorough history and physical exam as the diagnosis is entirely based on clinical symptoms and

signs. A risk assessment and potential HF etiologies should also be included. Regardless of EF, the signs of HF are similar. Fluid deposition (dyspnea, orthopnea, edema, and abdominal pain from hepatic congestion and ascites in the setting of right heart failure) or reduced cardiac activity cause symptoms to become more severe with exertion (fatigue, anorexia, and weakness) (Hajouli and Ludhwani, 2020). A nocturnal cough, weight loss, wheezing, palpitations, depression, syncope, bendopnea (breathing difficulties while sitting forward), and dizziness are only a some of the abnormal symptoms. Resting sinus tachycardia, diaphoresis, narrow heart pressure (less than 25 mmHg due to reduced cardiac output), and peripheral vasoconstriction are all signs of advanced heart failure (cold and pale extremities due to decreased perfusion). Peripheral edema (extremities edema, ascites, scrotal edema, and hepatosplenomegaly) as well as elevated jugular venous pressure (JVP) and respiratory obstruction also are signs of fluid overload (rales on exam and pleural effusions). An S3 gallop, a displaced apical impulse (laterally past the midclavicular line, indicating LV enlargement), and parasternal lift (right ventricular enlargement). HF symptoms and signs must be assessed at each clinic visit in order to track treatment response and stability over time. During each clinic visit, it's also useful to determine vital signs and assess volume status (Hajouli and Ludhwani, 2020).

1.2.5. Causes of Heart Failure Disease

HF may be caused by a variety of factors, including systemic disorders, a variety of cardiac conditions, and certain genetic defects. HF etiologies differ between low - and high countries, and patients can have a combination of etiologies (Yusuf *et al*., 2014). In high-income countries, ischemic heart disease and chronic obstructive pulmonary disease (COPD) are the most common underlying causes of HF. According to a systematic study for the

global burden of disease report, hypertensive heart disease, rheumatic heart disease, cardiomyopathy, and myocarditis are the main causes of HF in low-income countries (Savarese and Lund, 2017). Ischemic heart disease, COPD, hypertensive heart disease, and rheumatic heart disease account for more than two-thirds of the cases of HF

- **Coronary artery disease (CAD**): Ischemia both chronic and acute damages the myocardium directly and promotes remodeling and scar formation, resulting in insufficient diastole relaxation and reduced systole contraction, lowering contractility and cardiac output (CO). This scar tissue has also been linked to the formation of aneurysms, which impair contractile performance and relaxation even more. Dyssynchronous contraction of the infarcted segment, subsequent ventricle remodeling, ventricular dilatation with annular dilation, and mitral regurgitation are all common complications of myocardial infarction (MI), all of which increase the risk of HF and lower CO. In patients with CAD, many tachyarrhythmias, such as atrial fibrillation/flutter or non-sustained ventricular tachycardia, are widespread and can exacerbate cardiac function. HF is associated with CAD in more than 70% of cases (Purek *et al*., 2006). In patients with acute HF, CAD is a powerful indicator of mortality. However, the efficacy of coronary revascularization in reducing HF-related morbidity and mortality is still debatable, and viability testing may be useful in determining which patients will benefit from revascularization (Phillips *et al*., 2007).
- **High blood pressure (HBP):** HBP is an independent risk factor for coronary artery disease. Because of its high prevalence, HBP is a likely cause of HF in one-fourth to one-third of cases. HBP increases vascular

resistance by stimulating the renin-angiotensin-aldosterone system (RAAS). As a compensatory mechanism to maintain a normal CO, the heart must pump blood against a higher afterload caused by HBP, which causes left ventricular hypertrophy (LVH) by increasing myocardial mass. If blood pressure (BP) is not controlled, apoptosis and fibrosis can occur. LVH increases myocardial rigidity and may lead to ischemia leading to HFpEF or HFrEF controlling blood pressure is crucial for improving HF prognosis. The systolic blood pressure Intervention Trial (SPRINT) found that lowering systolic blood pressure to less than 120 mmHg had a 38 percent lower relative risk of heart failure in HBP patients (Group, 2015).

- **Chronic pulmonary obstructive disease (COPD):** COPD is increasing the risk of CAD and other diseases related to smoking, heart dysrhythmia and may cause pneumonic high blood pressure and right HF (Hajouli and Ludhwani, 2020).
- **Valvular heart disease**: In developed countries, valve disease degeneration can cause HF, while in low-income countries, rheumatic valve disease can cause HF. The ventricular afterload is increased by aortic and pulmonary stenosis and may cause HF. Due to persistent volume overload in the regurgitation of the valve, ventricular expansion and functional impairment could cause HF.
- **Cardiomyopathies (CMP):** CMP is a condition in which the heart muscle has functional and structural defects but no CAD, HBP, valve, or congenital heart disease. Dilated cardiomyopathy (DCM), hypertrophic cardiomyopathy (HCM), restrictive cardiomyopathy (RCM), arrhythmogenic right ventricular cardiomyopathy (ARVC), and other unclassified cardiomyopathies (isolated noncompaction of

the left ventricle [INLV] and Takotsubo syndrome are also in this category) are the five categories of cardiomyopathies that can be genetically modified or acquired. HFrEF, HFpEF, or HFmrEF are all possible outcomes of CMP (Hajouli and Ludhwani, 2020).

Congenital heart disease, myocarditis, infiltrative disease, peripartum cardiomyopathy, HIV, connective tissue disease, amyloidosis, substance abuse, long-term alcohol use, obesity, diabetes mellitus (DM), hyperthyroidism (can affect high-output HF), pulmonary hypertension (can cause right HF), and constrictive pericarditis (can cause HFpEF) pulmonary embolism (lead to right HF), and chemotherapies (like doxorubicin) (Hajouli and Ludhwani, 2020).

1.2.6. Diagnosis of Heart Failure

Initial analysis is significant. The following should be included in the original investigations (Ponikowski *et al*., 2016):

1) Basic blood estimations
2) 12-lead electrocardiography (ECG)
3) Chest X-ray
4) 2D echocardiography,

Basic blood estimations, the important tests to be considered for the basic blood work were (Ponikowski *et al*., 2016):

1) Complete blood count
2) Serum electrolytes (sodium, potassium, etc.)
3) Renal function test
4) Liver function test
5) Blood glucose (fasting plasma glucose and postprandial plasma glucose) Glycosylated hemoglobin (HbA1c)
6) Lipid profile

7) Thyroid function test Iron profile—serum iron, total iron-binding capacity, ferritin and folate.

1.2.6.1. Biomarkers

Measurement of B-type natriuretic peptide (BNP) in combination with physical examination findings can aid in the diagnosis of HF in cases where clinical confusion exists or echocardiography is not readily available (Yancy *et al*., 2013). BNP has unique cutoff values that are sensitive and specific enough to aid in the analysis of heart failure. The amounts of BNP and NT-proBNP must also be viewed with caution. Additional laboratory testing may be required at the time of diagnosis to rule out any possible causes of symptoms, determine the physiologic impact of HF, and plan appropriate care. A complete blood count, urinalysis, serum electrolyte, blood urea nitrogen, serum creatinine, and glucose levels, fasting lipid profile, liver function measure, and thyroidstimulating hormone level are all examples of standard laboratory tests that can be used to create a baseline for optimal therapy and evaluate treatment success (Lee and Auld, 2015). To rule out myocardial ischaemia as a source of acute heart failure (AHF), cardiac troponin may be used. Even when there is no obvious myocardial ischaemia or an acute coronary event, cardiac troponin levels are often elevated in patients with AHF, particularly when measured with high-sensitivity assays. AHF does, in reality, cause rapid myocardial necrosis and remodeling. Troponin levels should be used to assess prognosis, since higher levels are associated with worse results (Roberts *et al*., 2015). In AHF syndromes, a number of clinical factors and biomarkers are independent predictors of in-hospital complications and longer-term effects, but their impact on treatment is unclear. The easy-to-use AHF score, which focuses on co-morbidity

assessment, has been shown to provide useful insight into the short and long-term prognosis for AHF in hospitalized patients (Spinar *et al*., 2016).

1.3. Bacterial Infections

1.3.1. An Overview of Bacterial Infections

Bacteria are single-celled microbes that belong to the prokaryotic kingdom. Since they are simpler than most organisms, their cellular structure is simpler. They lack a nucleus and organelles which are membrane-bound. Bacteria are classified into several types depending on their characteristics, basic shapes and proportions (spheres, rods, and spirals) (length varies between 0.5 and 5 ml) (Berkley, 2021). Clinicians and microbiologists now often use phenotypic typing schemes to help understand bacterial morphology and staining properties (Gao *et al*., 2016). Bacteremia refers to the presence of live bacteria in the blood. Asymptomatic bacteremia may develop during routine everyday practices such as brushing one's teeth and following minor medical procedures. This clinically benign infections are transient in healthy people and have no long-term consequences. When the immune system's defense systems malfunction or become overwhelmed, bacteremia develops into a bloodstream infection that can manifest in a variety of clinical manifestations, and is identified as septicemia. Systemic inflammatory response syndrome (SIRS), sepsis, septic shock, and multiple organ dysfunction syndrome (MODS) are all symptoms of untreated and clinically significant bacteremia (Dagasso *et al*., 2018).

Sepsis is a leading cause of morbidity, death, and health-care costs in the United States, and it is a significant source of concern for health-care providers, whose payments are now partly dependent on sepsis performance criteria. Despite being often synonymous with bacteremia, sepsis has recently been redefined ('Sepsis') as a life-threatening dysregulated host immune

response to infection (Singer *et al*., 2016).. Among the numerous proven clinical and laboratory risk factors for CVD, several lines of evidence have shown that bacterial pathogens may play a major role in the pathogenesis of the heart disease (e.g. diabetes, hypertension, hyperlipidemia, dyslipidemia, and smoking). Bacterial infections can cause CVD either directly or indirectly by interfering with inflammatory and immunological pathways (Hogas *et al*., 2017). Infection has been shown to inhibit endothelial function directly by circulating endotoxins, to cause smooth muscle cell proliferation and local inflammation, and to stimulate the innate immune response (Banach *et al*., 2004). Induction of proinflammatory, hypercoagulability, and atherogenic responses, degradation of low-density lipoprotein, antigen mimicry between bacterial and host cells, induction of nutrient/vitamin malabsorption, and metabolic disruptions, including excess ammonia formation, are all indicators of bacterial infections' indirect harmful effects. To summarize, repeated bacterial infections cause an excess inflammatory reaction, which activates immune responses that adversely impact cardiovascular risk factors such as triglycerides, high density lipoprotein (HDL), C-reactive protein (CRP), heat shock proteins, cytokines, fibrinogen, and white blood cell count. *Helicobacter pylori*, *Chlamydia pneumonia*, *Mycoplasma pneumonia*, and *Porphyromonas gingivalis* are some of the bacteria linked to CVD risk (Matusiak *et al*., 2016).

Infections are a growing clinical problem that can lead to heart failure decompensation and, in many cases, life-threatening acute systemic disease (sepsis) and septic shock. In sepsis and refractory septic shock, the cardiovascular system plays a vital role in the progression of multi organ dysfunction. While sepsis-related intra-hospital deaths decreased from 35% in 2000 to 18% in 2002, one-third of patients die within one year of a septic

event. When compared to sepsis without heart dysfunction, sepsis with cardiovascular dysfunction has a considerably higher mortality risk (Kakihana *et al*., 2016). Infection causes cardiac decompensation which is a leading cause of death in people with heart failure (Alon *et al*., 2013). While infections are an uncommon cause of cardiovascular disease, bacteria and viruses may affect the pericardium (Adler *et al*., 2015), myocardium (Hemkens and Bucher, 2014), or even thrombi (Egeblad *et al*., 2005), as well as implants and devices (Nielsen *et al*., 2015). When bacteria infect cardiac tissue and/or valves, however, it induces extreme disorders that, despite modern antibiotics, are still associated with a high risk of morbidity and mortality (Olmos *et al*., 2013), frequently necessitating surgery (Revilla *et al*., 2007).

1.3.2. Bacterial Infections Associated with Heart Failure

The endocardium, myocardium, and pericardium are all affected by infectious diseases of the heart, which are a heterogeneous and diverse category of illnesses. And include a broad variety of clinical presentations. Bacteria, fungi, parasites, and viruses are just some of the microorganisms that can invade the heart, and they can affect several cardiac structures (Habib *et al*., 2015).

1.3.2.1 Infective endocarditis (IE)

Infective endocarditis (IE) is a potentially lethal disorder caused by infection and inflammation of the heart valves, which are often dysfunctional as a result of underlying disease. Patients' health will deteriorate if left untreated, and they will cause congestive heart failure (CHF). IE is more prevalent in the elderly, with 25%–50% of those over 60 years old developing it (McIntyre *et al*., 2017), with a higher frequency where a valve replacement is performed for IE. In developed countries, the prevalence of IE is 6–7 cases per 100,000, although it is possibly higher (6–10 cases per 100,000 life years)

in developing countries. When a mechanical heart valve or a bioprosthetic heart valve is implanted in IE patients, there is no significant difference in death rates; however, if the patient is younger than 60 years old, a mechanical heart valve is usually recommended, and if the patient is older than 60 years old, a bioprosthetic heart valve is commonly prescribed. Infection is caused mostly by bacteria and, in some cases, fungi. Depending on the infecting microorganism, the infection can be acute or subacute, and it usually progresses slowly at first, with unclear and unspecific symptoms. The diagnosis is complicated by the appearance of a low-grade fever, aches, pains, and fatigue (McIntyre *et al*., 2017). Acute onset is described by more virulent bacteria, severe symptoms, and rapid loss of infected valve(s) tissues. IE will result in myocardial, paravalvular, or annular abscesses, new intracardiac shunts, new cardiac murmurs, embolic infarctions, and other life-threatening complications (Singhal *et al*., 2013).

1.3.2.1.1 Pathophysiology:

The stable cardiac endothelium is resistant to bacteremia brought about by everyday behaviors including chewing and brushing teeth (Lockhart *et al*., 2008). However, following endothelial damage, the release of inflammatory cytokines and tissue factors, as well as related fibronectin expression, results in the development of a platelet-fibrin thrombus, which promotes bacterial adhesion (Widmer *et al*., 2006). Valve sclerosis, rheumatic valvulitis, and direct bacterial activity may all cause endothelium damage (particularly from Staphylococcus aureus) (Werdan *et al*., 2014). Bacterial adhesin proteins, such as fibronectin binding protein and staphylococcal clumping factors A and B, are essential determinants of pathogenicity and bacterial mediators of obedience (Veloso *et al*., 2013). Additional cycles of endothelial injury and

thrombus deposition are caused by bacterial invasion eventually resulting an infected vegetation.

1.3.2.2. Myocarditis (MC)

Infectious agents, systemic disorders, medications, and toxins with viral infections being the most prevalent cause in developing countries can all induce myocarditis refers to inflammation of the myocardium (Cooper Jr *et al*., 2014). Myocarditis can cause a wide variety of symptoms, including chest pain, palpitations, and heart failure, as well as cardiogenic shock and death (Bozkurt *et al*., 2016). In approximately 30% of cases, myocarditis will lead to DCM, which accounts for 9–16% of all nonischemic DCM in adults patients (Caforio *et al*., 2013).

1.3.2.2.1. Pathophysiology

Myocarditis (and its complications) are considered to be mostly immune-mediated. In infectious etiologies, for example, the microbial agent enters the body through the respiratory or gastroenteric tract and then binds to a particular receptor in the heart. Intracellular replication occurs as a result, resulting in cell damage and lysis. This process may lead to immune dysfunction, with molecular mimicry playing a key role, which can enhance cardiac damage. Dilated cardiomyopathy may develop if the damage is severe and prolonged (Baessler *et al*., 2018).

1.3.2.3. Pericarditis

Pericarditis is the most prevalent form of pericardial disorder, characterized by inflammation of the pericardial layers (Adler *et al*., 2015). It can be linked to pericardial effusion, which may cause problems with cardiac filling (tamponade). The disease may manifest itself in two ways: as a separate disorder or as a cardiac manifestation of a systemic illness (e.g., autoimmune or autoinflammatory diseases). Infectious and noninfectious causes of

pericarditis occur, but it is most generally idiopathic (Chang, 2017). The timing of pericarditis signs, as well as the prognosis, will vary significantly (Chiabrando *et al*., 2020).

1.3.2.3.1. Pathophysiology

The pericardium may be affected with the same infectious agents that infect the endocardium and myocardium. The most common cause of pericarditis is infection, which accounts for two-thirds of cases, with non-infectious conditions responsible for the remaining one-third (Troughton *et al*., 2004). When the pericardium becomes inflamed there is typically an accompanying increase in pericardial fluid, resulting in a collection large enough to be classified as a pericardial effusion. This occurs because of the inability of the ventricles to fill adequately due to the pericardial fluid compressing the heart, which can culminate in cardiovascular collapse. The pericardium is a flask-shaped sac that surrounds the heart and the proximal portions of the great vessels. It is made up of fibrous and serosal component layers with a combined thickness of 1–2 mm, appears smooth, and usually contains a small amount of fluid (approximately 50 mL) when viewed cross-sectionally (Rajiah, 2011). Also, it is also possible to have pericarditis in the absence of a significant pericardial effusion. The inflamed pericardium may also cause subjacent inflammation of the superficial myocardium, which then results in the ECG changes seen in pericarditis (Tunuguntla *et al*., 2019).

1.3.3. Symptoms of Bacterial Infections

1.3.3.1. Symptoms of Sepsis

Sepsis is characterized as an infection plus a systemic inflammatory response syndrome. As a result, early on in the progression of sepsis, patients

will show various vital sign changes: Fever is defined as a temperature above 38 °C, while hypothermia is defined as a temperature below 36 °C. Tachycardia is described as a heart rhythm that is greater than 90 beats per minute in adults and less than two standard deviations for age in pediatric patients. Tachypnea is characterized as a breathing rate of more than 20 breaths per minute in adults and more than two standard deviations for age in children (Mahapatra and Heffner, 2017). Severe sepsis signs and symptoms sepsis with end-organ dysfunction is referred to as severe sepsis. Signs and symptoms at this point can include: Altered mental status, oliguria or anuria, hypoxia, cyanosis and ileus.

Patients that undergo septic shock exhibit signs and symptoms of extreme sepsis, including hypotension. Blood pressure can be sustained at an early "compensated" stage of shock, and other symptoms of distributive shock, such as warm extremities, flash capillary refill (less than one second), and bounding bursts, commonly known as warm shock, may be present. This stage of shock can be reversed with rapid fluid resuscitation and vasoactive support. Hypotension develops as septic shock progresses to the uncompensated level, and patients can experience cool extremities, delayed capillary refill (more than three seconds), and thready pulses, a condition recognized as cold shock (Mahapatra and Heffner, 2017).

1.3.3.2. Symptoms Endocarditis

The two hallmark symptoms of infective endocarditis, fever and heart murmur, are present in about 90% and 75% of cases, respectively (TJ, 2016). Infectious endocarditis can present acutely with symptoms like low-grade fever, malaise, chills, sweating, dyspnea, back pain, arthralgias, and weight loss, or subacutely with symptoms like low-grade fever, malaise, chills, sweats, dyspnea, back pain, arthralgias, and weight loss that last weeks or

months. In 5 to 10% of patients, Splinter hemorrhage, conjunctival hemorrhage, Osler nodes, among other microembolic or immunologic phenomenon (distal vasculitic lesions of the fingers and toes), Janeway lesions (vasculitic lesions of the palms and soles) and Roth spots (hemorrhagic retinal lesions) are present (Chambers and Bayer, 2020).

1.3.3.3. Symptoms Myocarditis (MC)

A new or prior upper respiratory tract infection is the most frequent clinical presentation in an patient with suspected myocarditis (Halle *et al*., 2020). Overall, symptoms are highly variable, and they can include a previous flu-like infection with fevers, chills, diarrhea, or a lack of appetite. Chest pain, dyspnea, and palpitations are typical heart symptoms that can take days to occur (Group, 2011). If a pericardial effusion is present, patients often describe atypical chest pressure that worsens when they lean their upper body forward, indicating the possibility of a pericardial effusion (Halle *et al*., 2020). Myocarditis normally has subtle symptoms. Physical ability loss, nausea, dizziness, or new onset atrial or ventricular arrhythmias are some of the signs and symptoms. Any active patients may experience muscle soreness that is out of proportion to their recent level of exercise. When testing an patients a rise in heart rate of 5–10 beats per minute at rest may be a subclinical symptom of an active inflammatory phase (Halle *et al*., 2020).

1.3.3.4. Symptoms Pericarditis:

Chest pain was the most common presenting symptom, accompanied by cough (and dysphagia). Tachycardia was the most frequent physical test finding, followed by tachypnea. Patients with this condition were shown to have pericardial friction rub (Awan *et al*., 2017).

1.3.4. Causes of Bacterial Infections

In the treatment of a patient with bacteremia, as well as in identifying the infected patient population, determining the primary cause of infection is important. In hospitalized patients, common sources include the respiratory tract and indwelling catheters, especially central venous catheters. Community-acquired bacteremia is most commonly caused by untreated urinary tract infections. Soft tissue and intraabdominal infections are less prevalent in the preoperative surgical setting, although they are more common in the postoperative surgical setting. The most prevalent cause of gram-negative associated bacteremia is *Escherichia coli*, while the most common gram-positive organism is *Staphylococcus aureus* (Antonio *et al*., 2019).

1.3.5. Types of Bacterial Infections with Heart Failure

1.3.5.1. Bacterial of infectious Endocarditis: Most cases are caused by viridans streptococci, *Streptococcus gallolyticus*, *Staphylococcus aureus*, coagulase-negative staphylococci, HACEK organisms (*Haemophilus, Aggregatibacter*, *Cardiobacterium*, *Eikenella*, *Kingella*), and enterococci. Rarer organisms include pneumococci, *Candida*, gram-negative bacilli, and polymicrobial organisms (Galar *et al*., 2019).

1.3.5.2. Bacterial of Infectious Myocarditis: *chlamydia, Corynebacterium diphtheria, Klebsiella, Salmonella, Legionella*, *Mycobacterium tuberculosis, mycoplasma, staphylococcus, streptococcus A, Streptococcus pneumonia*, *Tryponema Pallidum and Haemophilus influenza* (Bejiqi *et al*., 2019).

1.3.5.3. Bacterial of Infectious Pericarditis: *Mycobacterium tuberculosis, Staphylococcus, Streptococcus, Haemophilus, Neisseria, Chlamydia*, *Legionella, Salmonella, Borrelia burgdorferi, Mycoplasma*, *Actinomyces, Nocardia, Tropheryma whippelii, Treponema and Rickettsia* (Hoit and Oh, 2016).

1.3.6. Diagnosis of Bacterial infections

1.3.6.1. Biomarkers of the Sepsis Diagnosis

The clinical and laboratory manifestations of sepsis (fever or leukocytosis, for example) are not predictable or unique. More common signs or laboratory criteria (e.g., arterial hypotension) are frequently late symptom that signal the onset of organ dysfunction and death. As a result, better sepsis markers are needed for clinical use (Meisner, 2005).). A biomarker is defined as "a biological characteristic that is objectively measured (i.e., with acceptable accuracy and reproducibility) and used as a marker for a physiological or pathological process, or the action of a medicine." Biomarkers are divided into two categories: prognostic and predictive. Patients' chances/risk of obtaining a certain result can be identified using prognostic markers, independent of treatment. Based on biomarker status, predictive markers will predict the potential benefit (efficacy) and/or risks (toxicity) of a therapy (Dupuy *et al*., 2013). CRP and procalcitonin (PCT), two of these biomarkers, follow the majority of the requirements for a successful biomarker and are routinely used in many laboratories. In the presence of tissue injury and inflammation, the liver produces CRP. (Simon *et al*., 2004). The study took into account the results of a complete blood count (CBC), CRP, or blood culture. White blood cell (WBC), neutrophils, monocytes, platelets, and mean platelet volume (MPV) were all extracted from the CBC (Tamelytė *et al*., 2019). Chest x-ray and urinalysis Either can be ordered to investigate for possible sources of infection Blood Cultures with or without other potential source cultures. At least 2 blood cultures are recommended, before administering antibiotics (Joseph, 2020).

1.3.6.2. Diagnosis of Endocarditis:

Major criteria include:

(1) Microorganisms consistent with IE from persistently positive blood cultures, blood cultures positive for typical microorganisms consistent with IE from two separate blood cultures.

(2) A transthoracic echocardiogram showed positive IE imaging.

(3) Cardiac computed tomography (CT) reveals definitive paravalvular lesions.

Minor criteria include:

(1) A predisposing cardiac disease or the use of injectable drugs.

(2) A fever of more than 38 degrees Celsius.

(3) Vascular lesions, such as massive arterial emboli, septic pulmonary infarcts, intracranial hemorrhage and conjunctival hemorrhages.

(4) Microbiological confirmation, positive blood culture, but not one of the main criteria mentioned above, or serological evidence of active infection with species consistent with IE (Ren *et al*., 2019).

1.3.6.3. Laboratory Findings

None of the numerous laboratory studies are diagnostic, and their positive predictive values are generally poor. In the diagnosis of IE, the examinations are just supportive. A high white cell count or other sepsis markers including a high erythrocyte sedimentation rate, CRP, or procalcitonin can be discovered. Chronic disease-related anemia may occur. Acute tubular necrosis, immune-complex mediated nephritis, or renal emboli may all induce a rise in creatinine levels (Hitzeroth *et al*., 2016).

1.3.6.4. Diagnosis Myocarditis

Acute myocarditis should be suspected in patients who have clinical signs and symptoms of the illness after a weak workup, particularly in young

patients (age 25-50) who have no history of cardiac disease (Leong *et al*., 2018). An ECG, echocardiogram, serum troponin, and BNP can all be performed as part of the initial assessment for acute myocarditis. Troponin elevation is found in more than half of the patients, and it is normally severe. BNP can be used to screen for symptoms of heart failure and ventricular stretch, which may mean myocarditis if the clinical picture is correct. An echocardiogram can be used to determine the severity of cardiac dysfunction and to rule out any possible causes, such as valvular disease (Al-Akchar and Kiel, 2021). Although a chest radiograph is neither sensitive nor specific for myocarditis, it may reveal an enlarged heart, pulmonary vascular obstruction, or pleural effusion. Other causes of chest pain can require a CT angiography examination. A complete blood count with differential showing eosinophilia in can also suggest eosinophilic myocarditis. CRP and erythrocyte sedimentation rate (ESR) are normally elevated but nonspecific (Al-Akchar and Kiel, 2021).

1.3.6.5. Diagnosis pericarditis:

Based on current European Society of Cardiology guidelines, a diagnosis is made. A minimum of two of four criteria are necessary for the diagnosis of acute pericarditis, according to current European Society of Cardiology guidelines (Adler *et al*., 2015):

- Chest pain
- Pericardial rub
- ECG changes
- Pericardial effusion, new or worsening
- Increased inflammatory markers (i.e., CRP, ESR, and WBC count elevation) as well as imaging evidence of pericardial inflammation (CT

scan, or cardiac magnetic resonance [CMR]) can help with diagnosis and disease monitoring (Adler *et al*., 2015).s

1.4. Antibiotics Susceptibility

1.4. 1. Uses of Antibiotics

Antibiotics are drugs that are used to cure or prevent bacterial and protozoan infections. A narrow-spectrum antibiotic would most likely be used. The price of the antibiotic would also influence the choice. Antibiotic therapy costs and toxicity can be reduced, as well as the chance of antimicrobial resistance forming, if the bacteria can be identified (Bojanić *et al*., 2018). Antibiotics can be used for non-complicated acute appendicitis to avoid surgery. Antibiotics may be given as a preventive measure (prophylactic) to at-risk populations like those with a weakened immune system (especially in human immune virus HIV cases to prevent pneumonia), those on immune suppressive drugs, cancer patients, and those undergoing surgery.(Page-Shipp *et al*., 2018). They're essential in the prevention of bacteremia and infective endocarditis in dental antibiotic prophylaxis. Antibiotics are often used to avoid infection in cases of neutropenia, particularly when it is caused by cancer (Schellack *et al*., 2017). Antibiotic treatment can be administered through a variety of routes. Antibiotics are usually taken orally. Antibiotics may be administered intravenously or by injection in more serious situations (Boyles *et al*., 2017). Topical application use has many advantages, including obtaining a large and continuous concentration of antibiotic at the site of infection, lowering the risk of systemic absorption and toxicity, and reducing the maximum amount of antibiotic available, lowering the risk of antibiotic misuse (Dunn *et al*., 2017). Surgical site infections have been shown to be reduced as topical antibiotics are applied to specific types of surgical wounds. However, there are certain

general reasons to be concerned with antibiotics applied topically (Teklay *et al*., 2016).

1.4.2. Antibiotics Sensitivity

Antibiotic susceptibility testing (AST) is normally performed in a laboratory (Giuliano *et al*., 2019). Antibiotics are chosen for susceptibility testing after a bacterium has been detected by microbiological culture (Reller *et al*., 2009). Methods of susceptibility testing include exposing bacteria to antibiotics and studying their reaction (phenotypic testing). Methods used can be qualitative, showing whether resistance is present or not, or quantitative, defining the concentration of antibiotic to which a bacterium is susceptible using a minimum inhibitory concentration (MIC) (van Belkum *et al*., 2019).

1.4.2.1. Phenotypic methods

In tests that depend on exposing bacteria to antibiotics, agar plates or dilution in agar or broth are used (Pulido *et al*., 2013). The antibiotics used would rely on the organism grown and the antibiotics present locally (Reller *et al*., 2009). The bacteria concentration added to the agar or broth (the inoculum) must be standardized to ensure that the results are accurate. This is done by measuring the turbidity of bacteria dissolved in saline or broth to McFarland standards solutions of the same turbidity as a suspension with a specific concentration of bacteria. The inoculum is applied to the growth medium until the proper concentration has been determined, which can be done visually or by photometry (Hombach *et al*., 2015). Choosing a bacteria strain, placing it on an agar plate, and seeing the bacteria grow near antibiotic-impregnated discs is the disc diffusion method (Syal *et al*., 2017). While modified methods are also used, this approach is known as the Kirby-Bauer method. Small paper discs containing antibiotic are put on a plate where bacteria are growing. If the antibiotic inhibits microbial growth a clear ring or

zone of inhibition can be seen around the disk. Bacteria are categorized as sensitive, intermediate, or resistant to an antibiotic by comparing the diameter of the zone of inhibition to defined thresholds that correlate with MICs. In this antibiotic susceptibility test, Mueller-Hinton agar is frequently used (Jorgensen and Turnidge, 2015). There are standards for how testing is done and how the results are interpreted (Reller *et al*., 2009). European Committee on Antimicrobial Susceptibility Testing (EUCAST) set standards for agar type and depth, incubation temperature, and method of analysis (Hombach *et al*., 2015). Disc diffusion is the simplest and cheapest method for determining susceptibility, and it can be easily adapted to test newly available antibiotics or formulations (Reller et al., 2009).

1.4.3. Causes of Antibiotics Resistance

1.4.3.1. Natural resistant

Antibiotic resistance (ABR) is characterized as a microorganism's ability to survive antibiotic exposure that would usually kill or stop them from growing (Li and Webster, 2018). The emergence of an antimicrobial-resistant phenotype is influenced by a variety of factors, including the microorganism's degree of resistance expression and its ability to tolerate resistance mechanisms, to mention a few chromosomal mutations (cross-resistance) or gene transfer among microorganisms through plasmids, transposons, integrons, and bacteriophages. Resistant microorganisms spread rapidly as resistance determinants are present on plasmids (Giedraitienė *et al*., 2011). To protect themselves from different agents, bacteria may use a variety of biochemical resistance mechanisms, the most important of which are enzymatic degradation, target alteration, decreased uptake, and overexpression of efflux pump proteins (Gajdács, 2019). Despite the fact that this is a normal occurrence that has been experienced in clinical practice since

the first-generation antibiotics (Monserrat-Martinez *et al*., 2019). Owing to the exponential growth and spread of resistance, as well as the lack of new medications to overcome it, ABR is now considered a global public medical issue (O'Neill, 2016).

1.4.3.2. Self-Medication

Self-medication is the use of medications or plants to cure health problems without consulting a doctor about the dosage, indication, path, or frequency. It also involves using a previously prescription drug to treat a recurring condition on a long-term basis (Bennadi, 2013). Self-medication is common for over-the-counter (OTC) medications, which are readily available at pharmacies without a doctor's prescription. Pressure relievers (acetaminophen), as well as cough and cold medications, are examples of these medications (Ehigiator *et al*., 2013). Self-medication is a global health issue with significant public health implications, including medication resistance and organ destruction, and it accounts for 2.9 - 3.7 % of global deaths (Osemene and Lamikanra, 2012). Self-medication is influenced by a variety of influences, including attitudes toward health care, education, insurance plans, cost savings, convenience, and age (Helal and Abou-ElWafa, 2017). Self-medication with OTC medications, it should be noted, can be safe and permissible if the consumer has sufficient knowledge of the prescription and the condition (Gutema *et al*., 2011). Self-medication, when done correctly and by knowledgeable people, will reduce down on time spent waiting for doctors as well as other insurance costs, such as consultation fees (Helal and Abou-ElWafa, 2017). OTC medications, on the other hand, are often regarded as dangerous when used irrationally, resulting in misdiagnosis or delayed diagnosis, various drug reactions, and, ultimately, a rise in disease burden in a population due to resistance (Sharma *et al*., 2015).

1.4.3.3. Clinical Misuse

One of the main factors contributing to the development of ABR is the misuse of antibiotics. Antibiotic misuse includes overuse, improper prescribing, self-medication, negligent use, and inaccurate dose or treatment length (Haddadin *et al*., 2019). Antibiotic misuse may be a result of patients' attitudes (Davey *et al*., 2002), As shown by the widespread use of antibiotics without a prescription or patients' complete disregard for doctors' orders. Neither the indication on the duration and dosage of treatments in the summary of product characteristics (Wogayehu *et al*., 2020). Community pharmacists still play a part in ensuring that antibiotics are used with caution (Gajdács *et al*., 2020). In the other hand, from the perspective of doctors, attempts should be made to optimize prescribing practices in order to prevent excessive antibiotic usage, especially in primary care (Bianco *et al*., 2018).

1.4.3.4. Environmental Pollution

Antimicrobial resistance (AMR) is a global health problem caused by the overuse of antibiotics in healthcare and animal farming, as well as the sluggish discovery of new antibiotics. Characterizing AMR in the environment, which is critical to identifying and avoiding risks to public health, has received a lot of attention recently. The existence of high-throughput platforms for detecting antimicrobial resistance genes (ARGs) has simplified and complicated this characterization (Williams *et al*., 2016). Researchers can now quickly detect and evaluate recognized ARGs in the environment, however due to current depth of sequencing technology, a large number of ARGs remain unknown and uncharacterized. Although new gene discoveries are crucial for preventing global AMR, the process is challenging due to the evolution of new resistance mechanisms as well as the spread of AMR in the environment due to horizontal gene transfer and the spread of

mobile genetic elements. Furthermore, various environments, such as the aquatic climate, have different resistance profiles depending on where they are located, and can serve as reservoirs for AMR, particularly because they are normally endpoints of agriculture runoff and wastewater treatment plant discharge. The aquatic environment is an effective way of incorporating and spreading AMR into the environment since most people get their drinking water from sea water, which is also where wastewater is discharged. Runoff from animal farms could end up in surface waters, resulting in AMR transmission between humans and animals (Williams *et al*., 2016).

1.4.3.5. Food Propduction

Food safety is a scientific course that focuses on preventing and managing food-borne diseases during the food manufacturing process, including transportation, packaging, handling, and preparation, as well as ensuring the quality and safety of foods intended for human consumption (Founou *et al*., 2016). Resistant food-borne infections are one of the most important public health problems related to the risk of antibacterial resistance developing in the food supply chain. Multiple types of resistant bacteria have been identified in food products and humans recently; however, certain essential and easy food safety measures, such as proper handwashing, convenient vegetable washing, effective cooking temperatures, and food storage conditions, can effectively minimize and monitor the spread of antibacterial resistance foodborne pathogens (Founou *et al*., 2016). Antibiotic residues in food products can cause allergic reactions, hepatotoxicity, mutagenicity, carcinogenicity, toxic symptoms, nephropathy, and antibacterial resistance, according to Antibiotic residues in food products can cause allergic reactions, hepatotoxicity, mutagenicity, carcinogenicity, toxic symptoms, nephropathy, and antibacterial resistance, according to (Mensah *et*

al., 2014). According to research, there are a variety of food-borne pathogens that are resistant to a variety of drugs and antibiotics (Hashempour-Baltork *et al*., 2019). Antibiotics are commonly used as growth additives in animals in both the developed and developing worlds. Antibiotics are mainly used in animals to stimulate growth and avoid infection, accounting for about 80% of antibiotics sold in the United States (Bartlett *et al*., 2013). Antimicrobial treatment of livestock is said to increase the animals' general health, resulting in higher yields and a higher-quality product (Michael *et al*., 2014). Antibiotics used in animals are consumed by humans by their food (Golkar *et al*., 2014). The transition of resistant bacteria from farm animals to humans was first recorded more than 35 years ago, when high rates of antibiotic resistance were discovered in both farm animals and farmers' intestinal flora (Bartlett *et al*., 2013). More recently, previous study shown that bacteria resistant to antibiotics in farm animals make their way to consumers through meat products.This happens as a result of the following events: 1) Antibiotics kill or suppress susceptible bacteria in food-producing organisms, allowing antibiotic-resistant bacteria to thrive; 2) resistant bacteria are transmitted to humans via the food supply; 3) These bacteria can cause infections in humans, which can be harmful to their health. Antibiotic use in agriculture has an effect on the microbiota in the environment (Control and Prevention, 2013).

1.4.4. Mechanism of antibiotic resistance

A-The modifications

Changes in the drug-related receptor and the position of the antibiotic relation's target regions differ, and they may include enzymes and ribosomes (Prashanth *et al*., 2012). Resistance to macrolide antibiotics is the most common form of resistance associated with changes in the ribosomal target (Shaikh *et al*., 2007). Mutations in penicillin-binding proteins beta-lactamase

enzymes have evolved penicillin resistance in strains of *Staphylococcus aureus, Streptococcus pneumoniae, Neisseria meningitides, and Enterococcus faecalis* (Southon *et al*., 2020).

B- Enzymatic Inactivation of Antibiotics

The majority of bacteria produce antibiotic degradation enzymes, and enzymatic inactivation is one of the most effective antibiotic resistance mechanisms (Pérez-Llarena and Bou, 2016). Beta-lactamases, aminoglycosidase, chloramphenicol, and erythromycin modifying enzymes are the most common examples (Suleiman *et al*., 2020).

C- Reduction of The Iinner and Outer Membrane Permeability

Reduced drug uptake into the cell or rapid ejection from the pump systems are caused by changes in the permeability of the internal and external membranes, which results in this process (Santajit and Indrawattana, 2016). Porin mutations that can occur in resistant strain proteins, for example quinolone resistance and aminoglycoside resistance can also be caused by a reduction in outer membrane permeability (Li *et al*., 2012).

D-Active Pumps System

In the tetracycline group of antibiotics, active pump system is the most important source of resistance. In an energy-dependent active pumping mechanism, tetracyclines are thrown out and cannot focus inside the cell (Li *et al*., 2020c). This resistance mechanism is in plasmid and chromosomal control. Quinolones, 14-membered macrolides, chloramphenicol, and beta-lactams are all resistant to active pumping systems (Guo *et al*., 2020).

E- Using an Alternative Metabolic Pathway

The most recent drug-susceptible pathway, unlike some of the target alterations in bacteria, does not require objective development (Fatahi-Bafghi, 2019). Instead of synthesizing folic acid, bacteria may prepare it from the

environment, making it resistant to sulfonamide and trimethoprim (Tan *et al*., 2020)

1.5. Nanotechnology Study

The required a new/novel and efficient drug delivery system that increases the therapeutic index of already used antimicrobial agents with reduced local and systemic side effects and without the development of microorganisms' resistant to these antimicrobial agents. Nowadays, the application of antimicrobial drugs loaded in nanosized vehicles (nanomedicine) has the potential to resolve these challenges that are associated with conventional therapy and delivery systems (Gupta *et al*., 2019). In nanomedicine, nano-sized vehicles (NVs) with various dimensions are applied for loading and conveying of antimicrobial drugs. These novel NVs have unique properties e.g. reduced prospects for the development of resistance by microorganisms, significantly enhanced therapeutic efficacy, more soluble in serum than free drugs, increased systemic drug circulation times, prolonged therapeutic effects, reduced adverse side effects on healthy tissues/cells and they can make use of combination therapy to convey multiple drugs on the same site-specific cell (Zhang *et al*., 2010). NVs are the vesicles or particles that have at least one dimension in the range between 1 and 100nm.

NVs have some unique and advanced physicochemical properties in comparison to the same bulk materials, individual atoms or molecules. These properties are mainly based on quantum effects and significantly raised surface area to volume ratio. In 2000, National Institutes of Health, USA launched the National Nanotechnology Initiative for supporting, coordinating and advancing research and development of nanoscale projects. "Nanotechnology is not simply working at even smaller dimensions; rather,

working at the nanoscale enables scientists to utilize the unique physical, chemical, mechanical, and optical properties of materials that naturally occur at that scale" (Weissig *et al*., 2014). Since prehistoric times, metals such as zinc (Zn), copper (Cu), gold (Au), titanium (Ti), and silver (Ag) have been used for therapeutic purposes because of their broad-spectrum activities against a number of microorganisms (Malarkodi *et al*., 2014). Recent advances in the field of nanotechnology have confirmed the importance of these metals, and nanoparticles (NPs) that exhibit antimicrobial properties have gained substantial scientific recognition as potent inhibitory agents for the growth of pathogens. To conquer the drug resistance phenomena of microbes, NPs exhibit multifunctionalities, such as the enhancement of intracellular accumulation of antimicrobial agents or the inhibition of biofilm formation (Huhand and Kwon, 2011) .

Various metal and metal oxide NPs, such as titanium dioxide (TiO2), silver oxide (Ag2O), copper oxide (CuO), zinc oxide (ZnO), gold (Au), silicon (Si), magnesium oxide (MgO), and calcium oxide (CaO), have been characterized for their efficient antimicrobial activities (Muzammil *et al*., 2018). The antimicrobial efficacy of metal oxide NPs is mainly attributed to the large surface area, which ensures that a wide range of reactions with bio-organics is available on the surface of cell (Mukherjee *et al*., 2011). The smaller the particle, the larger surface area to volume ratio it will have; thus, the augmentation of its chemical and biological activities can be enhanced by an increased area of contact of a metal with a microbe. The use of nanoscale metals has achieved a hundred-fold reduction in concentration with a simultaneous increase in antimicrobial properties; the reduction of the particle size from 10 μm to 10 nm increases the surface area of contact by a factor of 109 (Pal *et al*., 2007).

1.5.1. *Staphylococcus hominis* and it Resistance to Antibiotics.

Sepsis can be defined as the body responds to an infection usually bacteria invading the body and can be limited to a particular body region or can be widespread in the bloodstream which often called septicemia. The prevalence of septicemia was higher among among the gram-positive bacteria were: *Staphylococcus aureus, Staphylococcus epidermidis,* and *Staphylococcus* hominis, *Micrococcus luteus, Enterococcus faecalis* while the gram-negative bacteria were: *Klebsiella pneumoniae, Pseudomonas aeruginosa, Escherchia coli, Brucella melitensis , Salmonella typhi,* and *Proteus mirabilis* and antibiotic susceptibility profile showed that most of the isolated bacteria were resistant to more than one bacteria. Most of the isolated bacteria were gram-positive. The most of the bacteria isolated were resistant to most of the common antibiotics that however varieties of pathogens are responsible for sepsis, and antimicrobial resistance become a significant public health problem (Abdullah, 2020). By the newly redesigned colorimetric Vitek 2 compact system with an updated advanced expert system (AES) (bioMerieux, Marcy l'Etoile, France) was evaluated for its accuracy and rapidity to identify clinical isolates and to detect several antimicrobial resistances. The prevalence of septicemia was higher among the gram-positive bacteria and particular *Staphylococcus hominis* because there were 17 (17.5%) of the bacterial isolates. The antimicrobial susceptibility for *Staphylococcus hominis*, they had the highest sensitivity to Ciprofloxacin 16(94.1%), followed by (Rifampicin, Erythromycin, Tetracyclin). And they were highly resistant to Gentamicin13(76.3%) followed by (Amoxicillin, Meropenem, Vancomycin) (Thapa and Sapkota, 2019).

1.5.2. Meropenem

Meropenem is a broad spectrum, beta-lactam carbapenem antibiotic that acts by binding to the penicillin binding proteins and disrupting bacterial cell wall integrity and synthesis. Meropenem has a broad spectrum of activity against many aerobic and anaerobic gram-positive and gram-negative organisms, including *Staphylococcus aureus*, *Streptococcus pyogenes*, *Streptococcus agalactiae*, viridans group *streptococci*, *Enterococcus faecalis*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Proteus mirabilis*, *Bacteroides fragilis* and *Peptostreptococcus* species (LiverTox *et al*., 2012). Meropenem was approved for use in the United States in 1996 and is currently indicated for the treatment of severe or complicated skin, tissue, intraabdominal and urogenital infections as well as sepsis due to susceptible organisms. Its use is generally reserved for severe infections in hospitalized patients. The recommended dosage is 0.5 to 1 gram given intravenously every 8 hours, with dose adjustment for renal impairment. Meropenem is available in vials of 500 mg or 1 gram of lyophilized powder for injection in generic forms and under the brand name Merrem (LiverTox *et al*., 2012).

2.1. Materials

2.1.1. Chemicals

Table 1. Chemicals of the study

Chemicals	Company	Origin
ABO Reagents	AFCO	Jorden
AST FOR GRAM NEGATIVE	BIONMERIEUX	France
AST FOR GRAM POSTIVE	BIONMERIEUX	France
BNP ELISA KIT	Bioassay Technology Laboratory	Chine
Cholesterol	DIRUI	Chine
Creatinine kit	DIRUI	Chine
CRP kit	Boditech	Korea
Ethanol	Teeba	Iraq
GN card	BIONMERIEUX	France
GP card	BIONMERIEUX	France
Gram Staining kit	VSI	Iraq
HDL	DIRUI	Chine
Iodine	Areej Bagdad	Iraq
LDL	DIRUI	Chine
Random blood sugar kit	DIRUI	Chine
Triglyceride	DIRUI	Chine
Troponin kit	Boditech	Korea
Urea kit	DIRUI	Chine

2.1.2. Devices and Tools

Table 2: Devices and Tools of the study

Devices and Tools	Company	Origin
Auto-chemistry Analyzer	DIRUI	Chine
Autoclave	Labtech	Korea
BACT/ALERT 3D	BIONMERIEUX	France
Blood pressure device	Rossmax	Switzerland
Centrifuge	Gallenkamp	England
ECHO	Philips	Germany
Elisa UNO Human	Human	Germany
ECG	MAC-1600	Germany
FTIR-8400S	SHIMADZU	England
Fume Hood	FASTER Bio 4s	Italy
Glass wear	AFCO	Jorden
Hot plate magnetic stirrer	Labtech	Korea
Ichroma	Boditech	Korea
Incubator	Gallenkamp	England
Magnetic stereo	Heidolph	Korea
Micropipettes	Micropipette	Germany
Microscope	Olympus	Japan
Oven	Memmert	Germany
Refrigerator	LG	Korea
Sensitive balance	Kern	Germany
Shaker incubator	Gallenkamp	England
Vitek 2-compact	BIONMERIEUX	France
Vortex	Scientific Industries	Korea
Water Distling	GEL	Germany

2.1.3. The Media

2.1.3.1. Blood Agar

In 1000 ml of distilled water suspend 40g carry it to the boil to dissolve completely, autoclave at 121 °C for 15 minutes for sterilized, for this agar, cooling to 45-50 °C adds 7% of sterile defibrinated blood, this method fallowed as manufactured instruction.

2.1.3.2. Macconkey Agar

In 1000 ml suspend 51.55g of medium and water was been distilled. To dissolve the agar completely heating to boil with gently swirling, autoclave sterilization for 15 minutes at a pressure of 15 lbs (121°C). Without heating over. Cool to 45-50 °C and pour into petri dishes that are sterile. When inoculated, the surface of the medium should be dry.

2.1.3.3. Brain Heart Infusion Broth:

The media consisted, as a basal medium, of brain heart infusion broth and supplemented with 35% (v/v) glycerol. It was poured into 5 ml/tube, autoclaved, cooled and then preserved until used at 4 °C. The use of this medium was to sustain the isolate for a long time at 20 °C.

2.2.1. Patients

The case control study of patients with heart failure was conducted during period from October, 2020 to May, 2021. Seventy-one patients presented with heart failure in coronary care unit (CCU) in Heart Center of Al-Hussein Teaching Hospital, Al- Hussein Medical City/Kearbala Health Directorate. All patients were adults and their age > 40 and form both sexes who admitted as heart failure.

2.2.1.1. Collection Data

There were many important information and data that collected from

the patients like name, age, gender, weight, blood pressure, diabetes and blood group.

2.2.1.2. Collection Samples

About 10 ml of venous blood samples where taken from HF patients after admission to the CCU. There were important procedure of blood culturing done by Nutusi *et al* should be fallowed (Ntusi *et al*., 2010), like :

1- Confirming the patient's identity had been started and patient's identity was requested. To confirm identification, on the wall above the bed or in the patient notes.

2 -The procedure was described to the patient and the information of the plans was tolled. Often was gotten verbal permission.

3- The necessary materials for a blood culture was collected included blood culture bottles, syringe (10 ml), sterile gloves, tourniquet, adhesive strip, povidone iodine or alcohol solution (or other suitable skin disinfectant), sterile pack containing cotton/gauze swabs and sharps waste disposal bin.

4- A tourniquet was added, and an appropriate vein was chosen. Disinfection the hands with alcohol or washed them with soap and water. After that, hands were cleaned or rubbed until they were fully dry. Sterile gloves were putted.

5- Aseptic procedure was used; the puncture site was wiped with povidone or alcohol solution. The disinfectant was allowed to dry for 1 to 2 minutes. A green sterile cover was positioned over the blood culture site with an opening.

6 -A needle was carefully placed into the patient's blood vein, and a minimum of 10 ml of blood was obtained (adults). The blood culture would be the first blood specimen obtained if the vacutainer device was used.

7- The tourniquet was let go. The needle and syringe were taken out of the puncture wound. A dry swab was put on the puncture site and pressure was applied. Inoculate blood into culture bottle after disinfecting the top of the

blood culture bottle with an alcohol swab if blood was not extracted directly into the culture bottle with the vacutainer system. Often inoculate the blood culture tube before collecting blood for other examinations. Between collecting blood samples and inoculating the blood culture bottle.

8- To combine the blood and culture medium, the blood culture container was gently rotated (Avoided shake vigorously).

9- As soon as possible, the blood culture bottle was sent to the laboratory. And at the same time about 3.5 ml blood sample was transferred into gel tube (2ml) at room temperature and left to stand for at least fifteen minutes for clotting then centrifuged at 2500 rpm. Then serum was separated and divided into epindrop. And the remaining about (1.5ml) blood sample was put in the EDTA tube then put in shaker for at least fifteen minutes.

2.2.2. Estimation of Lipid Profile

Total Cholesterol (TC), Triglycerides (TG), High Density Lipoprotein (HDL-C) and Low Density Lipoprotein (LDL) were measured automatically in the Auto-Chemistry Analyzer CS-T180 followed method of (Young, 1997).

2.2.3. Estimation of Kidney Function Tests.

Creatinine and Urea were measured automatically in the Auto-Chemistry Analyzer CS-T180 followed method of (Young, 1997).

2.2.4. Identification of Heart Failure

2.2.4.1. Identification of Heart Failure by ECG and ECHO

The identification of heart failure patients by ECG and ECHO was done by the specialist doctor in the CCU.

2.2.4.2. Diagnosis of Heart Function Tests

2.2.4.2.1. Estimation Brain Natriuretic Peptide

According to manufacturing instruction:

1 -All reagents, standard solutions, and samples were made according to the directions. After that, all of the reagents were brought to room temperature before being used. At room temperature, the assay is carried out.

2 -After determining the number of strips needed for the assay, the strips were placed into the frames and used.

3 -In the standard well 50 µl of standard were added.

4 -In sample wells 40 µl of sample A were added, followed by 10 µl of anti-BNP antibody in sample wells, and finally 50 µl of streptavidin-HPR in sample and standard wells. The plate was then sealed and incubated for 60 minutes at 37 °C.

5- The sealer was removed and used wash buffer to wash the plate five times. For each shower, soak wells with at least 0.35 ml and wash buffer for 30 seconds to 1 minute. Aspirate both wells and wash 5 times with wash buffer, overfilling wells with wash buffer for automatic washing. Blot the plate onto paper towels or other absorbent material.

6- Substrate solution A of about 50 µl was added to each well, then 50 µl of substrate solution B to each well, then incubated plate filled with a new sealer at 37 °C in the dark for 10 minutes.

7- When 50 µl Stop Solution is added to each well, the blue color turns yellow almost immediately.

8- Within 10 minutes of applying the stop solution, the optical density (OD value) of each well was determined using a microplate reader set to 450 nm by spectrophotometer.

2.2.4.2.2. Estimation of Troponin

The procedure fallowed by McNeil (McNeil, 2007):

1- Using a transfer pipette 75 µl of human serum were transferred to an empty sample mixing tube, and 75 µl of detection buffer were added.

2 -The sample's cover was closed over the mixing tube, and the sample was properly mixed by shaking it about 10 times.

3- From the sample mixture75 µl were pipetted from it and loaded into the cartridge's sample well.

4 -The sample-loaded cartridge was left out for 12 minutes at room temperature.

5- The single-loaded cartridge was placed into the instrument's cartridge holder for ichroma tests. Before inserting the cartridge all the way into the cartridge holder, it was checked for proper orientation.

6 -To begin the scanning procedure for ichroma samples, the "Select" button on the instrument was pressed.

7 -The instrument for ichroma tests will automatically begin scanning the sample-loaded cartridge.

8- The results of the ichroma measurements were read on the instrument's display screen.

2.2.4.2.3 Estimation of C- Reactive Protein

According to manufacturing instruction:

1- A puncture on the top of the detection buffer tube was made by inserting an empty sample collector.

2 -A sample collector was used to draw a 10 microliter sample (human whole blood, serum, plasma, and control).

3 -The sample collector and tubing were assembled into one tube.

4 -Ten times or more is shaken until the sample was inverted out of the sample collector. The buffer and sample mixture were used within 30 seconds.

5 -The top cap was removed from the assembled tube. Before adding the reagents to the cartridge, 2 drops were discarded onto the paper towel.

6- Only 2 drops of the mixture were loaded into the cartridge's sample well.

7 -For ichroma measurements, the device was placed into the instrument's holder. Before inserting the cartridge all the way into the cartridge holder, it was checked for proper orientation. A special arrow has been drowned on the cartridge for this reason.

8 -For ichroma checks, the 'Select' or 'START' button on the instrument was pressed.

9-Cartridges have been inserted into the instrument for ichroma checks, and after 3 minutes, the instrument can begin scanning the sample-loaded cartridge.

10- For ichroma checks, the test result was read out on the instrument's display screen.

2.2.5. Estimation of Physiological Parameters.

2.2.5.1. Estimation of Complete Blood Counts

According to manufacturing instruction:

1. The samples were at room temperature in the first step.
2. It was invert by hand ten times until it is suspended.
3. It was run like a normal patient if the samples are barcoded (Caps lock was disabled).
4. The RUN button was pressed after the sample was placed on the analyzer. Results were printed after all samples had been examined.
5. "Stored Data" was select to print the information.

6. Output was Pressed.
7. Clear marks by pressing “Mark” then “All Clear” then “Cancel.

2.2.4.2. Estimation of Glucose

Glucose was measured automatically in the Auto-Chemistry Analyzer CS-T180 followed method of (Young, 1997).

2.2.4.3. Blood Pressure (Systolic and Diastolic)

This procedure was followed by Mersich, the pressure cuff is automatically inflated to about 220 mm of Hg and allowed to deflate slowly. The sensor picks up the oscillations from the artery near the surface, just below the compression cuff. The pressure reading at the inset of oscillations represents the systolic pressure after that diastolic pressure (Mersich, 2005).

2.2.5.4. Estimation of ABO Blood Group.

In this method, white porcelain support is divided into three parts, as for each part, a drop of donor or recipient blood is mixed with anti-A, anti-B and anti-D separately. The agglutination or blood clumping pattern can be visually observed from which the ABO and rhesus D (RhD) type of blood can be determined. The test completes in 5–10 min and is inexpensive, which requires only a small volume of blood typing reagents (Mujahid and Dickert, 2016).

2.2.6. Diagnosis of Bacteria

2.2.6.1. Blood Culture Samples

Blood culture bottles were used, and were inoculated with blood drawn from a peripheral vein. For the initial testing of the blood cultures, the BacT/ ALERT® 3D system (bioMeriéux, Marcy l'Etoile, France) was used. Gram staining was done on the positive blood culture bottles, and the bacteria were collected and inoculated on blood agar plates (BAP; Asan Pharmaceutical Co., Ltd., Seoul, Korea) and MacConkey agar plates (Becton Dickinson,

Sparks, MD, USA), followed by incubation at 35°C under a 5% CO2 atmosphere (Ha *et al*., 2018).

2.2.6.2. Conventional Workflow of Positive Blood Cultures

When the BacT/ALERT® 3D device indicated a positive signal, Gram staining was performed, accompanied by subculture on a sufficient solid agar medium. Following overnight incubation the colonies grown on the agar plates were used for ID and Antibiotic susceptibility testing (AST) using the commercial automated Vitek2 system (bioMeriéux). As the protocol for institution, the ID and AST results obtained using this traditional workflow were used as the standard for comparison. (Ha *et al*., 2018).

1. After primary organism isolation, there is minimal handling with a simple standardized inoculum
2. Place the inoculum into the VITEK® 2 Cassette at the Smart Carrier Station™
3. The VITEK® 2 Card and sample are linked via barcode
4. Once the Cassette is loaded, the instrument handles all subsequent steps for incubation and reading the results.

VITEK® 2 Compact is an automated biochemical-based tool that includes 48 biochemical features and is widely used in clinical laboratories for microbial detection (Książczyk *et al*., 2016). Microorganisms can be identified for up to 4 hours using VITEK® 2 Compact. Each well assesses a strain's metabolic function, including its ability to acidify, alkalize, and enzymatically hydrolyze substrates, as well as bacterial growth in the presence of inhibitors. The instrument detects bacterial growth and metabolic changes in the microwells using fluorescence-based instruments. The findings of the biotyping and biochemical-based methods was influenced by the conditions of bacterial incubation, such as media composition or pH (Książczyk *et al*., 2016). A

sterile microloop was used to collect a few colonies of a pure culture that had been grown on blood or macconkey agar for 18 to 24 hours. A bacterial suspension was calibrated to McFarland Turbidity Standard of 0.5–0.63 in 3 mL of a 0.45 percent sodium chloride solution using a VITEK® 2 DensiChek (bioMérieux, Warszawa, Poland). The GN card was placed on the cassette and placed in the instrument if the gram stain was negative, and the GP card was placed on the cassette and placed in the instrument if the gram stain was positive. The time between suspension preparation and card filling was less than 30 minutes to prevent turbidity modifications. The cards were incubated at 35.5 1 °C. Colorimetric measurements were taken automatically every 15 minutes when each card was taken out of the incubator. The results were read after 10 to 18 hours incubation (Morka *et al*., 2018).

2.2.7. Determination of Antibiotic Susceptibility

Antibiotic susceptibility testing determines a bacterial isolates susceptibility to a set of antibiotics. The cards were loaded into the Vitek 2 automatic reader-incubator after being inoculated. Identification and susceptibility cards were inoculated and interpreted as directed by the manufacturer where it written below. Colony counts were used to make sure the number and density of microorganisms inoculated into the Vitek cards were right (Bazzi *et al*., 2017).

- The microorganism was exposed to antibiotics and the examination determines whether or not the microorganism can grow in the presence of the antibiotics.
- The Minimum Inhibitory Concentration (MIC) an indicator of a microorganism's sensitivity or resistance to an antibiotic is reported to the clinician.

- Antibiotic susceptibility testing was used to detect antibiotic resistance processes in bacteria. Antibiotic resistance examination findings are used for clinicians to better assess the best care for the infection and the specific patient.

2.2.8.1 Preparation of Nanohyrbrid Meropenem.

Nanohybrid Meropenem The nanohybrid antibiotic was prepared using the process defined by Kolekar *et al* (Kolekar *et al*., 2011).

A. **Zinc Oxide Solution:** This solution was prepared by dissolving 1 gm of the Zinc Oxide in an amount of 50% ethanol, and after completing the dissolution process, the volume was completed to 50 ml using ethanol as well.

B. Meropenem Solution: This solution was prepared by dissolving 0.5 gm of the meropenem in an amount of 50% ethanol, and after completing the dissolution process, the volume was completed to 50 ml using ethanol as well.

C. Preparation of nanohybrid from zinc oxide layers with Meropenem Gel Solion exchange method: The techniques used previously published by Kolekar *et al* with the addition of 50 ml of the above-prepared Meropenem solution (both at the same time) drop by drop into zinc oxide solution and stirrer magnetically at room temperature for two hours before putting the mixture in the incubator. The vibration took conducted at 37°C for 18 hours before being placed in a 40°C incubator for 24 hours. After an hour, centrifuge the precipitate at 5000 rpm for 20 minutes to separate it. Then rinsed multiple times with distilled water before drying the precipitate at 40°C. It was then grounded in a ceramic mortar before being kept (Kolekar et al., 2011).

2.2.8.2. Preparation of Nutrient agar

According to manufacturing instruction:

1. In a beaker 28 gm of the dehydrated powder or lab-prepared media was added to 1000 ml of deionized water.
2. The suspension was then heated to boiling to dissolve the medium completely.
3. The dissolved medium was then autoclaved at 15 lbs pressure (121°C) for 15 minutes.
4. Once the autoclaving process is complete, the beaker was taken out and cooled to a temperature of about 40-45°C.
5. The media was then poured into sterile Petri dishes under sterile conditions.
6. Media were placed in the hot air oven at a lower heat setting for a few minutes to remove any moisture present on the plates before use.

2-2-8-3 Preparation of concentrates and petri dishes

1. Forty-two dishes were prepared, 12 of them are nanomeropenem and 12 of them were free meropenem.
2. Each of the free and nano dishes was been numbering and according to the concentrations were (0, 25, 50, 100, 200, 400) with duplicate each one concentration.
3. Two wells were made inside the media for all petri dishes.
4. Twelve tubes were Prepared, 6 of them are Free-Meropenem and 6 were Nano-Neropenem.

2.2.8.4. Preparation of Stock Solution

The stock solutions of the Free-Meropenem and the Nano-Meropenem were prepared separately, with a weight of 0.8 gm of the drug and placed in a test tube, and 2ml of distilled water was added to it to get a stock solution with

a concentration of 400 mg/ml, which will be used in the subsequent steps to prepare the concentrations used in this study.

2.2.8.5. Preparation of Antibiotic Concentrations:

The concentrations used in this study were prepared for each of the Free-Meropenem and Nano-Meropenem separately according to the method shown in Table 40.

Table 3: Preparation of drug concentrates

No. of tube	Distal Water (µl)	Stock Solution (µl)	Final Volume (µl)	Final Concentration (mg/ml)
1	1000	0	1000	0
2	937.5	62.5	1000	25
3	875	125	1000	50
4	750	250	1000	100
5	500	500	1000	200
6	0	1000	1000	400

2.2.9. Characterization of the Nanohybrid Antibiotic

The nanohybrid antibiotic under study was characterized by using several methods including Fourier transform infrared spectroscopy (FT-IR); X-ray diffraction (XRD); Atomic Force Microscope (AFM) and precise analysis of C, H and N elements.

1. **FT-IR**: The infrared spectrum for each of Nanohybrid-Meropenem and meropenem in free as well as the zinc oxide (ZnO) was assessed by making disk from the compound under study with potassium bromide (KBr) after grinded well, and was measured the infrared spectrum in a wave number range (400-4000) cm-1.
2. . **X-ray**: diffraction spectrum was used to characterize the Nanohybrid-Meropenem. XRD explains the difference in the thickness of the layer before and after the encapsulated process for meropenem antibiotic by using Brack's low ($n\lambda = 2dSin\theta$).

3. **Atomic Force Microscope (AFM)**: In order to measure the diameters, sizes and aggregation of the nanoparticles, the samples of the Nanohybrid-Meropenem were characterized by AFM.
4. . **Precise analysis of C, H and N elements**: C, H and N percentages in the Nanohybrid-Meropenem and meropenem free were analyzed.
5. **Scanning Electronic Microscope (SEM)**: was used to examine the outer surface of the Mero-ZnO nanocomposite as well as the layers of zinc oxide (ZnO).

2.2.10.Measurement of antimicrobial activity of Free-Meropenem and Nano-Meropenem: The method described by Egorove in yrear (1985) (Egorov, 1985) was followed to investigate about antimicrobial activity of Free-Meropenem and Nano-Meropenem as shown:

2.2.10.1. Media

2.2.10.1.1. Nutrient broth media: was prepared according to a company instruction which performed it by weighing 51.55 gm of media and dissolved with 1 L distilled water then autoclaved for 15 minutes. This media was used to activate the bacteria.

2.2.10.1.2. Muller Hinton ager media: was performed was prepared according to a company instruction by weighing 40.12 gm of media and dissolved by l L distilled water, then autoclaved for 15 minutes. This media was used to investigate the antimicrobial activity of Free- Meropenem and Nano- Meropenem against *Staphylococcus hominis.*

2.2.10.2. Activation of bacteria: *Staphylococcus hominis* was activated on nutrient broth before one hour of culturing.

2.2.10.3 Antimicrobial bioactivity assay: After the activation of the bacteria two wells had been done (with diameter 8 mm) for each dish (Muller Hinton agar) and add 100 µl from concentration of antibiotic to each well and 50 µl

was spread from suspension of activated bacteria on each petri dish and was been incubation at 37 ºC for one day and growth was seen, the diameter was observed for the inhibition zone round the well and it was measured by ruler.

2.3. Ethical management of studies

The study was conducted according to the standards recommended by the Department of Clinical Laboratories at the College of Applied Medical Sciences, University of Kerbala, to deal with biological substances and pathogenic germs. The samples in this study were collected from patients arriving at the Karbala Center for Heart Diseases and Surgery in Imam AI-Hussein Medical City in Karbala after obtaining the fundamental approvals from the hospital administration and its patients.

2.4. Statistical analysis

The results were analyzed statistically in SPSS to find out Chi-sequare , ANOVA (One away) at significance level (α) in (0.01and 0.05) and Coreelatuion (r).

3.1. General parameters

3.1. 1. Age

The results show that no significant differences ($P > 0.05$) between patients and controls all age groups except that there was only significant differences ($P < 0.05$) between patients and controls in the age group (50-59) as shown in the table 4.

Table 4: Distribution of the study sample according to age.

Age (Years)	Control N (%)	Patients N (%)	*P* value
40 – 49	9 (12.68 %)	6 (8.45 %)	0.4385
50 – 59	32 (45.07 %)	18 (25.35 %)	0.0477 *
60 – 69	15 (21.13 %)	18 (25.35 %)	0.6015
70 – 79	11 (15.49 %)	19 (26.76 %)	0.1441
80 – 89	4 (5.63 %)	9 (12.68 %)	0.1655
90 – 99	-	1 (1.41 %)	0.563
Total	71 (100 %)	71 (100 %)	
P value	0.00001 **	0.04707 *	

* means significance differences (P <0.05) ** means high significances differences (P <0.001)

This agreement with previous study that reported the major risk factor for (HF) and over all cardiovascular disease is age. Approximately 1% of individuals aged over 50 years are affected by HF, making HF is the major cause of mortality in the elderly (Benjamin *et al*., 2019). This is a matter of increasing concern in the United States, where the population aged 65 and over increased from 40 million in 2007 to 51 million in 2017 and is projected to reach 95 million in 2060 (Benjamin *et al*., 2019). Given this dramatic growth in the aged population, age-related HF represents one of the greatest challenges confronting global healthcare today (Li *et al*., 2020b). Both systemic and cardiac-specific changes in cellular physiology likely contribute to age related alterations in heart structure and function. Although, there is an increase in left ventricular wall thickness with age, this reflects an increase in size, and not number, of cardiomyocytes. In fact, aging is associated with a decrease in regenerative capacity, which may be compounded by an increase

in cell death. This in turn may be related to an age-dependent decline in mitochondrial function and accumulation of senescent cells. At the same time, elevated inflammatory activity likely drives the increase in myocardial fibrosis with age (Li *et al*., 2020b). Similar with previous study that found functional changes in aging adults hearts have been characterized, which include reports of diastolic and systolic dysfunction, and also electrical dysfunction, including the development of arrhythmias (Steenman and Lande, 2017). Collectively, both functional and electrical defects result in a high prevalence of heart failure, atrial fibrillation, and other CVDs, in aging patients (Steenman and Lande, 2017). Collectively, age-related oxidative stress results in significant cellular and structural changes, and these eventually lead to impaired cardiac functionality and development of CVD (Rodgers *et al*., 2019).

3.1.2. Gender

3.1.2.1. Gender According to The Study Sample

The results of the statistical analysis of table 5 showed that there were no significant differences ($P > 0.05$) between female in patients and controls groups, while there were high significant differences ($P < 0.001$). between patients and controls in both male group and in all patients and control. Although there were no significant differences ($P > 0.05$) between male and female in control group, while there were high significant differences ($P < 0.001$) between male and female in patients group whereas number of male is higher comparison to female.

Table 5: Distribution of the study sample according to gender

Gender	Control N (%)	Patients N (%)	Total	P value
Female	32	27	59	0.5150
Male	39	44	83	0.5831
Total	71	71	142	1.0000
P value	0.4061	0.04364 *	0.04401 *	

* means significance differences (P <0.05) ** means high significances differences (P <0.001)

Similar to the previous study that reported women had a lower risk of incident HF than men, in middle-aged to older individuals, but women had a higher HF risk than men in the oldest age groups. Men tended to be at higher risk of developing HF with reduced ejection fraction (HFrEF), and conversely, women were more likely to develop HF with preserved ejection fraction (HFpEF) (Magnussen et al., 2019). This distinction might be attributable to the predisposition of women to develop coronary microvascular dysfunction/endothelial inflammation and the predisposition in men to develop macrovascular coronary artery disease and myocardial infarction (Lam et al., 2019). These sex-related differences in HF phenotypes and underlying pathophysiology are also reflected in HF biomarker dissimilarities (Cediel et al., 2021).

3.1.2.2. Gender of Heart Failure Patients

From the statistical analysis of Table 6 the results showed that there were significant differences in the number of heart failure female patients without infection comparison to heart failure female patients with infection ($P < 0.05$). There were high significant differences in number heart failure male patients without infection comparison to heart failure male patients with infection ($P <0.001$) and high significant in all patients of heart failure without infection comparison to patients of heart failure with infection ($P < 0.001$). Recently there were significant increase in male number comparison to female in group of heart failure without infection ($P < 0.05$) where there were no

significant differences in male number comparison to female in group of heart failure with infection ($P > 0.05$).

Table 6: The gender of heart failure patients

Gender	Heart Failure Patients Without Infection N (%)	Heart Failure Patients With Infection N (%)	Total	*P* value
Female	20	7	27	0.0186 *
Male	35	9	44	0.00006 **
Total	55	16	71	0.00001 **
P value	0.0218 *	0.6170	0.0241 *	

* means significance differences (P <0.05) ** means high significances differences (P <0.001)

Disagreements with study that reported the management of sepsis in patients with HF represents a challenging and complex clinical conundrum. In contrast to previously reported literature, women with HF who develop sepsis have similar mortality to men despite fewer comorbidities and fewer predictors of poor outcomes. Furthermore, women with HF who develop sepsis receive a more aggressive implementation of the Surviving Sepsis Campaign than men, leading to more volume overload-related complications (Al Abbasi *et al*., 2020). Women with HF who developed sepsis receive a more aggressive implementation of the Surviving Sepsis Campaign than men, leading to more pulmonary edema events in women with HFpEF and more cardiogenic shock in women with HFrEF. A cautiously tailored approach is desperately needed for patients with HF who develop sepsis (Al Abbasi *et al*., 2020). Similar to the study that had been reported that women have lower sepsis related mortality than men (Garcia *et al*., 2016). However, in previous cohort, there was no difference in mortality between men and women with HF who develop sepsis. Women have a proportionally higher ratio of anti-inflammatory-to-pro-inflammatory cytokines, while men have higher levels of interleukin-6 (Babušíková *et al*., 2012). This translates to a better, more coordinated, and more organized immune response to infection in women as

well as lower mortality than in men. Furthermore, in one study, men had a higher prevalence of chronic comorbid conditions, such as coronary artery disease, HFrEF, and diabetes mellitus, which are known to be independent predictors for poor outcome and mortality for patients with sepsis regardless of the presence of heart failure or not. Therefore, despite having a better immunological response to infection, lower prevalence of HFrEF, and lesser comorbidities than men, women with heart failure that developed sepsis have similar mortality rates than men. This suggests that the presence of HF (a chronic debilitating condition) and its chronic neuroendocrine disarrangement are more critical in women than men (Al Abbasi *et al*., 2020).

3.1.3. The Weight

There were no significant differences in all weight results of statistical analysis of Table 7. There was an insignificances increase ($P > 0.05$) in the mean of weight in patients of heart failure comparison to the control, as the mean of weight for heart failure patients and the control (81.309 and 77.848) kg, respectively. Also from the results of the same table showed an insignificant decrease ($P > 0.05$) in the mean of weight in patients of heart failure with bacterial infection comparison to the heart failure without bacterial infection, as the mean of weight (74.375 and 81.309) kg, respectively.

Table 7: The weight (kg) of the study sample.

Patients of Heart Failure		Control	P value
Infection	Mean ± SD kg	Mean ± SD kg	
Without bacterial infection	81.309 ± 17.752	77.848 ± 16.609	0.3671
With bacterial infection	74.375 ± 12.643		0.4644
Total	79.746 ± 16.907	77.848 ± 16.609	0.5933
P value	0.1501		

* means significance differences ($P < 0.05$) ** means high significances differences ($P < 0.001$)

That similar to a previous study that show lower sympathetic activation and lower norepinephrine levels in obese patients with chronic HF than in

nonobese patients with HF. Considering that increased sympathetic activity is correlated with poorer clinical outcomes in patients with HF, these data may partially explain the mechanism of the obesity paradox in HF. More research about the role of norepinephrine and sympathetic activation in obese patients with HF will shed more light on this issue (Hamzeh *et al*., 2017). Other studies on neurohormonal activities are on progression and may partially explain the inverse relationship between obesity and mortality in patients with HF. It leads the obese patients to become symptomatic and present at earlier stages of HF (Lavie *et al*., 2016). That disagreements with study observed a graded association between increasing weight loss and decreasing risk of heart failure (Sundström *et al*., 2017). Adjusting for obesity-related comorbidities such as hypertension, DM, and low cardiorespiratory fitness, attenuated the association between obesity and HF in some cohorts (Pandey *et al*., 2017). Mechanisms linking obesity to HF include inflammation, insulin resistance, and hypertension, although obesity has a direct effect on LV mass independently from blood pressure (Carbone *et al*., 2017).

3.2. Lipid profile

3.2.1. Triglyceride (TG)

From the observation of the statistical analysis of the results of TG in Table 8 was founded that significant decrease ($P < 0.05$) in patients of heart failure without bacterial infection comparison to control, as the concentration of TG for patients for heart failure without bacterial infection and the control (136.762 and 180.844) mg /dl, respectively. Whereas insignificant decrease ($P > 0.05$) in patients of heart failure with bacterial infection in comparison to control as the concentration of TG for patients for heart failure with bacterial infection and the control (144.963 and 180.844) mg /dl, respectively. Lastly the result showed insignificantly increase ($P > 0.05$) in the patients of

heart failure with bacterial infection and those of heart failure without bacterial infection, as the concentration for TG (144.963 and136.762) mg /dl, respectively.

Table 8: TG mg /dl of the study sample

Patients of Heart Failure		Control	*P* value
Infection	Mean ± SD mg /dl	Mean ± SD mg /dl	
Without bacterial infection	136.762 ± 78.769	180.844 ± 81.11	0.0138 *
With bacterial infection	144.963 ± 111.010		0.2054
Total	138.61 ± 86.25	180.844 ± 81.11	0.0198 *
P value	0.7404		

* means significance differences (P <0.05) ** means high significances differences (P <0.001)

This is similar to the study that reported low serum TG level (<150 mg/dL, <1.7 mmol/L) was an independent predictor of cardiovascular death in women but not in men with chronic heart failure (Kozdag *et al*., 2013). This is disagreements with study that reported high serum triglycerides increase the risk of future heart failure, which is in accordance TG with another prospective observational study based on two population studies in Denmark showing that stepwise higher concentrations of non-fasting serum triglycerides were related to increased risk of heart failure (Varbo *et al*., 2018). High levels of triglycerides are also associated with overweight/obesity and diabetes which are known risk factors for ischemic heart disease and myocardial infarction frequently leading to heart failure with reduced ejection fraction. In one study showed that increasing levels of fasting serum triglycerides were significantly associated with increased risk of developing heart failure in the patients especially in oldest (Halldin *et al*., 2020).

3.2.2. High Density Lipoprotein (HDL)

The results of the statistical analysis in the Table 9 for HDL founded that high significant decrease (P < 0.001) in patients of heart failure comparison to control, as the mean of HDL for patients for heart failure and the control (44.323 and 57.024) mg /dl, respectively. Whereas insignificant

decrease (P > 0.05) in patients of heart failure with bacterial infection comparison to the patients for heart failure without bacterial infection, as the mean for HDL (42.5 and 44.854) mg /dl, respectively.

Table 9: HDL mg /dl of the study sample

Patients of Heart Failure		Control	P value
Infection	Mean ± SD mg /dl	Mean ± SD mg /dl	
Without bacterial infection	44.854 ± 12.008	57.024 ± 13.721	0.0001 **
With bacterial infection	42.5 ± 10.582		0.0005 **
Total	44.323 ± 11.671	57.024 ± 13.721	0.0001 **
P value	0.4816		

* means significance differences (P <0.05) ** means high significances differences (P <0.001)

This results corresponding with study that reported patients who were angiographical-diagnosis of coronary heart disease (CHD) and echocardiographical-diagnosis of left ventricular ejection fraction (LVEF)<45% were enrolled. Baseline characteristics were collected and association of total cholesterol (TC) and high density lipoprotein cholesterol (HDL-C) levels with rehospitalization for heart failure (HF) and all-cause mortality was assessed. Consistent to previous findings, results from one study also showed that CHD patients with reduced LVEF had relatively lower serum TC, LDL-C, and HDL-C levels (Zhao *et al*., 2017).

3.2.3. Low Density Lipoprotein (LDL)

As shown from the statistical analysis of Table 10 the results were significant decreased (P < 0.05) in the mean of LDL patients of heart failure comparison with control, as the mean of LDL for heart patients and the control (113.249 and 143.967) mg /dl, respectively. From the same Table the results of statistical analysis showed insignificances decrease (P > 0.05) in patients of heart failure with bacterial infection comparison to those of heart failure without bacterial infection as the mean of LDL (110.031 and 114.185) mg /dl, respectively.

Table 10: LDL mg /dl of the study sample

Patients of Heart Failure		Control	*P* value
Infection	Mean ± SD mg /dl	Mean ± SD mg /dl	
Without bacterial infection	114.185 ± 46.268	143.967±38.659	0.0026 *
With bacterial infection	110.031 ± 70.943		0.0347 *
Total	113.249 ± 52.278	143.967±38.659	0.0033 *
P value	0.7819		

* means significance differences (P <0.05) ** means high significances differences (P <0.001)

This is agreements with study that reported the Low HDL and LDL-C levels are closely related to poor prognosis of patients with severe or end-stage heart failure, which is not related to the etiology (Charach *et al*., 2018). Agreements with another study that reported increased levels of s-LDLcholesterol are a known very strong factor for development of atherosclerotic coronary heart disease, which in young middle-aged men more often than in young middle-aged women, lead to obstructive coronary artery disease (Chiha *et al*., 2015), often proceeding to acute coronary syndrome with myocardial infarction resulting in heart failure with reduced ejection fraction. Lowering LDL-cholesterol has proven beneficial for reducing major cardiac coronary events in both men and women (Collaboration, 2015).

3.2.4. Totaled Cholesterol (TC)

From the observations of the results of statistical analysis in Table 11 they showed that there were high significant decreases ($P < 0.001$) in the mean of TC in patients of heart failure comparison to control, as the mean of TC for heart patients and control (160.423 and 206.396) mg /dl, respectively. In the same table the result of statistical analysis also showed insignificant decreases ($P > 0.05$) in patients of heart failure with bacterial infection comparison to those of heart failure without bacterial infection (153.303 and 162.532) mg /dl, respectively.

Table 11: TC mg /dl of the study sample

Patients of Heart Failure		Control	*P* value
Infection	Mean ± SD mg /dl	Mean ± SD mg /dl	
Without bacterial infection	162.532 ± 52.506	206.396±36.404	0.0001 **
With bacterial infection	153.303 ± 51.302		0.0001 **
Total	160.423 ± 52.009	206.396±36.404	0.0001 **
P value	0.5361		

* means significance differences (*P* <0.05) ** means high significances differences (*P* <0.001)

This is disagreements with study that reported the patients with hypercholesterolaemia and high levels of LDL-cholesterol and an increased risk of coronary artery disease. One study reported that in this group of patients there was an increased risk of heart failure in both men and women and most of the patients had coronary artery disease and nearly 40% had suffered from myocardial infarction (Hovland *et al*., 2017). In general, one study has 2 major findings. First, they observe that in CHD patients with LVEF<45%, higher baseline TC and HDL-C levels are associated with lower risk of rehospitalization for HF symptoms deterioration and all-cause mortality. Second, underlying mechanisms associated with these favorable effects of higher baseline TC and HDL-C levels may be different. Future randomized controlled trials are necessary to evaluate whether increasing TC and HDL-C levels will confer cardiovascular benefits in CHD patients with reduced LVEF. Agree with The mechanisms underlying these findings are attributed to the protective effects of cholesterol on HF patients. For example, cholesterol on the 1 hand is a major energy resource, and in HF patients, energy-deprivation superimposes hypo-perfusion would promote renal and liver dysfunction which in turn cause HF symptom deterioration (Valentova *et al*., 2016).

3. 3 Kidney Function Tests

3.3.1. Creatinine

The results of the statistical analysis of Table 12 showed that there were a hight significant increase ($P < 0.001$) in the concentration of Creatinine in patients of heart failure comparison to the control, as the rate of Creatinine for heart patients and the control (1.343 and 0.845) mg /dl, respectively. The results of the same statistical Table also showed an insignificant decrease ($P > 0.05$) in the concentration of Creatinine in patients of heart failure with bacterial infection comparison to the heart failure without bacterial infection, as the of concentration of Creatinine (1.331 and 1.347) mg /dl, respectively.

Table 12: The concentration of Creatinine (mg /dl) of the study sample.

Patients of Heart Failure		Control	*P* value
Infection	Mean ± SD mg /dl	Mean ± SD mg /dl	
Without bacterial infection	1.347 ± 0.747	0.845 ± 0.285	0.0004 **
With bacterial infection	1.331 ± 0.729		0.0015 *
Total	1.343 ± 0.737	0.845 ± 0.285	0.0003 **
P value	0.9398		

* means significance differences (P <0.05) ** means high significances differences (P <0.001)

This is agreements with study that reported most prognostically important comorbidity in patients with HF is chronic kidney disease (CKD). Close to 10% of the UK adult population have CKD. This proportion increases to over 50% in patients with chronic heart failure (CHF) (Damman and Testani, 2015).

3.3.2. Urea

The results in Table 13 of the statistical analysis showed that there was high significant decreases ($P < 0.001$) in the consentration of Urea in patients of heart failure comparison to the control, as the consentration of Urea for heart failure patients and the control (62.658 and 32.454) mg /dl, respectively. While there was insignificant inecrease ($P > 0.05$) in the consentration of Urea in patients of heart failure with bacterial infection comparison to the heart

failure without bacterial infection, as the mean of Urea (63.256 and 62.481) mg /dl, respectively

Table 13: The concentration of Urea (mg /dl) of the study sample

Patients of Heart Failure		Control	*P* value
Infection	Mean ± SD mg /dl	Mean ± SD mg /dl	
Without bacterial infection	62.481 ± 35.998	32.454 ± 6.469	0.0001 **
With bacterial infection	63.256 ± 26.499		0.0001 **
Total	62.658 ± 33.884	32.454 ± 6.469	0.0001 **
P value	0.9366		

* means significance differences (P <0.05) ** means high significances differences (P <0.001)

This is agreements with study that decumented AHF is one of the most common comorbidities in acute myocardial infarction (AMI) and is associated with adverse prognosis (Ibanez *et al*., 2018). Both blood urea nitrogen (BUN) and creatinine (Cr) are metabolic end products of nitrogen-containing substances in the human body. As they are small molecules, they can be freely filtered through the glomerulus. Normally, Cr is hardly reabsorbed in the tubules, while approximately 30% to 40% of BUN is reabsorbed (Matsue *et al*., 2017). Similar with previous study demonstrated that high BUN levels were associated with poor cardiovascular (CV) outcomes in patients with compensated HF. However, both renal parenchymal damage and high BUN levels at discharge were required for poor CV outcomes. The results of one study highlight the importance of paying attention not only to the baseline BUN level but also to changes in this value and in the serum Cr levels over time, in order to improve long-term survival in acute HF patients (Jujo *et al*., 2017).

3.4. Heart Function Tests

3.4.1. C-Reactive Protein (CRP)

The results of the statistical analysis of Table 14 showed that there was a high significant increase (P < 0.001) in the mean of CRP in patients of heart failure comparison to the control, as the mean of CRP for heart patients and

the control (46.013 and 4.454) mg /l, respectively. The results of the same statistical table also showed an insignificant decrease ($P > 0.05$) in the mean of CRP in patients of heart failure with bacterial infection comparison to the heart failure without bacterial infection, as the rate of CRP (43.478 and 45.4662) mg /l, respectively.

Table 14: CRP mg /l of the study sample.

Patients of Heart Failure		Control	*P* value
Infection	Mean ± SD mg /l	Mean ± SD mg /l	
Without bacterial infection	45.4662 ± 57.545	4.454 ± 1.845	0.0001 **
With bacterial infection	43.478 ± 53.333		0.0001 **
Total	46.013 ± 56.361	4.454 ± 1.845	0.0001 **
P value	0.9020		

* means significance differences (P <0.05) ** means high significances differences (P <0.001)

This is accordance with study that reported patients with IE, elevated CRP levels at hospital admission and vegetation length at diagnosis were predictors of in-hospital death in patients with IE, independent of other prognostic variables, specifically taking into account the patient characteristics and complications, including the development of heart failure and embolic events (Nunes *et al*., 2018). This is similar with another study that documented CRP are commonly used clinical markers of inflammation and used for differential diagnosis and monitoring of bacterial infectious diseases. CRP is closely related to infection and related to many factors in the diagnosis of sepsis. Therefore, CRP can be used as an essential auxiliary index for the diagnosis of sepsis (Arellano-Navarro *et al*., 2018).

3.4.2. Brain natriuretic peptide (BNP)

The statistical analysis of the result in Table 15 showed that there was a significant increase ($p < 0.05$) in the mean of BNP in patients of heart failure comparison to the control, as the mean of BNP for heart failure patients and the control (218.84 and 89.039) ng/ dl, respectively. Also from the same Table

15 results showed an insignificant decrease ($P > 0.05$) in the mean of BNP in patients of heart failure with bacterial infection comparison to the heart failure without bacterial infection, as the mean of BNP (197.48 and 226.11) ng/ dl, respectively.

Table 15: BNP ng/ dl of the study sample.

Patients of Heart Failure		Control	*P* value
Infection	Mean ± SD ng/ dl	Mean ± SD ng/ dl	
Without bacterial infection	226.11 ± 250.02	89.039 ± 175.87	0.0070 **
With bacterial infection	197.48 ± 82.99		0.0239 *
Total	218.84 ± 219.55	89.039 ± 175.87	0.0036 *
p value	0.6549		

* means significance differences (P <0.05) ** means high significances differences (P <0.001)

This is accordance with study that documented serum levels of CRP and BNP have shown to predict adverse outcomes in patients with HF, both in HF with reduced ejection fraction (HFrEF, LVEF <50%) and in HF with preserved ejection fraction (HFpEF, LVEF >50%). Although CRP and NT-proBNP provide independent and complementary insight into cardiorespiratory fitness (CRF), whether CRP and/or BNP also independently predict the degree of CRF impairment in HF patients is not yet established. They hypothesize that two biomarkers, CRP, and BNP, by acting as surrogates for different pathophysiologic mechanisms, inflammation and myocardial strain, respectively, will independently predict the degree of CRF impairment in patients with HF across the spectrum of LVEF including both HFrEF and HFpEF (van Wezenbeek *et al*., 2018). This study agreements with previous study that documented in addition to conventional markers of infection and inflammation, such as procalcitonin, CRP , or leukocyte count, some markers of heart failure, such as BNP, have been suggested to facilitate the diagnosis of septic cardiomyopathy (Charpentier *et al*., 2004). A recent investigation conducted in 900 patients revealed that BNP and cardiac troponin are substantially correlated with the development of septic shock

(with or without septic cardiomyopathy). In investigation of previous study, BNP was superior to troponin in predicting 90-day mortality in patients with septic shock. Both BNP and cTNT, however, failed to detect septic cardiomyopathy with a sufficient specificity in this investigation (Masson *et al*., 2016).

This is agreements with study that documented natriuretic peptides are peptide hormones mostly released by the heart muscles in response to increased volume status and wall stress, which are key elements in cardiovascular physiology (Okamoto *et al*., 2019). Brain natriuretic peptide (BNP) is a commonly measured natriuretic peptide, which is released in conditions that leads to volume expansion and increased myocardial wall pressure. The physiological functions of BNP include relaxation of vasomotor tone, inhibition of sympathetic activity, reduction in cardiac preload, increase in renal blood flow, and increase in natriuresis and diuresis (Potter *et al*., 2009). Plasma BNP has become an important tool in clinical decision-making regarding diagnosis, management, and risk stratification of heart failure (Ibrahim and Januzzi, 2015, Maisel *et al*., 2018).

3.4.3. Troponin

The results of the statistical analysis of Table 16 showed that there was a high significant increase ($P < 0.001$) in the concentration of troponin in patients of heart failure without bacterial infection in comparison to the control, as the concentration of Troponin for heart patients without bacterial infection and the control (924.526 and 0.100) ng/ml, respectively. And high significant increase ($P < 0.001$) in the results of the same statistical table in the concentration of troponin in patients of heart failure with bacterial infection comparison to the control, as the concentration of troponin for heart patients with bacterial infection and the control (383.97 and 0.100) ng/ml,

respectively. There was high significant decrease ($P < 0.001$) in the concentration of troponin in patients of heart failure with bacterial infection comparison to the heart failure without bacterial infection, concentration of Troponin (383.97 and 924.526) ng/ml, respectively.

Table 16: Troponin (ng/ml) of the study sample

Patients of Heart Failure		Control	*P* value
Infection	Mean ± SD ng/ml	Mean ± SD ng/ml	
Without bacterial infection	924.526 ± 175.346	0.100 ± 0.00	0.0001 **
With bacterial infection	383.97 ± 57.446		0.0001 **
Total	802.713 ± 157.934	0.100 ± 0.00	0.0001 **
P value	0.0001 **		

* means significance differences ($P < 0.05$) ** means high significances differences ($P < 0.001$)

This is accordance to with previous study that documented detecting cardiac troponin (cTn) with high clinical sensitivity and high specificity for myocardial tissue. Moreover, many studies were capable of early cTn detection, when necrosis is minimal or even in the absence of cell necrosis by different mechanisms (increased myocyte turnover or increased cell wall permeability among others). Due to these features, cTn has become the standard biomarker for myocardial damage and the preferred biomarker for diagnosing acute myocardial infarction (Cediel *et al*., 2020). In addition, individuals in the HF population frequently have increased concentrations of cTn. In up to 93% of patients with acute HF and up to 74% of patients with stable chronic HF, cTn concentrations are above the 99th percentile of the reference value (Eggers and Lindahl, 2017). In another study that reported relationship of this myocardial injury in intubated patients with sepsis which was reflected by a positive troponin level to duration of mechanical ventilation in patients admitted to ICU. In other study 36% of the patients had elevated troponin, whereas Bessiere *et al* described the prevalence of positive troponin in patients admitted with sepsis to be around 61% (Bessière *et al*., 2013). which was similar to the study by Sheyin *et al* (60.5%) (Sheyin *et al*., 2015).

Prior studies on sepsis and septic shock presented conflicting data on the association of clinical outcomes with troponin elevation. Various studies including those by Vallabhajosyula *et al* (Vallabhajosyula *et al*., 2017), Yang *et al* (Yang *et al*., 2016) and Sheyin *et al* (Sheyin *et al*., 2015) have concluded that troponin elevation was associated with adverse outcomes and increased mortality in patents admitted with sepsis (Abdalla *et al*., 2019).

3.5. Physiological parameters

3.5.1. Complete Blood Count (CBC)

3.5.1.1. White Blood Cell (WBC)

The statistical analysis of the result in Table 17 showed that there was a significant increase ($P < 0.001$) in the mean of WBC in patients of heart failure comparison to the control, as the mean of WBC for heart failure patients and the control (12.670 and 7.133) 10^3/ µl, respectively. Also from the same table 4 results showed an insignificant decrease ($P > 0.05$) 10^3/ µl in the mean of WBC in patients of heart failure with bacterial infection comparison to the heart failure without bacterial infection, as the mean of WBC (13.143 and 12.529) 10^3/ µl, respectively.

Table 17: The number of WBC (10^3/ µl) of the study sample.

Patients of Heart Failure		Control	*P* value
Infection	Mean ± SD10^3/ µl	Mean ± SD10^3/ µl	
Without bacterial infection	12.529 ± 4.822	7.133 ± 2.093	0.0001 **
With bacterial infection	13.143 ± 9.033		0.0006 **
Total	12.670 ± 5.972	7.133 ± 2.093	0.0000 **
P value	0.7195		

* means significance differences (P <0.05) ** means high significances differences P <0.001)

This is similar with study that reported positive association between elevated WBC count and an increased level of CHD risk in the middle aged and elderly population (Chen *et al*., 2018). And agreements with another study that documented chronic inflammation is a key feature of atherosclerosis, and WBC count is a marker of inflammation that is widely available in clinical

practice. Moreover, WBC counts, especially monocytes, were independent risk factors of CVDs. Thus, WBC could be a readily available and informative marker for CVDs in asymptomatic individuals (Kim *et al*., 2017). There were insignificant differences between the patients of heart failure with bacterial infection and the patients of heart failure without bacterial infection that agreements with the study that reported this factor may lack specificity for the diagnosis of infections complicated by heart failure. In particular, a considerable number of the patients with infections had no increases in (WBC count) (Drees *et al*., 2012). It also similar with previous several studies indicate that higher leucocyte count in HF are negative prognostic markers. In middle-aged men, leucocyte count is associated with long-term incidence of HF hospitalizations, and large population studies indicate that higher neutrophil count is associated with the development of incident HF (Shah *et al*., 2017). In another study with ischaemic left ventricular (LV) dysfunction, a leucocyte counts of >7000 cells/μL is an independent predictor of all-cause mortality. In a prospective observational study of a community-based cohort, elevated leucocyte count was associated with an increased risk of incident HFpEF (Gong *et al*., 2018).

3.5.1.2. Red Blood Cell (RBC)

As shown in the Table 18 there were no significant differences ($P > 0.05$) in all the results. There was insignificant decrease ($P > 0.05$) in the mean of RBC in patients of heart failure comparison to the control, as the rate of RBC for heart failure patients and the control (4.639 and 4.637) 10^6/μl, respectively. In the same table 6, the result showed that was insignificant increase ($P > 0.05$) in patients of heart failure with bacterial infection comparison to those of heart failure without bacterial infection as the mean of RBC (4.771 and 4.636) 10^6 /μl, respectively.

Table 18: The number of RBC (10^6 / µl) µl of the study sample.

Patients of Heart Failure		Control	*P* value
Infection	Mean ± SD10^6 /µl	Mean ± SD10^6 /µl	
Without bacterial infection	4.636 ± 0.671	4.637 ± 0.558	0.9943
With bacterial infection	4.771 ± 1.032		0.5566
Total	4.639 ± 0.761	4.637 ± 0.558	0.9893
P value	0.5360		

* means significance differences ($P < 0.05$) ** means high significances differences ($P < 0.001$)

The most important function of RBCs is to deliver oxygen to organs and tissues (Wang *et al*., 2020). This accordance with study that reported clinical evidence that anemia is associated with a series of severe complications in cardiovascular disease (CVD) (which as risk factor for HF) such as thromboembolic events (*e.g*., venous thrombosis). However, therapeutic interventions aimed to increase the circulating number of RBCs (*e.g*., by transfusion of blood or by administration of erythropoiesis-stimulating agents (ESAs) to stimulate the production of RBCs by the bone marrow), were not always effective in the tested cohorts (Yin *et al*., 2017). In another study showed an elevated MCV, RDW, and RBC count were significantly associated with more severe coronary artery stenosis. (Wang *et al*., 2020). Stenosis of the coronary artery, which may lead to myocardial infarction or sudden cardiac death, reduces blood flow and oxygen to the heart muscle (Paradis *et al*., 2014). This disagreements with study that reported erythrocyte changes were common in patients with heart failure and can be influenced by a variety of factors (Murphy, 2014).

3.5.1.3. Hemoglobin (HgB)

The results in Table 19 of statistical analysis showed that there was insignificanct increase ($P > 0.05$) in the mean of HgB concentration in patients of heart failure comparison to the control, as the mean of HgB concentration for heart failure patients and the control (12.804 and 12.79) g/dL, respectively. While there was insignificant inecrease ($P > 0.05$) in the mean of HgB in

patients of heart failure with bacterial infection comparison to the heart failure without bacterial infection, as the mean of HgB (12.943 and 12.763) g/dl, respectively.

Table 19: HgB (g/dl) of the study sample

Patients of Heart Failure		Control	*P* value
Infection	Mean ± SD g/dL	Mean ± SD g/dL	
Without bacterial infection	12.763 ± 1.826	12.79± 1.48	0.812
With bacterial infection	12.943 ± 2.678		0.872
Total	12.804 ± 2.029	12.79 ± 1.48	0.951
P value	0.7572		

* means significance differences (P <0.05) ** means high significances differences (P <0.001)

This is in agreement with study that documented Hb concentration and mean corpuscular volume were highest among HFpEF compared to the two other phenotypes (Akintunde *et al*., 2021). In agreements also with another study that founded the presence of anemia is associated with a special risk for patients with any form of proatherosclerotic condition and heart disease. Anemia became a new therapeutic target in patients with cardiovascular pathology, improving oxygen supply. Complete blood count abnormalities and hemorheological parameters represent useful, inexpensive, widely available tools for the management and prognosis of patients with coronary heart disease, heart failure, hypertension, arrhythmias, and stroke (Mozos, 2015). In addition, cardiac echo parameters of diastolic function such as left atrial dimension was worse in anemic patients than in non-anemic patients. This is disagreements with study that reported anemic patients might be in more advanced stage in HF compared with non-anemic patients (Okuno *et al*., 2019). To make up for the deficiency in the HF patients or due to the medications.

3.5.1.4. Hematocrit (HCT)

From the observation of the results of statistical analysis in Table 20 showed that there was insignificant decrease (P > 0.05) in the percent of HCT

in patients of heart failure comparison to the control, as the rate of HCT for heart failure patients and the control (40.659 and 39.448) %, respectively. In the same Table 8 the result showed that was insignificances increase ($P > 0.05$) in patients of heart failure with bacterial infection comparison to those of heart failure without bacterial infection as the mean of HCT (42.006 and 40.267) %, respectively

Table 20: HCT % of the study sample

Patients of Heart Failure		Control	*P* value
Infection	Mean ± SD %	Mean ± SD %	
Without bacterial infection	40.267 ± 5.481	39.448 ± 4.205	0.4629
With bacterial infection	42.006 ± 8.778		0.1719
Total	40.659 ± 6.342	39.448 ± 4.205	0.3205
P value	0.3380		

* means significance differences (P <0.05) ** means high significances differences (P <0.001)

That disagreements with this study that documented the association of HCT with the short-term outcomes of acute decompensated HF has remained largely elusive. In another study, the association of HCT with the outcomes of AHF patients, i.e., re-hospitalization, was examined, and a higher HCT was indicated to be linked to a reduced risk of cardiac-associated events in patients with AHF. In one results also suggest that, similar to BNP and serum creatinine, HCT may serve as an independent prognostic factor for patients with AHF (Yan *et al*., 2020). Due to weakened left ventricular systolic function accompanied by a decreased glomerular filtration rate and increased reabsorption of water and sodium by renal tubules, the blood volume is frequently increased, subsequently resulting in sodium retention and dilute anemia, as well as decreased hemoglobin and HCT (Waldum *et al*., 2012). Thus, HCT is an indicator reflecting the severity of anemia and sodium retention, which are linked to kidney dysfunction and affect the prognosis of patients with HF (Alexandrakis and Tsirakis, 2012). While the exact mechanisms underlying the association between HCT and the prognosis of

patients with AHF remain elusive, multiple factors are likely to be implicated. For instance, the association between HCT and kidney function may be involved (Ter Maaten *et al*., 2016). An another finding indicate that a short-term change in HCT concentration is an independent risk factor for mortality in patients hospitalized with AHF. The top tertile of HCT change (ΔHCT > 1.5%) during hospitalization is associated with a lower risk of mortality (Zhou *et al*., 2017).

3.5.1.5. Mean Corpuscular Volume (MCV)

From the statistical analysis in Table 21 the results showed that there was insignificant decrease ($P > 0.05$) in the mean of MCV in patients of heart failure comparison to the control, as the rate of MCV for heart patients and the control (86.703 and 85.5) fl, respectively. Recently there was insignificant increase ($P > 0.05$) in patients of heart failure with bacterial infection comparison to those of heart failure without bacterial infection as the mean of MCV (87.843 and 86.371) fl, respectively.

Table 21: MCV (fl)of the study sample

Patients of Heart Failure		Control	*P* value
Infection	Mean ± SD fL	Mean ± SD fL	
Without bacterial infection	86.371 ± 6.842	85.5 ± 7.324	0.5749
With bacterial infection	87.843 ± 4.745		0.2506
Total	86.703 ± 6.428	85.5 ± 7.324	0.3976
P value	0.4241		

* means significance differences (P <0.05) ** means high significances differences (P <0.001)

This is disagreements with previous study that documented the proposes for the first time that MCV is an independent predictor of mortality in patients with AHF. A large-scale, multi-center study, however, is required to confirm the present results and to elucidate the mechanisms underlying the observed correlations between macrocytosis and poor prognosis in AHF. One possible explanation is that macrocytosis is merely a biomarker for malnutrition, which is often associated with end-stage HF (Ueda *et al*., 2013)

3.5.1.6. Mean Corpuscular Hemoglobin (MCH)

The results of statistical analysis in Table 22 showed that there were insignificants decrease ($P > 0.05$) in the mean of MCH in patients of heart failure comparison to the control, as the rate of MCH for heart patients and the control (27.498 and 27.757) pg, respectively. Recently there was insignificances increase ($P > 0.05$) in patients of heart failure with bacterial infection comparison to those of heart failure without bacterial infection as the mean of MCH (27.606 and 27.467) pg, respectively.

Table 22: MCH (pg) of the study sample

Patients of Heart Failure		Control	*P* value
Infection	Mean ± SD pg	Mean ± SD pg	
Without bacterial infection	27.467 ± 2.851	27.757 ± 2.967	0.6503
With bacterial infection	27.606 ± 2.344		0.8594
Total	27.498 ± 2.730	27.757 ± 2.967	0.6623
P value	0.8592		

* means significance differences (P <0.05) ** means high significances differences (P <0.001)

This is similar with study that showed the demand to be emphasized that even in non-anemic [according to the World Health Organization (WHO) definition] patients with MCV, MCH, and MCHC above the lower limit of normal. An observed considerable prevalence of ID irrespective of the presence of anemia or abnormal red cell indices (RCI) suggests that although disordered iron homeostasis represents one of the causes of anemia in HF (Van Veldhuisen *et al*., 2011), many patients with cardiac failure and concomitant ID will not develop haematological abnormalities. Importantly, in one study confirms that in patients with HF, ID should not only be perceived as a cause of anemia, but an equivalent comorbidity that can occur without haematological abnormalities, and is generally more frequent than anemia (Wong *et al*., 2016).

3.5.1.7. Mean Corpuscular Hemoglobin Concentration MCHC

The results of statistical analysis in Table 23 showed that there was insignificant increase ($P > 0.05$) in the results of MCHC in patients of heart failure without bacterial infection comparison to the control, as the rate of MCHC for heart patients and the control (32.037 and 32. 412) g/dl, respectively. While significant decrease ($P < 0.05$) in the mean of MCHC in patients of heart failure with bacterial infection in comparison to the control, as the mean of MCHC for heart patients and the control (31.393 and 32.412) g/dl respectively. Recently there was insignificant decrease ($P > 0.05$) in patients of heart failure with bacterial infection in comparison to those of heart failure without bacterial infection as the mean of MCHC (31.393 and 32.037) g/dl, respectively.

Table 23: MCHC (g/dl) of the study sample

Patients of Heart Failure		Control	*P* value
Infection	Mean ± SD g/dl	Mean ± SD g/dl	
Without bacterial infection	32.037 ± 1.546	32.412 ± 1.274	0.2437
With bacterial infection	31.393 ± 1.764		0.0254 *
Total	31.892 ± 1.608	32.412 ± 1.274	0.1055
P value	0.1599		

* means significance differences (P <0.05) ** means high significances differences (P <0.001)

This is disagreements with the study that reported of one study is the association between the presence as well as persistence of relative hypochromia (as defined by low MCHC levels, a readily available parameter in complete blood count analysis) and increased risk of 5-year all-cause mortality. This was especially notable in non-anemic patients with HF, a sub-group for whom no clinical consensus yet exists regarding approach, monitoring and treatment. Furthermore, they observed significant impairment in functional activity in patients with relative hypochromia and heightened inflammatory (Tkaczyszyn *et al*., 2018). Disagreements too with study that showd conclusion, relative hypochromia is a strong and independent predictor

of increased mortality in AHF. Given the direct link to diagnostic (endoscopy) and therapeutic interventions to treat functional iron deficiency, relative hypochromia deserves increased attention as an inexpensive and universally available biomarker (Kleber *et al*., 2019).

3.5.1.8. Platelet (PLT)

From the observation of the results of statistical analysis in Table 24 showed that there was insignificant decrease ($P > 0.05$) in the mean of PLT in patients of heart failure comparison to the control, as the rate of PLT for heart patients and the control (282.632 and 244.787) µl, respectively. Recently there was insignificances increase ($P > 0.05$) in patients of heart failure with bacterial infection comparison to those of heart failure without bacterial infection as the mean of PLT (322.0 and 271.18) µl, respectively.

Table 24: PLT (µl) of the study sample

Patients of Heart Failure		Control	*P* value
Infection	Mean ± SD µl	Mean ± SD µl	
Without bacterial infection	271.18 ± 91.213	244.787 ± 54.83	0.1360
With bacterial infection	322.0 ± 288.959		0.1413
Total	282.632 ± 157.378	244.787 ± 54.83	0.1829
P value	0.2585		

* means significance differences (P <0.05) ** means high significances differences (P <0.001)

This is disagreement with previous study that showed low PLT is a risk factor for all-cause death and HF prehospitalization. It had been Demonstrated that thrombocytopenia (< 100.000/microliter) was associated with 1-year death in patients who were first diagnosed as having HF with reduced EF (<40%) (Mojadidi *et al*., 2016). Previous studies revealed that acute heart failure (AHF) was evoked not solely by cardiac problems but also by systemic physiological changes. The PLT may reflect those systemic changes and indicate the severity of AHF. Patients with AHF with preserved and reduced EF, and showed that thrombocytopenia was associated with worse prognosis in such patients. The conclusion results of previous study showed that lower

PLT was associated with poor prognosis in patients with AHF. PLT is widely measured in clinical settings and can be readily available for use as a risk marker in AHF (Yamaguchi *et al*., 2018).

3.5.1.9. Lymphocyte (LYM)

As shown from the statistical analysis of Table 25 the results were significantly decreased ($P < 0.001$) in the mean of LYM % patients of heart failure comparison with control, as the mean of LYM % for heart patients and the control (20.139 and 36.021) %, respectively. From the same table the results of statistical analysis showed insignificances increase ($P > 0.05$) in patients of heart failure with bacterial infection comparison to those of heart failure without bacterial infection as the mean of LYM % (23.193and 19.480) %, respectively.

Table 25: LYM % of the study sample

Patients of Heart Failure		Control	*P* value
Infection	Mean ± SD %	Mean ± SD %	
Without bacterial infection	19.480 ± 12.991	36.021 ± 7.522	0.0001 **
With bacterial infection	23.193 ± 11.274		0.0001 **
Total	20.329 ± 12.638	36.021 ± 7.522	0.0001 **
P value	0.3046		

* means significance differences (P <0.05) ** means high significances differences (P <0.001)

This is accordance with the results of previous study confirmed the prognostic role of lymphopenia in patients with AHF demonstrating how a simple and routine test may predict the patients' outcome and underscoring the importance of the immune system in the pathophysiology of AHF. Recent evidence suggesting that lymphocytes count differs according to pharmacological therapy support this hypothesis (Carubelli *et al*., 2017). It also agreements with another study that confirms previous observations that low lymphocyte count, part of routine blood testing may be useful to identify outpatients with heart failure at higher risk of death providing an additional

tool for identifying patients in need of close supervision (Marçula *et al*., 2015).

3.5.1.10. Neutrophil (NEUT)

From the statistical analysis of Table 26 the results of showed that there was a high significant increase ($P < 0.001$) in the percentage of NEUT in patients of heart failure comparison to the control, as the percentage of NEUT for heart patients and the control (70.129 and 55,290) %, respectively. The results of the same statistical table also showed an insignificant decrease ($P > 0.05$) in the percentage of NEUT in patients of heart failure with bacterial infection comparison to the heart failure without bacterial infection, as the rate of NEUT (68.012 and 70.745) %, respectively.

Table 26: NEUT % of the study sample

Patients of Heart Failure		Control	*P* value
Infection	Mean ± SD %	Mean ± SD **%**	
Without bacterial infection	70.745 ± 13.862	55.290 ± 8.387	0.0001 **
With bacterial infection	68.012 ± 13.850		0.0002 **
Total	70.129 ± 13.808	55.290 ± 8.387	0.0001 **
P value	0.4899		

* means significance differences ($P < 0.05$) ** means high significances differences ($P < 0.001$)

This is similar with previous study that showed neutrophils play a significant role following myocardial infarction (MI), the most common cause of HF. Neutrophils infiltrate the infarcted myocardium and mediate tissue damage (Soehnlein *et al*., 2017). A few studies have shown that neutrophils may play a significant role in experimental models of myocarditis (Woudstra *et al*., 2017, Bracamonte-Baran *et al*., 2017). In most myocarditis, an innate response mediated by monocytes/macrophages and neutrophils plays a significant role in priming the auto-immune process but also in triggering tissue damage and repair (Bracamonte-Baran *et al*., 2017). Agreements with another study that documented elevated neutrophil count is associated with higher risk of major adverse cardiac events including myocardial infarction

and early development of heart failure. Neutrophils contribute to cardiac damage through a number of mechanisms, including attraction of other immune cells and release of inflammatory mediators (Gopalkrishna *et al*., 2020).

3.5.1.11. Red cell Distribution Width-Coefficient of Variation (RDW-CV)

The results of the statistical analysis of Table 27 showed that there was a significant increase ($P < 0.001$) in the percentage of RDW-CV in patients of heart failure in comparison to the control, as the percentage of RDW-CV for heart patients and the control (15.369 and 13.196) %, respectively. The results of the same statistical table also showed an insignificant decrease ($P > 0.05$) in the percentage of RDW-CV in patients of heart failure with bacterial infection in comparison to the heart failure without bacterial infection, as the percentage of RDW-CV (14.887 and 15.509) %, respectively.

Table 27: RDW-CV % of the study sample

Patients of Heart Failure		Control	*P* value
Infection	Mean ± SD %	Mean ± SD %	
Without bacterial infection	15.509 ± 3.238	13.196 ± 1.954	0.0004 **
With bacterial infection	14.887 ± 2.345		0.0107 *
Total	15.369 ± 3.055	13.196 ± 1.954	0.0003 **
P value	0.4775		

* means significance differences (P <0.05) ** means high significances differences (P <0.001)

RDW-CV was higher in the HFrEF group without etiology of MI and correlated with LVEF (Gujytė *et al*., 2021).

3.5.1.12. Red cell Distribution Width-Standard Deviation (RDW-SD)

The results of the statistical analysis of Table 28 showed that there was a significant increase ($p < 0.001$) in the mean of RDW-SD in patients of heart failure comparison to the control, as the rate of RDW-SD for heart patients and the control (49.253 and 45.215) fl, respectively. The results of the same statistical table also showed an insignificant decrease ($P > 0.05$) in the mean of RDW-SD in patients of heart failure with bacterial infection comparison to

the heart failure without bacterial infection, as the rate of RDW-SD (49.175 and 49.276 5) fl, respectively.

Table 28: RDW-SD (fl) of the study sample

Patients of Heart Failure		Control	*P* value
Infection	Mean ± SD fl	Mean ± SD fl	
Without bacterial infection	49.276 ± 6.967	45.215 ± 6.116	0.0069 **
With bacterial infection	49.175 ± 4.841		0.0282 *
Total	49.253 ± 6.517	45.215 ± 6.116	0.0034 **
P value	0.9570		

* means significance differences (P <0.05) ** means high significances differences (P <0.001)

This is similar to the study that showed decreased red blood cell deformability among patients with higher RDW values impairs blood flow through the microcirculation, resulting in the diminution of oxygen supply at the tissue level, particularly among patients suffering from myocardial infarction treated with urgent revascularization (Bujak *et al*., 2015). Agreements with another study that documented the red blood cell distribution width (RDW) is a simple, rapid, inexpensive and straightforward hematological parameter, reflecting the degree of anisocytosis in vivo. The currently available scientific evidence suggests that RDW assessment not only predicts the risk of adverse outcomes (cardiovascular and all-cause mortality, hospitalization for acute decompensation or worsened left ventricular function) in patients with acute and chronic heart failure (HF), but is also a significant and independent predictor of developing HF in patients free of this condition. Regarding the biological interplay between impaired hematopoiesis and cardiac dysfunction, many of the different conditions associated with increased heterogeneity of erythrocyte volume (*i.e*., ageing, inflammation, oxidative stress, nutritional deficiencies and impaired renal function), may be concomitantly present in patients with HF, whilst anisocytosis may also directly contribute to the development and worsening of HF. In conclusion, the longitudinal assessment of RDW changes over time

may be considered an efficient measure to help predicting the risk of both development and progression of HF (Lippi *et al*., 2018).

3.5.1.13. Platelet Distribution Width (PDW)

As shown in the Table 29 the results of the statistical analysis for RDW showed that there was insignificanct decrease ($P > 0.05$) in the group patients of heart failure control, as the mean of RDW for heart patients and the control (14.270 and13.666) fl, respectively. The result of statistical analysis in the same table also showed insignificances increase ($P > 0.05$) in patients of heart failure with bacterial infection comparison to those of heart failure without bacterial infection (13.843 and14.394) fl, respectively.

Table 29: PDW (fl) of the study sample

Patients of Heart Failure		Control	*P* value
Infection	Mean ± SD fl	Mean ± SD fl	
Without bacterial infection	14.394 ± 3.707	13.666 ± 2.283	0.3120
With bacterial infection	13.843 ± 2.970		0.8188
Total	14.270 ± 3.542	13.666 ± 2.283	0.3725
P value	0.5876		

* means significance differences ($P < 0.05$) ** means high significances differences ($P < 0.001$)

This disagree with this study that reported high PDW is an independent predictor of adverse prognosis in patients with HF (Sato *et al*., 2020b). Increased levels of PDW are presumed to be associated with atherosclerosis, CAD, cerebrovascular disease, and systemic inflammatory disease (Li *et al*., 2020a). These diseases play key roles in the pathophysiology of HF (Ponikowski *et al*., 2016). Another study that found the associations between red blood cell distribution width and prognosis in patients with HF have been reported, as the prognostic impact of PDW has been unclear in HF patients (Watanabe *et al*., 2020).

3.5.1.14. Mean platelet volume (MPV)

The observations of the results of statistical analysis in Table 30 showed that there was insignificant increase ($P > 0.05$) in the group patients of heart

failure control, as the mean of MPV for heart patients comparison the control (10.280 and10.181) fl, respectively. In the same table the result of statistical analysis also showed insignificances increase in patients of heart failure with bacterial infection comparison to those of heart failure without bacterial infection (10.318 and10.200) fl, respectively.

Table 30: MPV (fl) of the study sample

Patients of Heart Failure		Control	*P* value
Infection	Mean ± SD fl	Mean ± SD fl	
Without bacterial infection	10.200 ± 1.972	10.181 ± 1.182	0.9601
With bacterial infection	10.318 ± 1.120		0.7006
Total	10.280 ± 1.662	10.181 ± 1.182	0.7590
P value	0.8202		

* means significance differences (*P* <0.05) ** means high significances differences (*P* <0.001)

This is disagreements with the analysis of the other study they conclude that platelet count was significantly lower in study group as compared to control group (normal healthy controls or non-cardiac chest pain patients). MPV and PDW were significantly higher in study group compared to control group. This change suggests the role of Platelets in heart disease by Platelet activation and Coronary thrombosis leading to myocardial infarction (Gandhi and Gamit, 2019). They are consistent with previous findings that the mean platelet volume is increased at time of admission with an acute myocardial infarction (Gandhi and Gamit, 2019). In another study, they investigated the relationship between the mean platelet volume (MPV) with mortality and heart failure (HF)-related hospitalization in stable chronic HF outpatients with reduced ejection fraction (HFrEF) (Kaya *et al*., 2017). Platelet volume indices correlate to severity of heart failure and have prognostic value for both cardiac and thrombotic events in patients with congenital heart disease (Sato *et al*., 2020a).

3.5.1.15. Platelet Large Cell Ratio (P-LCR)

As shown in the Table 31there were no significant differences in all the results. There was insignificant decrease ($P > 0.05$) in the percentage of P-LCR in patients of heart failure comparison to the control, as the percentage of P-LCR for heart failure patients and the control (28.369 and 28. 403) %, respectively. In the same Table the result showed that there was insignificant increase ($P > 0.05$) in patients of heart failure with bacterial infection comparison to those of heart failure without bacterial infection as the percentage of P-LCR (28.981 and 28.190) %, respectively.

Table 31: P-LCR % of the study sample

Patients of Heart Failure		Control	*P* value
Infection	Mean ± SD %	Mean ± SD %	
Without bacterial infection	28.190 ± 9.705	28.403 ± 8.254	0.9164
With bacterial infection	28.981 ± 7.775		0.8159
Total	28.369 ± 9.259	28.403 ± 8.254	0.9857
P value	0.7660		

* means significance differences (P <0.05) ** means high significances differences (P <0.001)

Platelets play key roles both in the pathogenesis of atherosclerosis and in the development of acute thrombotic events. Platelet size correlates with platelet activity and can be assessed by platelet volume indices, which are mean platelet volume (MPV), platelet distribution width (PDW), and Platelet-large cell ratio (P-LCR) (Alkhateeb *et al*., 2018). Disagreements with study that documented platelet volume indices, including MPV, PDW, and P-LCR, increased significantly in patients with severe CAD compared with those with significant and nonsignificant CAD. These indices were higher in patients with significant coronary stenosis than insignificant CAD, although this increase was not statistically significant. These results were in agreement with previous study that showed a prognostic and diagnostic value for that the elevated platelet volume indices in patients with CAD (Alkhateeb *et al*., 2018).

3.5.1.16. Plateletcrit (PCT)

From the statistical analysis in Table 32 the results showed that there was insignificant increase ($P > 0.05$) in the percentage of PCT in patients of heart failure comparison to the control, as the percentage of PCT for heart patients and the control (0.276 and 0.247) %, respectively. Recently there was insignificances increase ($P > 0.05$) in the percentage of PCT patients of heart failure with bacterial infection comparison to those of heart failure without bacterial infection as the percentage of PCT (0.32 and 0.264) %, respectively.

Table 32: PCT % of the study sample

Patients of Heart Failure		Control	*P* value
Infection	Mean ± SD %	Mean ± SD %	
Without bacterial infection	0.264 ± 0.095	0.247 ± 0.049	0.3432
With bacterial infection	0.32 ± 0.271		0.1369
Total	0.276 ± 0.152	0.247 ± 0.049	0.2880
P value	0.1982		

* means significance differences (P <0.05) ** means high significances differences (P <0.001)

This is disagreements with study that reported increased MPV, PLC, P-LCR and PCT were observed in CAD group compared to control group (Khode *et al*., 2012). Statistically significant lower PCT was also observed in AMI/UA patients compared to healthy control groups (Majumder *et al*., 2018). Disagreements with study that showed larger platelets are hemostatically active and act as risk factors for developing coronary thrombosis leading to myocardial infarction. Platelet count and platelet volume indices can provide a signature for the prethrombotic state in ischemic heart disease. Measurement of platelet count and platelet volume indices may be of some benefit in detecting those patients at higher risk of acute coronary syndrome (Majumder *et al*., 2018).

3.5.2. Glucose

The results of the statistical analysis of Table 33showed that there were hight significant increase ($P < 0.001$) in the concentration of Glucose in

patients of heart failure comparison to the control, as the concentration of Glucose for heart patients and the control (202.336 and 137.924) mg/dl, respectively. The results of the same statistical table also showed an insignificant decrease ($P > 0.05$) in the concentration of Glucose in patients of heart failure with bacterial infection comparison to the heart failure without bacterial infection, as the of concentration of Glucose (188.808 and 206.344) mg/dl, respectively.

Table 33: The concentration of Glucose (mg/dl) of the study sample

Patients of Heart Failure		Control	*P* value
Infection	Mean ± SD mg/dl	Mean ± SD mg/dl	
Without bacterial infection	206.344 ± 96.648	137.924 ± 42.49	0.0002 **
With bacterial infection	188.808 ± 66.495		0.0021 *
Total	202.336 ± 90.505	137.924 ± 42.49	0.0002 **
P value	0.4995		

* means significance differences (P <0.05) ** means high significances differences (P <0.001)

This is agreements with study that reported clinical implications of findings are numerous. Firstly, the measurement of RBS in the Emergency Department is simple and provides very useful information in predicting the hospital course and prognosis of AHF. Therefore, it can potentially be used as a tool amongst other tools for risk stratification in AHF patients. Secondly, HG in the context of AHF was found to be predictive of the development of new-onset DM (Sud *et al*., 2015). This should encourage treating physicians to screen patients with abnormal glucose levels for DM following the acute phase of HF. Finally, as HG is an independent predictor of short-term adverse outcomes in the context of AHF, this should raise interest in studies examining the efficacy of aggressive glycemic control on the outcomes of AHF patients. Despite the general recommendation by the American Diabetes Association to aim for strict glycemic control in any hospital admission regardless of the primary diagnosis (Care, 2015), the evidence for this practice in AHF is weak (Aljohar *et al*., 2018). Also agreemwnts with onther study that showed

diabetic patients have an increased risk of developing heart failure because of the effect of the metabolic derangements of diabetes on the cardiovascular system. Furthermore, the metabolic risk of diabetes in heart failure is heightened by the effect of most anti-diabetic medications, as the use of certain anti-diabetic agents increase the risk of mortality and hospitalisation for heart failure both in patients with and without heart failure (Fadini *et al*., 2015).

3.5.3. Systolic Blood Pressure (SBP)

As shown in the Table 34 there were no significant differences in all the results. There was insignificant decrease ($P > 0.05$) in the of Systolic blood pressure (in patients of heart failure comparison to the control, as the rate of Systolic blood pressure for heart failure patients and the control (138.816 and 129.03) mmHg, respectively. In the same table the result showed that was insignificant increase ($P > 0.05$) in the Systolic blood pressure in patients of heart failure with bacterial infection comparison to those of heart failure without bacterial infection as of Systolic blood pressure (138.25 and 138.98) mmHg, respectively.

Table 34: Systolic blood pressure (mmHg) of the study sample

Patients of Heart Failure		Control	*P* value
Infection	Mean ± SD	Mean ± SD mmHg	
Without bacterial infection	138.98 ± 33.502 mmHg	129.03 ± 11.35	0.1032
With bacterial infection	138.25 ± 32.900		0.1525
Total	138.816 ± 33.134	129.03 ± 11.35	0.1023
P value	0.9388		

* means significance differences (P <0.05) ** means high significances differences (P <0.001)

This is similar with findings from one study that documented that among hospitalized patients with HFrEF whose SBP was stable during hospitalization, a discharge SBP of <130 mm Hg was associated with a significantly higher risk for 30-day all-cause mortality that remained significant during longer follow-up. The associations with all-cause and HF

readmissions, on the other hand, were weak and nonsignificant at 30 days, but became significant at 12-month follow-up and during the overall follow-up of 6 years. We also observed that when patients with SBP <110 mm Hg were excluded, SBP 110 to 129 mm Hg was associated with a significantly higher risk of 30-day and 12-month all-cause mortality. These findings suggest that in patients with HFrEF, SBP <130 mm Hg, even SBP values between 110 and 129 mm Hg, are associated with poor outcomes (Arundel *et al*., 2019). The association of a low SBP with mortality was also more pronounced in the subgroup without hypertension among older patients with HF with preserved EF (Tsimploulis *et al*., 2018).

3.5.4. Diastolic Blood Pressure (DBP)

The results of statistical analysis in Table 35 showed that there was insignificant decrease ($P > 0.05$) in the Diastolic blood pressure in patients of heart failure comparison to the control, as the Diastolic blood pressure for heart patients and the control (86.281 and 84.19) mmHg respectively. Recently there was insignificances dncrease ($P > 0.05$) in Diastolic blood pressure of patients of heart failure with bacterial infection comparison to those of heart failure without bacterial infection as the mean of Diastolic blood pressure (85.25 and 86.581) mmHg respectively.

Table 35: Diastolic blood pressure (mmHg) of the study sample

Patients of Heart Failure		Control	*P* value
Infection	Mean ± SD mmHg	Mean ± SD	
Without bacterial infection	86.581 ± 17.613	84.19 ± 10.88	0.4842
With bacterial infection	85.25 ± 19.250		0.8062
Total	86.281 ± 17.862	84.19 ± 10.88	0.5365
P value	0.7952		

* means significance differences (P <0.05) ** means high significances differences (P <0.001)

This is agreements with previous study indicate that higher DBP levels are preferred in patients with HFpEF. The other study suggested that the risk of all-cause death and major cardiovascular events was nonsignificantly

higher in patients with a DBP of ≥ 90 mm Hg compared to those with a DBP of 80–89 mm Hg (Tsujimoto and Kajio, 2018). In one study extend these findings by demonstrating that, at any given SBP, 1) low DBP is cross-sectionally associated with prevalent myocardial damage, 2) low DBP is prospectively associated with near-term progression of myocardial damage, 3) low DBP is prospectively associated with incident CHD events (and mortality), but, as expected, not with incident stroke, and 4) the association between low DBP and incident CHD appears to be strongest among those with evidence of preceding myocardial damage at baseline. Considered in isolation, each of these 4 findings are of clinical importance; however, taken together, they form a compelling argument that excessively low DBP may directly harm the myocardium (McEvoy *et al*., 2016).

3.5.5. Blood Groups of Study Sample

Table 36: The Blood Groups of Study Sample

Blood Groups	Control N (%)	Patients N (%)	Total	*P* value
A	30 (42.25 %)	17 (23.94 %)	47 (33.10%)	0.05793
B	15 (21.13 %)	20 (28.17 %)	35 (24.65%)	0.3980
AB	9 (12.68 %)	6 (8.45 %)	15 (10.56%)	0.4385
O	17 (23.94 %)	28 (39.44 %)	45 (31.69%)	0.1010
Total	71 (100 %)	71 (100 %)	142 (100%)	1.0000
P value	0.00417 *	0.00289 **	0.00042 **	

* means significance differences (P <0.05) ** means high significances differences (P <0.001)

In one study observed that individuals with blood group A and B were at higher risk of developing thromboembolic diseases, but lower risk of hypertension, when compared with O-group individuals. Individuals with blood group A were at higher risk of developing hyperlipidemia, atherosclerosis, and heart failure compared with blood group O, whereas individuals with blood group B were at higher risk of myocardial infarction compared with individuals with blood group O (Groot *et al*., 2020).

3.5.6. The Blood Groups of Patients.

From the observation of the statistical analysis in Table 37 found that most common blood group in heart failure patients with bacterial infection was O and in significances differences from other blood group type.

Table 37: The Blood Groups of Patients

Blood Groups	Heart Failure Patients Without Bacterial Infection N (%)	Heart Failure Patients With Bacterial Infection N (%)	Total	*P* value
A	16 (29.09 %)	1 (6.25 %)	17 (16.34%)	0.00027 **
B	16 (29.09 %)	4 (25.00 %)	20 (19.23%)	0.0072 **
AB	6 (10.91 %)	0 (0.00 %)	6 (5.77 %)	0.0587
O	17 (30.90 %)	11 (68.75 %)	28 (26.92%)	0.2568
Total	55 (100 %)	16 (100 %)	71 (100%)	0.00019 **
P value	0.1179	0.0013 **	0.0057 **	

* means significance differences (*P* <0.05) ** means high significances differences (*P* <0.001

This is similar with study that showed patients with blood type O have been reported to have 25–30% lower blood plasma levels of the von Willebrand factor (vWF) than those with non-O blood types (Dentali *et al*., 2013). Taken together, these factors suggest that a person's blood type may affect the disease pathophysiology, particularly concerning sepsis and its association to coagulation and immunology. Therefore, they hypothesized that blood type O sepsis patients have a higher risk of death, and that this effect is stronger in the severe septic shock groups because they are characterized by a more severe coagulation dysfunction (Hasegawa *et al*., 2020).

3.6. Microbiological Tests

3.6.1. Bacterial Isolations

From observation the results of Table 38 that the most common genius in heart failure patients is *Staphylococcus* and in significant differences from other genius, while the most species heart failure patients is *Staphylococcus hominis ssp hominis* in significance differences from other species.

Table 38: The bacterial species that isolated from heart failure patients

Genus	Species	Total
Acinetobacter	*baumanii*	1
Gardnerlla	*vaginalis*	1
Kocuria	*kristinae*	1
Pseudomonas	*stutzeri*	3
Staphylococcus	*hominis* ssp hominis	5
	sciuri	2
	lentus	1
	haemolayticus	2
Total		16
P value		0.00079 **

* means significance differences (P <0.05) ** means high significances differences (P <0.001)

Another study on patients with infective endocarditis that microbiological findings were: *Streptococcus* sp., n (%) 12 (34.3%) *Streptococcus pyogenes*, n (%) 1 (2.9%) *S. agalactiae*, n (%) 1 (2.9%) Non-haemolytic *Streptococci*, n (%) 10 (28.6%) *Staphylococcus* sp., n (%) 9 (25.7%) *Staphylococcus aureus*, n (%) 2 (5.9%), negative coagulase *staphylococci*, n (%) 7 (20.0%) *Enterococcus* sp., n (%) 5 (14.3%) *Enterococcus faecalis*, n (%) 3 (8.6%) *E. faecium*, n (%) 1 (2.9%) (Kreitmann *et al*., 2020). Non-haemolytic *Streptococci* belonged to the following species: S*treptococcus* oralis, *S. mutans*, *S. gallolyticus*, *S. agalactiae, S. homans*, *S. bovis, S. parasanguinis.* Negative coagulase *Staphylococci* belonged to the following species: *Staphylococcus epidermidis*, *S. hominis* and *S. warneri* (Kreitmann *et al*., 2020).

3.6.2. Antibiotics susceptibility Tests

3.6.2.1. Antibiotics Susceptibility for Gram Positive Bacteria

From observation the resultes of Table 39 of Antibiotics susceptibility profile for Gram positive bacteria in heart failure patients were found that Cephalexin Cefpirome were resistance to the all species had been isolated.

Table 39: Antibiotics susceptibility profile of Gram positive bacteria by vitek (R-resistance, I-intermediate, S-sensitive).

Antibiotics	*Staphylococcus hominis* ssp hominis (1)	*Staphylococcus hominis* ssp hominis (2)	*Staphylococcus hominis* ssp hominis (3)	*Staphylococcus hominis* ssp hominis (4)	*Staphylococcus hominis* ssp hominis (5)	*Staphylococcus haemolayticus* (1)	*Staphylococcus haemolayticus* (2)	*Staphylococcus sciuri* (1)	*Staphylococcus sciuri* (2)	*Staphylocoous lentus*	R %	I %	*S* %
Benzylpenicillin	R	R	R	R	R	R	R	R	R	S	90	0	10
Clindamycin	S	S	S	S	R	R	R	I	R	I	40	20	40
Erythromycin	R	R	R	R	R	R	R	S	R	S	80	0	20
Fusaid acid	R	R	S	R	R	R	R	S	R	S	70	0	30
Gentamicin	S	I	S	S	S	S	R	S	S	S	10	10	8-
Levofloxacin	S	I	S	R	S	S	R	S	S	S	20	10	70
Linezolid	S	S	S	S	S	S	R	S	S	S	10	0	90
Moxifloxacin	S	I	S	I	S	S	R	S	S	S	10	20	70
Nitrofuranation	S	S	S	S	S	R	S	S	S	S	10	0	90
Oxacillin	R	R	R	R	R	R	R	R	R	S	90	0	10
Rifampicin	S	S	S	S	S	S	S	S	S	S	0	0	100
Ticoplanin	S	S	I	S	S	S	S	S	S	S	0	10	90
Tetracycline	S	R	S	R	S	S	S	S	R	S	30	0	70
Tigecycline	S	S	S	S	S	S	S	S	S	S	0	0	100
Tobramycin	S	S	S	S	S	S	R	S	S	S	10	0	90
Trimethoprim/sulfamethoxazole	R	R	R	S	S	R	S	S	S	S	40	0	60
Vancomycin	S	S	S	S	S	S	S	R	S	S	10	0	90
Amoxicillin+	R	R	R	R	R	R	R	R	R	S	90	0	10
Amoxicillin/clavulanic Acid+	R	R	R	R	R	R	R	R	R	S	90	0	10
Ampicillin+	R	R	R	R	R	R	R	R	R	S	90	0	10
Ampicillin/sulbactam+	R	R	R	R	R	R	R	R	R	S	90	0	10
+Carbencillin	R	R	R	R	R	R	R	R	R	S	90	0	10
+Azithromycin	R	R	R	R	R	R	R	S	S	S	70	0	30
Cefazolin	R	R	R	R	R	R	R	R	R	S	90	0	10
Cephalexin	R	R	R	R	R	R	R	R	R	R	100	0	0
Cefepime	R	R	R	R	R	R	R	R	R	S	90	0	10
Cefixime	R	R	R	R	R	R	R	R	R	S	90	0	10
Cefatotaxime	R	R	R	R	R	R	R	R	R	S	90	0	10
Cefoxitin	R	R	R	R	R	R	R	R	R	S	90	0	10
Cefotetan	R	R	R	R	R	R	R	R	R	S	90	0	10
Cefpirome	R	R	R	R	R	R	R	R	R	R	100	0	0
Ceftazidime	R	R	R	R	R	R	R	R	R	S	90	0	10
Ceftriaxone	R	R	R	R	R	R	R	R	R	S	90	0	10
Ciprofloxacin	S	I	S	R	S	S	R	S	S	S	20	10	70
Clarithromycin	R	R	R	R	R	R	R	S	S	S	70	0	30
Cloxacillin	R	R	R	R	R	R	R	R	R	S	90	0	10
Diclxacillin	R	R	R	R	R	R	R	R	R	S	90	0	10
Doripenem	R	R	R	R	R	R	R	R	R	S	90	0	10
Ertapenem	R	R	R	R	R	R	R	R	R	S	90	0	10
Doxycycline	S	S	S	S	S	S	S	S	S	S	0	0	100
Flucloxacillin	R	R	R	R	R	R	R	R	R	S	90	0	10
Lmipenem	R	R	R	R	R	R	R	R	R	S	90	0	10
Meropenem	R	R	R	R	R	R	R	R	R	S	90	0	10
Methicillin	R	R	R	R	R	R	R	R	R	S	90	0	10
Minocycline	S	R	S	S	S	S	S	S	S	S	10	0	90
Ofloxacin	S	I	S	R	S	S	R	S	S	S	20	10	70
Oxacillin mic	R	R	R	R	R	R	R	R	R	S	90	0	10
Piperacillin	R	R	R	R	R	R	R	R	R	S	90	0	10
Piperacillin/tazobactam	R	R	R	R	R	R	R	R	R	S	90	0	10
Ticarcillin	R	R	R	R	R	R	R	R	R	S	90	0	10
Cefalotin	R	R	R	R	R	R	R	R	R	S	90	0	10
Ticarcillin/ Clavlanic Acid	R	R	R	R	R	R	R	R	R	10	90	0	10
Cefalexin	R	R	R	R	R	R	R	R	R	S	90	0	10

Other study reported that S. hominis faound to be resistance to (96.9 %) penicillin, (92.2%) oxacillin, (98.4%) erythromycin, (84.4 %) cefoxitin, (85.9 %) clindamycin, (79.7 %) levofloxacin, (79.7%) moxifloxacin, (62.5%) trimethoprim/sulfamethoxazole, (9.4%) gentamicin, (9.4%) rifampicin. While there were no resistance to vancomycin and linezolid (0%) (Cui *et al*., 2019). *S. haemolyticus* faound to be resistance to (100 %) penicillin, (100%) oxacillin, (91.7%) erythromycin, (91.7%) cefoxitin, (50 %) clindamycin, (100 %) levofloxacin, (100%) moxifloxacin, (66.7%) trimethoprim/sulfamethoxazole, (75%) gentamicin, (16.7%) rifampicin. While there were no resistance to vancomycin and linezolid (0%) (Cui *et al*., 2019). The results of other study showed that *S. sciuri* be resistance to (1 %) penicillin, (1%) oxacillin, (1 %) erythromycin, (1%) cefoxitin, (1 %) clindamycin, (1 %) levofloxacin, (1%) moxifloxacin, (0%) trimethoprim/sulfamethoxazole, (1%) gentamicin, (0%) rifampicin. While there were no resistance to vancomycin and linezolid (0%) (Cui *et al*., 2019). *S. haemolyticus* showed: 10 species that resistance to benzyl penicillin, 6 species to ampicillin, 3 species to oxacillin, 2 species to cefoxitin, 1 species to ciprofloxacin, 1 to species to norfloxacin, 2 species to gentamicin, 1 species to erythromycin, 4 species to tetracycline, 1 species to trimethoprim/sulfamethoxazole. While no resistance to doxycycline, and chloramphenicol (Boamah *et al*., 2017). *S. sciuri* 39 species resistance to benzyl penicillin13 species resistance to ampicillin, 32 species resistance to oxacillin, 16 species resistance to cefoxitin, 1 species resistance to ciprofloxacin, 6 species resistance to norfloxacin, 11 species resistance to gentamicin, 20 species resistance to erythromycin, 85 species resistance to tetracycline, 59 species resistance to doxycycline, 11 species resistance to chloramphenicol, 10 species resistance to trimethoprim/sulfamethoxazole

(Boamah *et al*., 2017). *S. lentus* appeare 14 species resistance to benzyl penicillin, 51 species resistance to oxacillin, 3 species resistance to cefoxitin, 3 species resistance to ciprofloxacin, 43 species resistance to norfloxacin, 5 species resistance to erythromycin; 42 species resistance to, tetracycline; 47 species resistance to doxycycline, 3 species resistance to chloramphenicol,3 species resistance to trimethoprim/sulfamethoxazole. Where there were no resistance to ampicillin, and no resistance to gentamicin too (Boamah *et al*., 2017).

3.6.2.2. Antibiotics Susceptibility for Gram Negative Bacteria

From the observed of the results of the antibiotics susceptibility of gram negative bacteria showed that *Pseudomonas stutzer* (1) was sensitive to all antibiotic of gram negative card Where the second isolate of *Pseudomonas stutzer* (2) was sensitive to all antibiotic except the minocycline was intermediate to it and the third isolate of *Pseudomonas stutzer* (3) was sensitive to all antibiotic present. *Acinetobacter baumanii resistant* to all the antibiotic except one Minocycline it was sensitive to it as showed in table 40.

Table 40: Antibiotics susceptibility profile of Gram negative bacteria by vitek (R-resistance, I-intermediate, S-sensitive)

Antibiotics	*Pseudomonas stutzer* (1)	*Pseudomonas stutzer* (2)	*Pseudomonas stutzer* (3)	*Acinetobacter baumanii*	R %	I %	S %
Gentamicin	S	S	S	R	25	0	75
Tobramycin	S	S	S	R	25	0	75
Trimethoprim/sulfamethoxazole	S	S	S	R	25	0	75
Cefepime	S	S	S	R	25	0	75
Ceftazidime	S	S	S	R	25	0	75
Ciprofloxacin	S	S	S	R	25	0	75
Imipenem	S	S	S	R	25	0	75
Meropenem	S	S	S	R	25	0	75
Minocycline	S	I	S	S	0	25	75
Piperacillin	S	S	S	R	25	0	75
Piperacillin/tazobactam	S	S	S	R	25	0	75
Ticarcillin	S	S	S	R	25	0	75
Ticarcillin/ Clavlanic Acid	S	S	S	R	25	0	75
Amikacin	S	S	S	R	25	0	75

Another studies show that *Pseudomonas stutzer* showed sensativity (S) to Amikacin, (S) Aztreonam (S) Cefepime, (S) Ceftazidime, (S) Ciprofloxacin, (S)Gentamicin, (S) Imipenem, (S)Piperacillin/tazobactam, (S) Trimethoprim/sulfamethoxazole (Halabi *et al*., 2019). *Acinetobacter* (A.) species are ubiquitous gram-negative coccobacilli and usually cause nosocomial infections, principally ventilator-associated pneumonia and catheter-associated bacteremia, as well as soft tissue and urinary tract infections. Community-acquired infections by *Acinetobacter baumannii* are increasingly reported (Wong *et al*., 2017). *Acinetobacter baumanii* showed resistance to Piperacillin, Piperacillin-tazobactam, Ticarcillin, Ticarcillin-clavulanate, Cefotaxime, Ceftriaxone, Ceftazidime, Imipenem, Ciprofloxacin, Levofloxacin, Gentamicin and Tobramycin. While it showed sensative to Amikacin, Doxycycline and Trimethoprim/sulfamethoxazole. It is only Intermediate to Tetracycline (Lahmidi *et al*., 2020). *Acinetobacter baumanii* showed resistance to Ampicillin, 11 out of 11 (100)%, Penicillin, 10 out of 10 (100) %, Piperacillin/tazobactam, 5 out of 6 (83.3) %, Sulbactam, 5 out of 7 (71.4) %, Carbapenems, 6 out of 9 (66.7) %, Quinolones, n 4 out of 8 (50) %, Aminoglycosides, 4 out of 11 (36.4) % and Colistin, 0 out of 7 (0) % (Ioannou *et al*., 2021).

3.7. Nanotechnology Study

3.7.1. Infrared spectrum (FTIR)

3.7.1.1. Infrared spectrum (FTIR) for zinc oxide (ZnO)

FT-IR spectrum of zinc oxide showed indistinct bands at 400-500 cm-1 which attributed to the metal bond Zn-O vibration as shown in Figure 1 (Voicu et al., 2013).

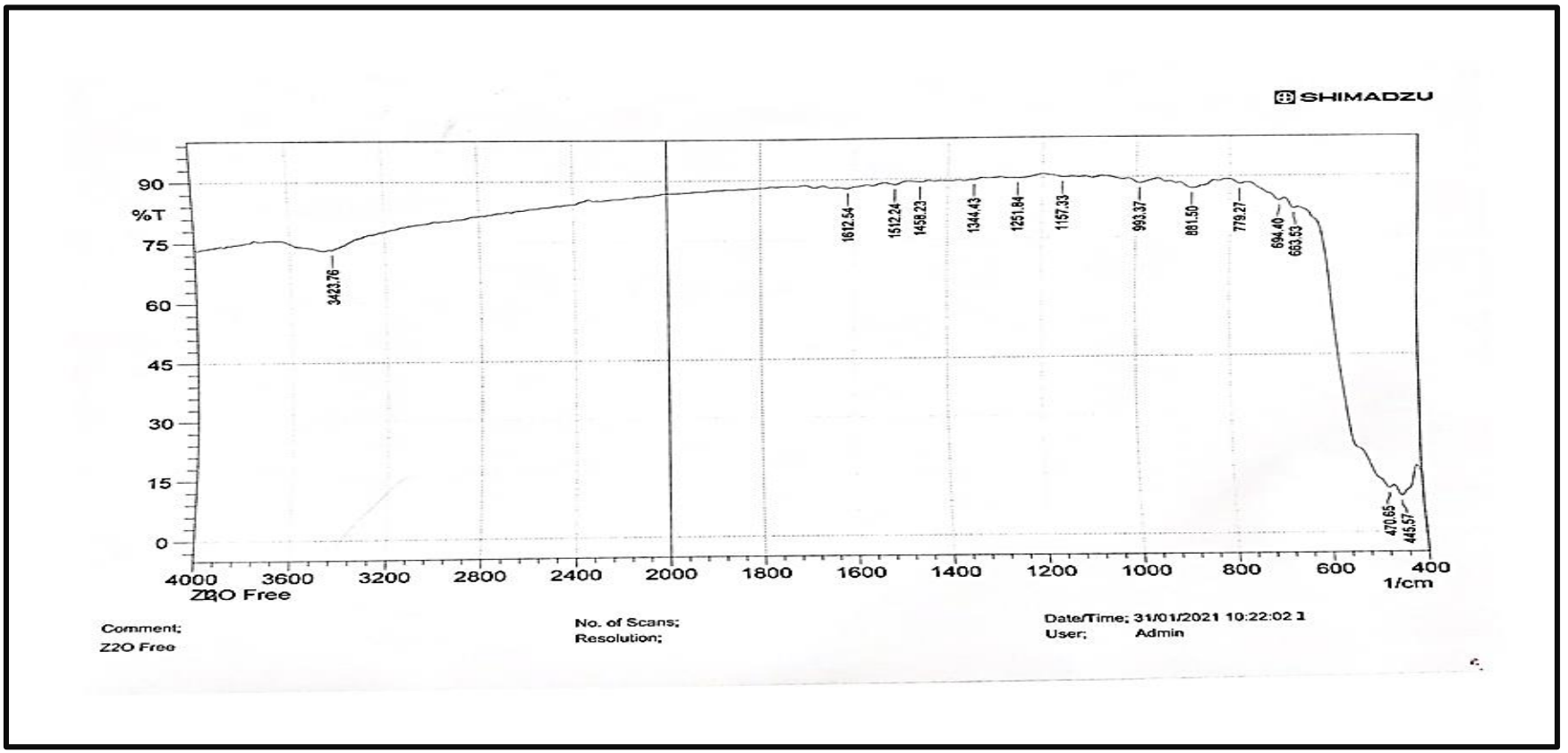


Figure 1: Infrared spectrum (FTIR) for zinc oxide (ZnO)

3.7.1.2. Infrared Spectrum (FTIR) for Free-Meropenem.

Infrared spectrum (q2FT-IR) of free meropenem antibiotic: The absorption band at 3568 for phenolic (O-H) stretching. The two bands around 3477 and 3404 attributed to (O-H) stretching for carboxylic acid group. The band at 3203 due to (N-H) stretching. The band at 3020 assigned to carboxylic (O-H) which intermolecularly hydrogen bonded. The bands at 29787, 2935 and 2847 attributed to (C-H) aliphatic stretching. The strong band around1749 due to carboxylic (C=O) stretching. The medium band at 1653 for amidic (C=O) stretching. The band at 1579 assigned to olefinic (C=C) stretching. The band around 1452 assigned to (CH3) bending. The band at 1390 for (C-N) stretching. The band at 1284 for (C-O) stretching of carboxylic group. The band around 1147 for (C-O) stretching of phenol. The weak band at 665 due to (CS) stretching. This similar to the previous study that reported same the results (Rashid *et al*., 2018).

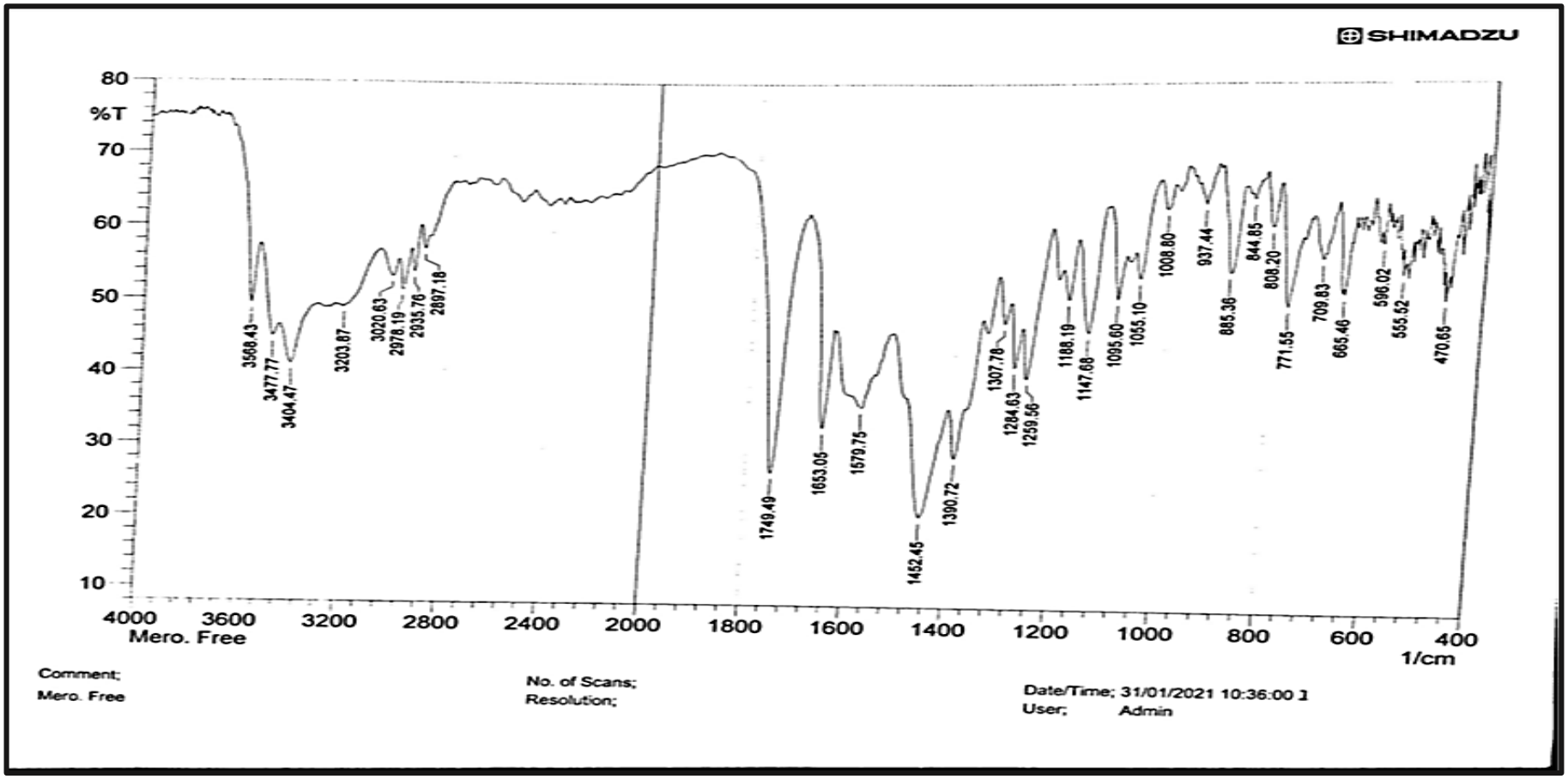


Figure 2: Infrared spectrum (FTIR) for free-Meropnem antibiotic

3.7.1.3. Infrared spectrum (FTIR) for Nano-Meropenem.

FT-IR spectrum of nano meropenem: The absorption band at 3373 attributed to phenolic (O-H) stretching, carboxylic (O-H) stretching and (N-H) stretching (overlapped). The band at 2918 attributed to (C-H) aliphatic stretching. The band around1635 because of carboxylic (C=O) stretching and amidic (C=O) stretching (overlapped). The band of olefinic (C=C) stretching was shifted to lower frequency around 1550. The band of (N-H) bending appeared at 1510. The band for (CH3) bending was shifted to higher frequency around 1462. The band for (C-N) stretching was shifted to higher frequency around 1400. The band for (C-O) stretching of carboxylic group was shifted to higher frequency at 1288. The band for (C-O) stretching of phenol was shifted to lower frequency around 1126 infrared spectrum (FTIR) for Nano-Meropenem.

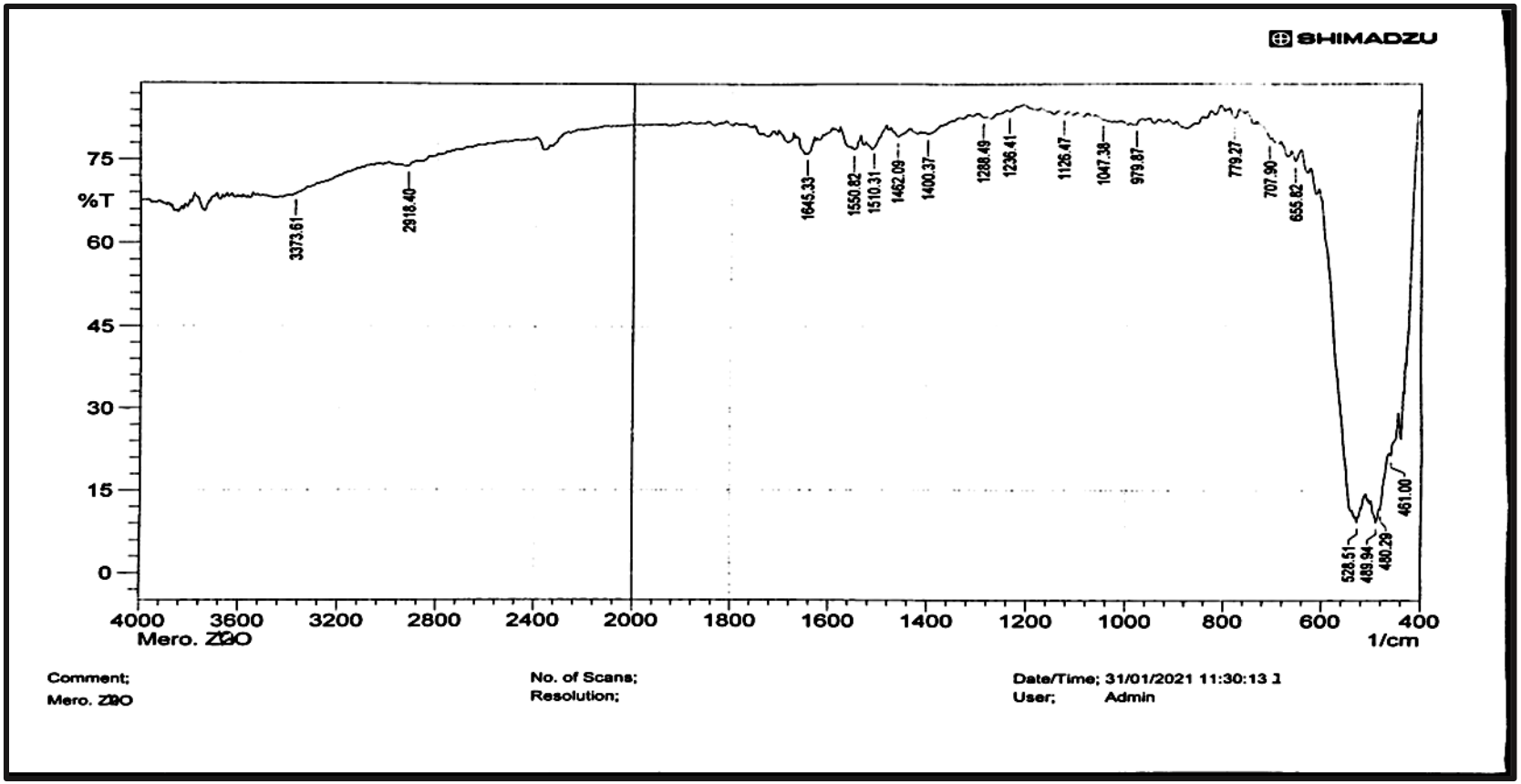


Figure 3: Infrared spectrum (FTIR) for nano meropnem

3.7.2. Characterization by using X-ray diffraction spectrum (XRD)

The spectrum of XRD of zinc oxide (carrier) and the nanohybrid antibiotic (MERO-ZnO) were studied to find the difference in the thickness of the ZnO layers before and after the intercalation of meropenem between ZnO layers. Figure 4 illustrated XRD of free meropenem while Figure 5 showed the XRD spectrum of MERO-ZnO, results confirmed that meropenem was intercalated between ZnO layers.

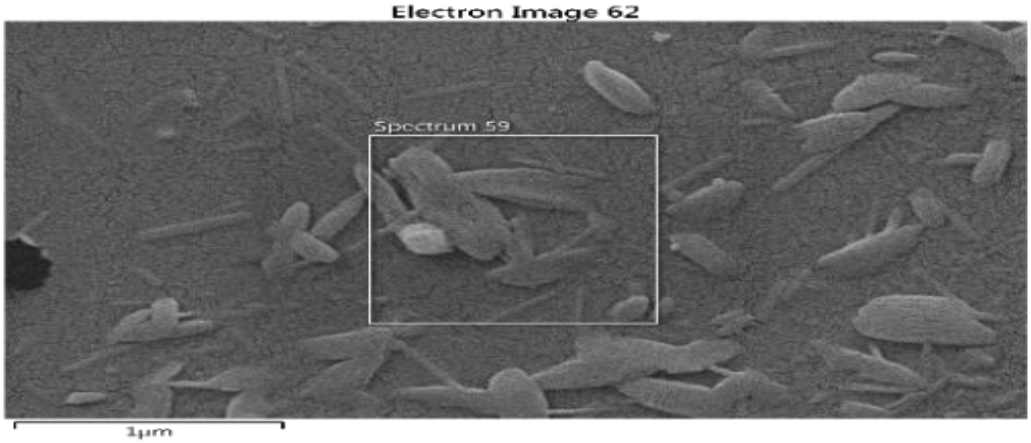


Figure 4: X-ray diffraction spectroscopy of Free-Meropenem.

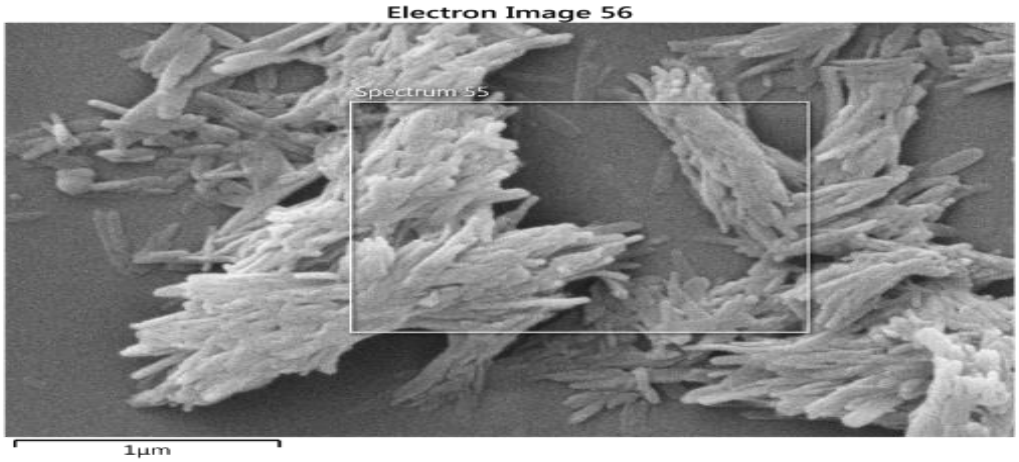


Figure 5: X-ray diffraction spectroscopy of Nanohybrid-Meropenem.

3.7.3. Characterization by using Atomic Force Microscope (AFM)

AFM was used to study the outer surface of the nanohybrid-meropenem. Figure 6 (A) showed a two dimensional image of the surface section of the nanohybrid antibiotic indicating the successful of preparation of nanohybrid antibiotic where the elevation of molecular assemblies of up to 145.7 nm. Figure 6 (B) showed semispherical forms of Meropenem-ZnO in the three dimensional images. The results obtained in this study agreements with the previous study done by Sasikumar *et al* (Sasikumar *et al*., 2016).

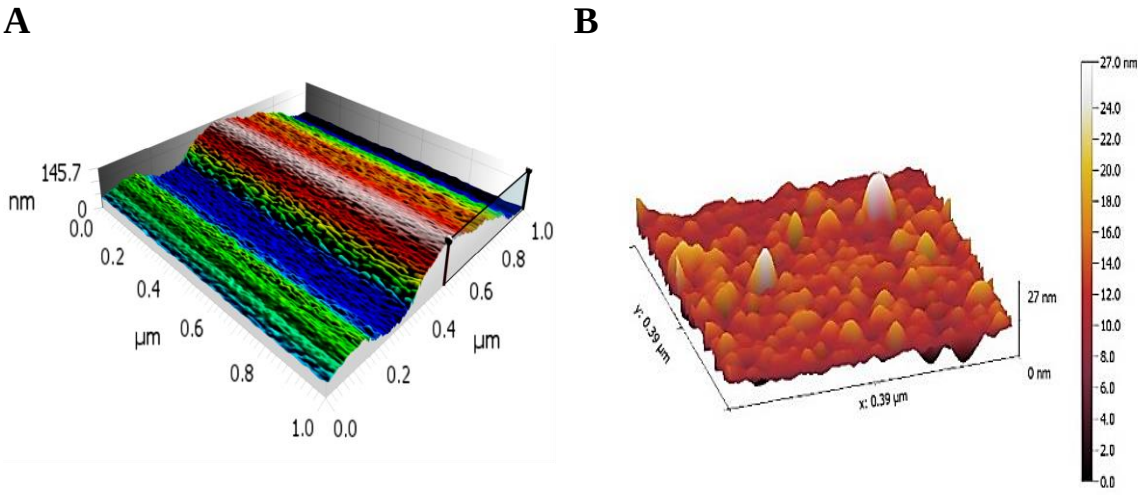


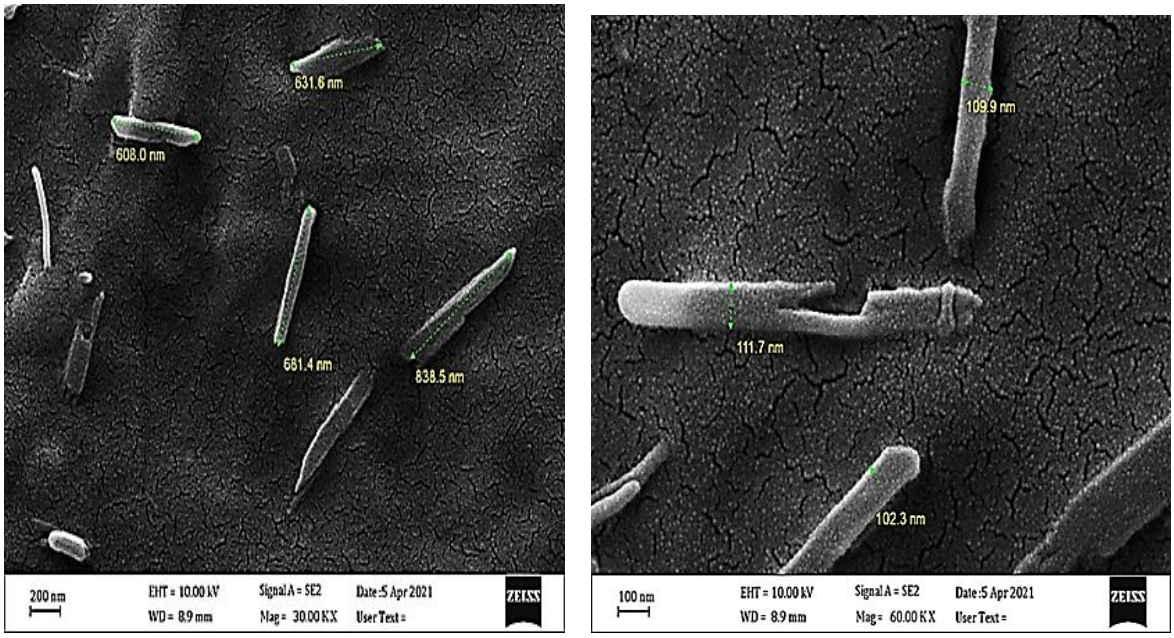
Fig. 6: (A) Two-dimensional and (B) three-dimensional, image of the MEM-Zn.

3.7.4. Characterization by using Scanning Electronic Microscope (SEM):

The Figure 8 shows the scanning electron microscope image for the layers of zinc oxide, where it was observed that the clear-cut hexagonal shapes in which the oxide leaves appear superimposed on top of each other in irregular shapes and sizes (Bashi *et al*., 2013),and that these irregular shapes convert into different geometric shapes interspersed with spaces when the hybrid nanocomposite (Mero-Zno) is formed resulting from the direct

interaction of the zinc oxide layers with the meropenem antibiotic, which indicates the success of the process of encapsulated of the antibiotic into the zinc oxide the Figure 5.

(A) (B)



(C) **(D)**

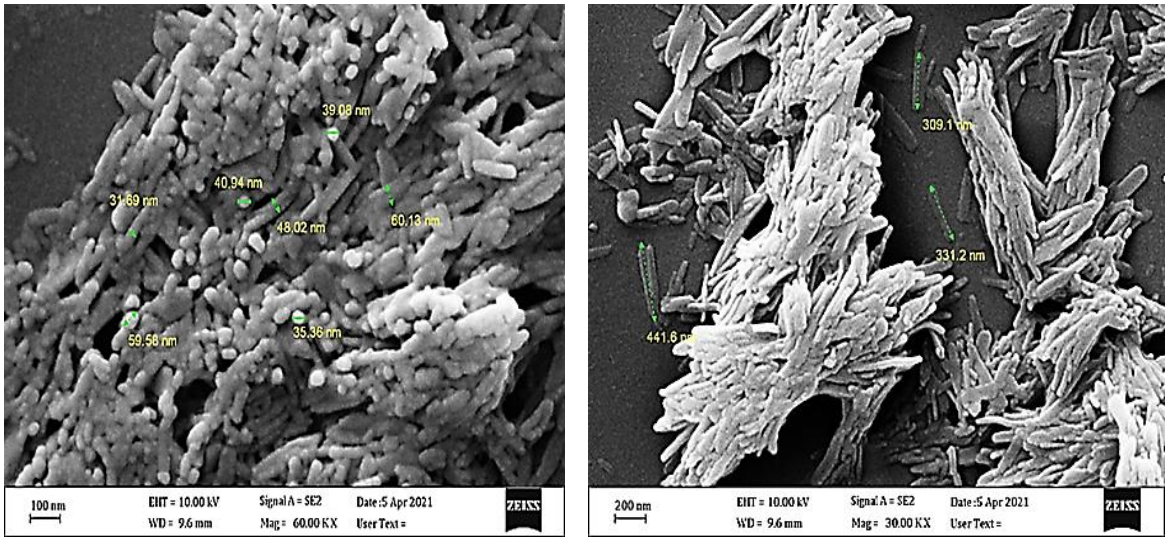


Fig7: (A) and (B) Scanning Electron Microscope (SEM) image of Zinc Oxide layers and (C) and (D) Meropenem-ZnO.

3.7.5. Precise Analysis of Elements in the Nanohybrid Antibiotic

Chemical elements analysis showed that the percentages of Carbon, Hydrogen, Nitrogen and Sulphur were 49.20, 5.52, 9.15 and 0 % for Free-Meropenem, while they were 17.74, 2.19, 3.39 and 0 % for Nano-Meropenem. These results indicate that the level of meropenem loaded between the zinc oxide layers was 36 % (Table 41 and 42).

Table 41: The components of Free-Meropenem.

147.TXT
Eager 300 Summarize Results

Date : 2021/05/03 at 03:25:16
Method Name : Nitrogen/Carbon/Hydrogen/Sulphur
Method Filename : N C H S system.mth

Filename	AS Method	Vial
147(Z15)		

#	Group	Sample Name	Type	Weig.	Pro.F	---
57	9	147	UNK	2.079	6.25	---

Component name	Element %
Nitrogen%	9.152077675
Carbon%	49.20296097
Hydrogen%	5.529557228
Sulphur%	0

1 Sample(s) in Group No : 9

Component Name	Average	Std. Dev.	% Rel. S. D.	Variance
Nitrogen%	9.152077675	0	0.0000	0.0000
Carbon%	49.20296097	0	0.0000	0.0000
Hydrogen%	5.529557228	0	0.0000	0.0000
Sulphur%	0	0	0.0000	0.0000

Table 42: The components of Nano-Meropenem

148.TXT
Eager 300 Summarize Results

Date : 2021/05/03 at 03:25:26
Method Name : Nitrogen/Carbon/Hydrogen/Sulphur
Method Filename : N C H S system.mth

Filename	AS Method	Vial
148Z15)		

#	Group	Sample Name	Type	Weig.	Pro.F	---
58	10	148	UNK	2.532	6.25	---

Component name	Element %
Nitrogen%	3.39694047
Carbon%	17.74459457
Hydrogen%	2.192493677
Sulphur%	0

1 Sample(s) in Group No : 10

Component Name	Average	Std. Dev.	% Rel. S. D.	Variance
Nitrogen%	3.39694047	0	0.0000	0.0000
Carbon%	17.74459457	0	0.0000	0.0000
Hydrogen%	2.192493677	0	0.0000	0.0000
Sulphur%	0	0	0.0000	0.0000

3.7.6. Antimicrobial Activity of Meropenem

The results of the statistical analysis in Table 43 showed that there are high significant differences ($P \leq 0.001$) in the diameters of inhibition zone of the free ciprofloxacin against *Staphylococcus hominis ssp hominis* at all concentrations that used compared with the control. In addition, there were increasing in inhibition zone when the concentration was increased. The diameters of inhibition zone to Free-Meropenem were (53.25, 56.0, 63.50, 75.0 and 84.0) mm of the following concentrations (25, 50, 100, 200 and 400) mg/ml; respectively. When we used the Nano-Meropenem there are a high significant differences ($P \leq 0.001$) in the diameters of inhibition zone of the nano ciprofloxacin against *Staphylococcus hominis ssp hominis* at all concentrations that used compared with the control. In addition, there are increasing in inhibition zone when the concentration was increased. The diameters of inhibition zone to Nano-Meropenem were (11, 17.25, 21, 23.5, and 23.5) mm of the following concentrations (25, 50, 100, 200, and 400) mg/ml; respectively. An other hand, when we compare between Free-Meropenem and Nano-Meropenem to each concentration, the results refer to high significant differences ($P \leq 0.001$) in the following all concentrations.

Table (43): The inhibitory efficacy of (Meropenem) against *(Staphylococcus hominis ssp hominis)* isolated from heart failure patient

Concentration (mg/ml)	Inhibition Zone (mm)		*P* value
	Meropenem (Free)	Meropenem (Nano)	
O (Control)	0 ± 0.00	0 ± 0.00	1.0000
25	53.25 ± 1.25	11.00 ± 1.63	0.0000 **
50	56.00 ± 1.82	17.25 ± 2.75	0.0000 **
100	63.50 ± 1.29	21.00 ± 1.82	0.0000 **
200	75.00 ± 1.82	23.5 ± 1.91	0.0000 **
400	84.00 ± 1.82	23.5 ± 2.88	0.0000 **
P value	0.0000 **	0.0000 **	
LSD	1.93	2.83	

The numbers refer to mean ± Standard Deviation * refers significance differences ($P \leq 0.05$) ** refers high significance differences ($P \leq 0.001$)

That is agreaments with Fadwa *et al* who report the results found the antibiotics Meropenem was found to be very effective on *P. aeruginosa* ATCC 2785 with MIC value 0.6 μg/mL with SD ±0.2 and *P. aeruginosa* (MRO-17-29) the clinical isolated strain was found to be resistant with MIC value 16 μg/ml with SD±0. Whereas, the tested *P. aeruginosa* (MRO-17-3) strain isolated from urine sample was found to be intermediate susceptible to ciprofloxacin antibiotic with MIC value 3.33μg/mL with SD±1.15 (Fadwa *et al*., 2021). Fosfomycin (FOS) is a unique mechanism-based inhibitor of bacterial wall formation (Falagas *et al*., 2016). In most cases, FOS is used in conjunction with at least one other active substance. The association benefits from an increase in FOS's bactericidal activity, as well as the avoidance of AMR and the reduction of side effects due to lower dosages. The following are some examples of commonly used empirical combination regimens that include FOS: FOS + Carbapenems (Antonello *et al*., 2020).

Carbapenems Forty-four papers evaluating FOS in combination with carbapenems. Carbapenems are β-lactamantibiotics that work by attaching to penicillin-binding proteins to stop bacteria from making cell walls. Carbapenems are -lactams used intravenously to treat serious infections as a "last resort." The breakpoints for imipenem (IMI) are ≤ 2 μg/mL for *Enterobacterales, Acinetobacter* spp., *S. pneumoniae* and ≤ 0.001 μg/mL for *Pseudomonas* spp. and *Staphylococcus* spp. Meropenem breakpoints are ≤2 μg/mL for *Enterobacterales, Acinetobacter* spp., *Pseudomonas* spp., *S. pneumoniae* and ≤4 μg/mL for *Staphylococcus* spp. Ertapenem (ERT) breakpoints are ≤0.5 μg/mL for *Enterobacterales, S. pneumoniae* and ≤4 μg/mL for *Staphylococcus* spp (org/clinical_breakpoints, 2020).

3.8.The Correlations between parameters of the study.

From then observations of the results of statistical analysis in Table 44 showed that there was significant correlation at (0.01) between RBC and both HGB and HCT, as it was positive correlation (0.728 and 0.792), respectively. In the same time there was significant correlation at (0.01) between HGB and HCT and between MCV and MCH as it was positive correlation too (0.893 and 0.890), respectively. Significant correlation at (0.01) also can be seen between PDW and both MPV and P-LCR as it was positive correlation (0.733 and 0.737), respectively. Significant correlation at (0.01) also can be seen between RDW-CV and RDW-SD as it was positive correlation (0.626). At the same time there was significant correlation at (0.05) between MPV and P-LCR, as it was positive correlation (0.503).

Table 44: Correlation between CBC parameters in patients of heart failure without bacterial infections.

	WBC	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	LYM	NEUT	RDW-CV	RDW-SD	**PDW**	**MPV**	**P-LCR**	**PCT**
WBC	1	0.025	0.087	0.119	0.136	0.099	0.021	-0.131	-0.093	0.302	0.026	0.124	0.030	0.019	0.038	0.036
RBC	-	1	0.728**	0.792**	-0.406	-0.342	-0.035	-0.139	0.163	-0.205	0.027	-0.220	-0.094	0.023	0.046	-0.070
HGB	-	-	1	0.893**	0.216	0.334	0.315	-0.317	0.205	-0.176	-0.287	-0.188	0.081	0.095	0.180	-0.241
HCT	-	-	-	1	0.156	0.156	0.041	-0.365	0.164	-0.204	-0.166	-0.100	0.058	0.095	0.163	-0.269
MCV	-	-	-	-	1	0.890**	0.136	-0.322	-0.018	0.004	-0.289	0.274	0.343	0.181	0.338	-0.251
MCH	-	-	-	-	-	1	0.391	-0.249	-0.009	0.059	-0.482	0.077	0.174	-0.026	0.170	-0.264
MCHC	-	-	-	-	-	-	1	-0.019	0.054	0.043	-0.257	-0.319	-0.017	0.059	-0.142	-0.008
PLT	-	-	-	-	-	-	-	1	-0.194	0.009	0.195	0.086	-0.143	-0.234	-0.096	0.795**
LYM	-	-	-	-	-	-	-	-	1	-0.226	-0.109	-0.225	0.213	0.272	0.255	-0.005
NEUT	-	-	-	-	-	-	-	-	-	1	0.029	0.097	-0.142	-0.125	-0.063	-0.158
RDW-CV	-	-	-	-	-	-	-	-	-	-	1	0.626*	0.207	0.349	0.040	0.310
RDW-SD	-	-	-	-	-	-	-	-	-	-	-	1	0.281	0.056	0.328	0.107
PDW	-	-	-	-	-	-	-	-	-	-	-	-	1	0.733**	0.737**	0.168
MPV	-	-	-	-	-	-	-	-	-	-	-	-	-	1	0.503*	0.145
P-LCR	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	0.119
PCT	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1

* The correlation is significant at 0.05 level (2-tailed) ** The correlation is significant at 0.01 level (2-tailed)

Heart failure is one of the most common causes of cardiovascular mortality in the world and a frequent cause of hospitalization in patients over the age of 65 (Ponikowski *et al*., 2016). The high prevalence of normocytic normochromic anemia in the studied patients (69.28%) may be due to the fact that HF is a chronic disease characterized by the increased level of pro-inflammatory cytokines that mediate the occurrence of anemia and comorbidities present in these patients (Zaharie *et al*., 2017). Agreements with study that reported patients with HF studying over 64 years have significantly lower values of erythrocyte counts, Hb, Ht, compared with corresponding healthy population with the same age and sex (STUDENT and MIRELA, 2018). Low and high levels of Hct, Hb and RBCs were associated with vascular smooth muscle dysfunction, and low Hct levels were associated with abnormal vascular structure. Increases in the levels of HCT, Hb and RBCs within normal ranges may decrease the risk of cardiovascular disease. HCT level of 43.0–48.9%, Hb level of 14.7–16.8 g/dL and RBCs level of 4.82–5.24 × 10^6/μL may be the optimal target levels for maintenance of vascular function and vascular structure (Kishimoto *et al*., 2020). Changes in Hb, HCT, and plasma volume correlate with invasive haemodynamics and clinical outcomes in hospitalized HF patients (Vaduganathan *et al*., 2014, Breidthardt *et al*., 2017, Chouihed *et al*., 2019). The positive correlation between PDW with MPV of the current study agreements with results study that show PDW is also a specific marker of platelet activation and increases in heterogeneity of platelet volume distribution. Vagdatli *et al*. reported that MPV and PDW were elevated together in platelet activation but emphasized that PDW is a more specific marker (Vagdatli *et al*., 2010). In the study of Rechcński *et al*., PDW was found to be an independent risk factor for cardiac mortality and for the occurrence of either death, recurrent MI, or need for another

revascularization procedure (Rechciński *et al*., 2013). PLCR is another marker related to platelet volume, and it is an indicator of the largest platelet fraction. An increase in PLCR usually occurs together with an increase in the number of newly produced platelets, which are the largest platelet type. PLCR is usually correlated with MPV, but it is more sensitive to the increase in platelet size. Babu showed that PLCR is inversely proportional to platelet count and directly related to MPV and PDW (Babu *et al*., 2004). An increase in PLCR may indicate the presence of platelet aggregates, microerythrocytes, and giant platelets. PLCR can serve as useful prognostic factors for long-term mortality in patients after acute MI. Rechcński *et al*. advocated that PDW and PLCR are prognostic factors after MI and suggested that they could be better than other markers, particularly MPV (Rechciński *et al*., 2013).

Agreements with previous study that showed RBCs display a physiological size heterogeneity in adult human blood, which is usually measured in terms of RBC distribution width (RDW). This simple and straight forward parameter can thus be expressed both in absolute value, as the standard deviation (SD) of erythrocyte volumes (RDW-SD), or as the coefficient of variation (RDW-CV) of erythrocyte volumes [*i.e*., (RDW-SD)/ (MCV)*100]. The normal range of RDW-CV is 11.5-14.5% but often varies according to the technique used for its assessment by the different commercially available hematological analyzers (Salvagno *et al*., 2015).

The results of the statistical analysis in the table 45 showed that there was significant correlation at (0.01) between MCHC and MCH, as it was positive correlation (0.733). From the same Table 45 that there were significant correlations at (0.05) between PLT and RBC, HGB and HCT, as it was positive correlation (0.625, 0.574 and 0.575), respectively. Also there were significant correlation at (0.01) and at (0.05) between NEUT and both WBC and LYM, as it were positive and inverse correlation (0.969 and -0.555), respectively. There was significant correlation at (0.05) between PDW and RDW, as it was positive correlation (0.622). At the last time there were significant correlation at (0.05) between PCT and RBC, HGB and HCT, as it was positive correlation (0.654, 0591 and 0.574), respectively.

Table 45: Correlation between CBC parameters in patients of heart failure with bacterial infections.

	WBC	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	LYM	NEUT	RDW-CV	RDW-SD	**PDW**	**MPV**	**P-LCR**	**PCT**
WBC	1	0.166	0.166	0.153	-0.274	-0.074	0.175	0.147	-0.480	0.969**	-0.019	-0.095	0.061	0.087	0.114	0.132
RBC	-	1	0.954**	0.795**	-0.261	-0.008	0.204	0.625*	0.101	0.007	0.249	0.068	0.021	-0.048	-0.133	0.654*
HGB	-	-	1	0.831**	-0.012	0.211	0.306	0.574*	0.117	0.029	0.117	0.060	-0.127	-0.176	-0.263	0.591*
HCT	-	-	-	1	-0.010	-0.174	-0.205	0.575*	0.304	0.065	-0.070	0.188	-0.299	-0.369	-0.205	0.574*
MCV	-	-	-	-	1	0.702**	0.057	-0.088	0.137	-0.233	-0.156	0.314	-0.442	-0.391	-0.435	-0.116
MCH	-	-	-	-	-	1	0.733**	-0.104	-0.135	-0.087	-0.011	-0.014	-0.177	-0.082	-0.377	-0.075
MCHC	-	-	-	-	-	-	1	-0.099	-0.270	0.139	-0.027	-0.428	0.081	0.163	-0.176	-0.046
PLT	-	-	-	-	-	-	-	1	0.475	-0.075	0.361	0.433	-0.234	-0.298	-0.319	0.992**
LYM	-	-	-	-	-	-	-	-	1	-0.555*	-0.116	0.196	-0.306	-0.302	-0.166	0.455
NEUT	-	-	-	-	-	-	-	-	-	1	-0.150	-0.186	0.066	0.109	0.179	-0.098
RDW-CV	-	-	-	-	-	-	-	-	-	-	1	0.719**	0.622*	0.482	0.320	0.419
RDW-SD	-	-	-	-	-	-	-	-	-	-	-	1	0.176	0.022	0.088	0.428
PDW	-	-	-	-	-	-	-	-	-	-	-	-	1	0.931**	0.847**	-0.149
MPV	-	-	-	-	-	-	-	-	-	-	-	-	-	1	0.896**	-0.200
P-LCR	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	-0.253
PCT	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1

* The correlation is significant at 0.05 level (2-tailed) ** The correlation is significant at 0.01 level (2-tailed)

The positive correlation between PLT and RBS in the current study agreemnts with study that conducted that NRBC may be considered as a parameter that sums up hypoxic and inflammatory changes during sepsis as in this condition hypoxemia occurs together with the increase of known stimulators of the bone marrow like erythropoietin. Similarly to immature red blood cells, immature platelets were also released by the bone marrow. Previously the immature platelet fraction (IPF) was found to predict sepsis (De Blasi *et al*., 2013) and it was also found that the IPF is useful for discriminating septic patients fromnon-septic patients, but not for the determination of sepsis severity (Park *et al*., 2016).

The positive correlation between WBC and NEUT aggreements with other previous studies that condected the WBC is the most commonly used metric to investigate infection, but is also the least useful. Septic shock may cause either leukocytosis or leukopenia. Many septic patients exist between these two extremes, with a normal WBC (such patients often develop leukocytosis in a delayed fashion). For example, half of patients presenting to the hospital with bacteremia may have a normal WBC (Seigel *et al*., 2012). Thus, while a substantially abnormal WBC may suggest the presence of infection, a normal WBC reveals little. If the WBC is extremely low, then determination of the absolute neutrophil count must be made (the absolute number of mature neutrophils plus bands present). Neutropenia is generally defined as an absolute neutrophil count below 500/microliter, or a count in the range of 500–1,000/microliter which is decreasing. Patients with neutropenia often fail to manifest focal signs of infection. There must be a high index of suspicion for infection in patients with neutropenia (for example, the mere presence of fever generally indicates the need for broad-spectrum antibiotics)

(Farkas, 2020). Sepsis represents a severe derangement of the immune response to infection, resulting in neutrophil dysfunction. The mechanism of this phenomenon has not been indicated clearly. Complement activation, impairment of neutrophil migration, and endothelial lesions are involved in this progress. Alterations of cytokines, chemokines, and other mediators contribute to neutrophil dysfunction in sepsis. At the mean time, neutrophil dysfunction promotes sepsis and even leads to organ failure. Mechanism studies, clinical practice, and strategies to interrupt dysregulated neutrophil function in sepsis are desperately needed (Feltz de Faria, 2020).

Agreements with results that reported the haematological parameters are an important tool of diagnosis that reveals the state of health of fish species. Therefore, the bacteriosis resulted in impaired homeostasis and consequently dynamic balance between production and destruction of erythrocytes which favoured the installation of anaemia with negative consequences. With the help of the haematological indices the erythrocytes constants (MCV, MCH, MCHC) for the blood of the sturgeon were calculated. In another study, there was a significant increase in MCHC value, due to macrocytic anaemia; the adaptation response of blood to the significantly reducing the number of erythrocytes and the haemoglobin content was prompt materialized in increasing HEM and CHEM (Docan *et al*., 2017). Similar to the study that reported infection also interferes with anticoagulant and procoagulant systems by stimulating the coagulation system forming thrombin and leading to consumptive coagulopathy and disseminated intravascular coagulopathy (DIC). Also in this study, the prevalence of anemia (Hb < 10 g/dL) among patients with septicemia was 40.8% (in total 196 patients). The changes of Hb/Hct and WBC correlated with the initial number including platelet count, however platelet count

abnormality correlated with partial thromboplastin time (PTT) may have been due to DIC causing fibrin formation. Similar to one subgroup study found that elderly patients and patients with underlying chronic lung diseases had more severe anemia (Bumpensil and Kantisap, 2018). Therefore, the two indices PDW and RDW have diagnostic power in the discrimination of bacteremia. The results indicate that the elevated PDW, RDW values observed at the onset of inflammation are significantly associated with the presence of bacteremia (Zhang *et al*., 2016). RDW and PDW together can be used as biomarker for sepsis and early institution of antibacterial therapy (Mohan *et al*.).

As shown from the statistical analysis of Table 46 that there were significant correlation at (0.05 and 0.01) between TC and both HDL and LDL, as it was positive correlation (0.661 and 0.937), respectively. Also there was significant correlation at (0.05) between LDL and HDL, as it was positive correlation (0.534). There was significant correlation at (0.05) between Urea and Creatinine, as it was positive correlation (0.548). Lastly there was high significant correlation at (0.01) between DBP and SBP, as it was positive correlation (0.709).

Table 46: Correlation between some parameters in patients of heart failure without bacterial infections.

	Age	Weight	CRP	Troponin	BNP	TC	TG	HDL	LDL	Creatinine	**Urea**	**Glucose**	**SBP**	**DBP**
Age	1	-0.202	-0.071	0.053	0.095	-0.147	-0.387	0.093	-0.127	0.275	0.028	-0.312	-0.067	0.081
Weight	-	1	-0.073	0.074	0.187	0.100	0.289	0.033	-0.003	0.061	0.273	0.271	0.101	0.036
CRP	-	-	1	-0.065	-0.131	-0.249	-0.162	-0.112	- 0.174	0.119	0.208	0.113	-0.011	0.061
Troponin	-	-	-	1	0.090	0.059	- 0.035	- 0.037	0.042	0.044	-0.010	0.138	-0.073	-0.186
BNP	-	-	-	-	1	0.272	- 0.042	0.041	0.260	0.189	0.215	0.169	-0.045	-0.215
TC	-	-	-	-	-	1	0.377	0.661*	0.937**	-0.036	-0.170	0.198	0.326	0.160
TG	-	-	-	-	-	-	1	0.214	0.351	-0.069	-0.187	0.202	0.120	0.087
HDL	-	-	-	-	-	-	-	1	0.534*	-0.085	-0.272	0.095	0.126	0.166
LDL	-	-	-	-	-	-	-	-	1	-0.075	-0.234	0.189	0.300	0.117
Creatinine										1	0.548*	-0.078	0.288	0.147
Urea											1	-0.111	0.055	0.015
Glucose												1	0.173	0.130
SBP													1	0.709**
DBP														1

* The correlation is significant at 0.05 level (2-tailed) ** The correlation is significant at 0.01 level (2-tailed)

Similar to in other study reported that has two major findings. First, they observe that in CHD patients with LVEF<45%, higher baseline TC and HDL-C levels are associated with lower risk of prehospitalization for HF symptoms deterioration and all-cause mortality. Second, underlying mechanisms associated with these favorable effects of higher baseline TC and HDL-C levels may be different. Future randomized controlled trials are necessary to evaluate whether increasing TC and HDL-C levels will confer cardiovascular benefits in CHD patients with reduced LVEF (Zhao *et al*., 2017). HF is attributed to coronary heart disease (CHD) (Najafi *et al*., 2007), which now affects more than 10 million people in China. Theoretically, reducing TC and LDL-C levels would not only decrease the incidence of CHD as evidenced by previous clinical trials but may also improve HF patients' outcomes (Zhao *et al*., 2017). Disagreements with Nakagomi *et al* who reported that HDL-C was inversely correlated with LDL-C ($r = -0.408$; $p = 0.004$) while agreement with same study that conducted LDL-C was positively correlated with total cholesterol ($r = 0.910$; $p < 0.0001$). Among the classical plasma lipid parameters, it has been reported that LDL-C is in HF and associated to poorer prognosis (Nakagomi *et al*., 2014). Another study show that HF patients reduced with higher HDL-C (Cai *et al*., 2016). Similar to the previous study that show clinical systolic and diastolic heart failure appear to be 2 distinct syndromes of chronic heart failure. The myocardial structural and primary functional derangements are distinctive in these 2 syndromes, although hemodynamic consequences, clinical presentations, signs and symptoms, and prognosis are similar. The neurohormonal abnormalities are also similar in both of these syndromes. Although there have been considerable advances in the management of systolic heart failure, the management of DHF remains

primarily to relieve symptoms (Chatterjee and Massie, 2007, Gao *et al*., 2014). Agreements with results of Cleland *et al* study who conducted that changes in creatinine, transient increases in urea may be associated with an adverse outcome (Cleland *et al*., 2012). Renal dysfunction is common in patients with acute heart failure and is likely to be a major determinant of the response to diuretics and the deployment of life-saving therapies such as ACE inhibitors and aldosterone receptor antagonists. However, it is the underlying chronic severity of renal dysfunction, rather than transient changes, which is the major determinant of prognosis (Cleland *et al*., 2012).

From observations the results of statistical analysis in Table 47 showed that there was significant correlation at (0.05) between Age and BNP, as there was inverse correlation (- 0.527). Also there were high significant correlations at (0.01) between CRP and both TG, and creatinine, as there was positive correlation (0.731, 0.894), respectively. While there were significant correlations at (0.05) between CRP with HDL, LDL, and Urea, as there were inverses, and positive correlations (- 0.505, -0.505 and 0.664), respectively. From observation the same Table 47 there were there were high significances correlation at (0.01) between Creatinine with TG and significances correlation at (0.05) between Glucose with Weight, as there was positive correlation (0.763, 0.593), respectively.

Table 47: Correlation between some parameters in patients of heart failure with bacterial infections.

	Age	Weight	CRP	Troponin	BNP	TC	TG	HDL	LDL	Creatinine	**Urea**	**Glucose**	**SBP**	**DBP**
Age	1	0.271	0.371	0.197	- 0.527*	- 0.021	0.234	0.050	- 0.106	0.275	0.205	-0.484	0.124	-0.141
Weight	-	1	0.104	0.299	0.116	- 0.053	- 0.099	0.194	0.005	-0.161	-0.337	0.593*	-0.039	-0.209
CRP	-	-	1	- 0.160	- 0.039	- 0.375	0.731**	- 0.540*	- 0.505*	0.894**	0.664*	-0.069	0.045	0.091
Troponin	-	-	-	1	0.200	- 0.094	- 0.191	0.329	- 0.203	0.198	-0.126	0.109	0.153	0.047
BNP	-	-	-	-	1	- 0.017	0.185	- 0.287	0.058	0.154	0.252	0.305	-0.211	0.094
TC	-	-	-	-	-	1	0.173	0.702**	0.898**	-0.059	-0.158	0.050	-0.082	-0.174
TG	-	-	-	-	-	-	1	0.308	0.009	0.763**	0.484	0.015	-0.231	-0.032
HDL	-	-	-	-	-	-	-	1	0.610*	-0.259	-0.422	0.004	0.200	-0.131
LDL	-	-	-	-	-	-	-	-	1	-0.272	-0.248	-0.039	-0.246	-0.355
Creatinine										1	0.736**	-0.057	-0.067	0.071
Urea											1	-0.152	-0.122	0.124
Glucose												1	-0.094	0.099
SBP													1	0.695*
DBP														1

* The correlation is significant at 0.05 level (2-tailed) ** The correlation is significant at 0.01 level (2-tailed)

Similar to the previous study that show BNP can play an important role as a biomarker in septic shock, BNP increases in diseases other than sepsis or cardiac failure, on the other hand, limiting its utility as a primary prognostic diagnostic in sepsis patients. BNP is relatively easy to obtain as a laboratory test and has the potential to identify patients with imminent cardiovascular compromise and those at high risk for mortality. Further relationships regarding laboratory value and correlation with severity of illness need to be established with larger prospective studies to develop consensus regarding a cutoff point for optimum sensitivity and specificity in predicting in-hospital mortality related to sepsis (Bhandari and Cunningham, 2020). Agreement with the guidelines of other study that show primary care patients with BNP above a certain cut-off (irrespective of sex or gender) should be referred for further diagnostics. One might question whether the use of one single cut-off level for BNP (not taking into account age and gender) is specific enough for daily practice. Since this cut-off was established for maximizing the sensitivity, it might be hypothesized that one rigorous, non-age-specific, cut-off of elevated BNP results in many false positive cases at higher ages and that too many older patients will undergo additional diagnostic tests or are referred to a cardiologist for further investigation. Therefore, there is a need to adjust the reference values (Keyzer *et al*., 2014).

The current results conducted that inverses correlation between CRP with both HDL and LDL, while positive correlation between CRP and TG. Agreement with study done by Bermudes *et al* data who suggest that in septic pediatrics patients, an inverse correlation exists between the severity of inflammation (as measured by serum CRP values) and TC or HDL (Bermudes *et al*., 2018). Agreement in the another cohort observational study about the

correlation of CRP with both HDL and LDL but disagreement in the correlation of CRP with TG, where study 60 severe sepsis patient were enrolled and their lipid profile and CRP compared on first and third and seventh days in order to determine prognostic condition of patients. Comparison of the demographic parameters between patients showed uniform distribution. The HDL and LDL and TG values from the first day until the seventh gradually will reduce and CRP value from the first to seventh day will increase. The same study demonstrated that the degree of inflammation correlates with the severity of hypocholesterolemia (Hazrati *et al*., 2018).

The current results showed that was positive correlation between CRP with both Creatinine and Urea. Similar to the previous study that reported septic shock with higher serum concentration of C-reactive protein (CRP), urea, and creatinine, and higher mortality rate (Costa *et al*., 2019).

In this study show that positive correlation between Weight and Glucose this agreement with results done by Magkose *et al* who reported that obese patients are usually accompanied by insulin resistance, so the basal insulin secretion value of these patients is higher than that of normal people (Magkos *et al.*, 2016). Similar to other study that conducted the fasting insulin value of patients in this group before weight loss is of 26.96 ± 1.98 uu/ml (normal reference value of Insulin radioimmunoassay (RIA) method is of 5 - 20 uu/ml). It was confirmed that there was insulin resistance in this group of patients. Hyperinsulinemia is caused by insulin resistance or insulin insensitivity (Burt Solorzano *et al*., 2018). Hyperinsulinemic blood syndrome is the common pathogenesis basis of coronary heart disease, hypertension, hyperlipidemia, Type-2 diabetes, obesity, cerebral stroke, etc., which is the most harmful to cardiovascular disease (Alfadda *et al.*, 2012). Agreement

with other studies that show the regulation of lipid metabolism and glucose metabolism after losing weight, the response sensitivity of tissue to insulin is enhanced, and the fasting blood glucose and serum insulin level are decreased (Kong *et al*., 2020). Clinically, obese and T2D patients have an increased risk of and significant morbidity and mortality from infections and sepsis for reasons that are poorly understood (Frydrych *et al.*, 2018).

The positive correlation between Creatinine and HDL in this study agreements with study that conducted creatinine serum has a positive relationship with triglycerides serum, thus the increase in creatinine serum can also increase triglycerides serum in patients (Aliviameita, 2018).

Conclusions

- The most common bacterial species which isolated from heart failure pateints was *Staphylococcus hominis ssp hominis*.
- Most bacterial isolates were resistant to Meropenem
- CRP had irreversible correlation with both HDL and LDL, while reversible correlation with TG, Creatinine and Urea in heart failure with bacterial infections.
- Reversible correlation between creatinine with TG and between glucose with weight in heart failure with bacterial infections.
- Nano-Meropenem was very effected agniast bacteria by made varaiaty of inhibation zones for different concentrations, so nanotechnology was very impotant technique in facing the crisis of resistance antbiotic.

Recommendations

- Blood culturing test should be done before any antbiotic givin to the sepsis suspected patients to avoid occure of more resistance.
- Conducting study about association of the troponin with bacterial infection.
- Conducting study in the relationship between TG and creatinine.
- Conducting study about MCHC in bacterial infection.

References

ABDALLA, M., SOHAL, S. & BAHA'A AL-AZZAM, W. M. J. J. O. C. M. R. 2019. Effect of troponin I elevation on duration of mechanical ventilation and length of intensive care unit stay in patients with Sepsis. 11**,** 127.

ABDULLAH, S. M. Z. 2020.Common bacterial causes of Septicemia and their antibiotic susceptibility profile in Erbil, Iraq.

ADLER, Y., CHARRON, P., IMAZIO, M., BADANO, L., BARON-ESQUIVIAS, G., BOGAERT, J., BRUCATO, A., GUERET, P., KLINGEL, K. & LIONIS, C. 2015. European Society of C 2015 ESC guidelines for the diagnosis and management of pericardial diseases: the task force for the diagnosis and Management of Pericardial Diseases of the European Society of Cardiology (ESC) endorsed by: the European Association for CardioThoracic Surgery (EACTS). *Eur Heart J*, 36**,** 2921-64.

AKINTUNDE, A. A., AKINLADE, M. O. & AWORANTI, O. W. 2021. Disordered iron homeostasis among nigerians with chronic heart failure: Pattern, prevalence, and clinical correlates. *Journal of Clinical and Preventive Cardiology*, 10**,** 17.

AL-AKCHAR, M. & KIEL, J. 2021. Acute myocarditis. *StatPearls [Internet]*.

AL ABBASI, B., TORRES, P., RAMOS-TUAREZ, F., CHEN, K., AVILA, G., CEKA, E., CHACON, A. R., DE DIEGO, G., BORNMANN, C. R. & GHUMMAN, W. J. C. 2020. Implementation of the Surviving Sepsis Campaign in Patients With Heart Failure: Gender-Specific Outcomes. 12.

ALEXANDRAKIS, M. G. & TSIRAKIS, G. J. I. S. R. N. 2012. Anemia in heart failure patients. 2012.

ALFADDA, A. A., FATMA, S., CHISHTI, M. A., AL-NAAMI, M. Y., ELAWAD, R., MENDOZA, C. D. O., JO, H., LEE, Y. S. J. M. & CELLS 2012. Orosomucoid serum concentrations and fat depot-specific mRNA and protein expression in humans. 33**,** 35-41.

ALIVIAMEITA, A. Relationship Between Renal Function Test Serum and Lipid Profile in Patients with Diabetes Mellitus. Journal of Physics: Conference Series, 2018. IOP Publishing, 012011.

ALJOHAR, A., ALHABIB, K. F., KASHOUR, T., HERSI, A., AL HABEEB, W., ULLAH, A., ELASFAR, A., ALMASOOD, A., GHABASHI, A. & MIMISH, L. J. J. O. T. S. H. A. 2018. The prognostic impact of hyperglycemia on clinical outcomes of acute heart failure: Insights

from the heart function assessment registry trial in Saudi Arabia. 30**,** 319-327.
ALKHATEEB, M., KADDAR, T. J. R. J. O. P. & TECHNOLOGY 2018. Increased platelet volume indices is associated with the severity of coronary artery disease. 11**,** 2168-2172.
ALON, D., STEIN, G. Y., KORENFELD, R. & FUCHS, S. 2013. Predictors and outcomes of infection-related hospital admissions of heart failure patients. *PloS one,* 8**,** e72476.
ANTONELLO, R. M., PRINCIPE, L., MARAOLO, A. E., VIAGGI, V., POL, R., FABBIANI, M., MONTAGNANI, F., LOVECCHIO, A., LUZZATI, R. & DI BELLA, S. J. A. 2020. Fosfomycin as Partner Drug for Systemic Infection Management. A Systematic Review of Its Synergistic Properties from In Vitro and In Vivo Studies. 9**,** 500.
ANTONIO, M., GUDIOL, C., ROYO-CEBRECOS, C., GRILLO, S., ARDANUY, C. & CARRATALÀ, J. 2019. Current etiology, clinical features and outcomes of bacteremia in older patients with solid tumors. *Journal of geriatric oncology,* 10**,** 246-251.
ARELLANO-NAVARRO, C. E., HUERTA-RAMÍREZ, S., ELIZALDE-BARRERA, C. I., RUBIO-GUERRA, A. F., GARRO-ALMENDARO, A. K. & GONZÁLEZ-MORENO, F. J. J. M. I. D. M. 2018. Value of C-reactive protein (CRP)/albumin index in the diagnosis of sepsis. 34**,** 188-195.
ARUNDEL, C., LAM, P. H., GILL, G. S., PATEL, S., PANJRATH, G., FASELIS, C., WHITE, M., MORGAN, C. J., ALLMAN, R. M. & ARONOW, W. S. J. J. O. T. A. C. O. C. 2019. Systolic blood pressure and outcomes in patients with heart failure with reduced ejection fraction. 73**,** 3054-3063.
AWAN, A., TIRUNEH, F., WESSLY, P., KHAN, A., IFTIKHAR, H., BARNED, S. & LARBI, D. 2017. Acute pericarditis: descriptive study and etiology determination in a predominantly African American population. *Cureus,* 9.
BABU, E., BASU, D. J. I. J. O. P. & MICROBIOLOGY 2004. Platelet large cell ratio in the differential diagnosis of abnormal platelet counts. 47**,** 202-205.
BABUŠÍKOVÁ, E., LEHOTSKÝ, J., DOBROTA, D., RAČAY, P. & KAPLÁN, P. J. P. R. 2012. Age-Associated Changes in Ca 2+-ATPase and Oxidative Damage in Sarcoplasmic Reticulum of Rat Heart. 61.
BAESSLER, B., LUECKE, C., LURZ, J., KLINGEL, K., VON ROEDER, M., DE WAHA, S., BESLER, C., MAINTZ, D., GUTBERLET, M. &

THIELE, H. 2018. Cardiac MRI texture analysis of T1 and T2 maps in patients with infarctlike acute myocarditis. *Radiology,* 289**,** 357-365.
BANACH, M., MARKUSZEWSKI, L., ZASŁONKA, J., GRZEGORCZYK, J., OKOŃSKI, P. & JEGIER, B. 2004. The role of infection in the pathogenesis of atherosclerosis. *Przeglad epidemiologiczny,* 58**,** 671-676.
BAPTISTA, P. V., MCCUSKER, M. P., CARVALHO, A., FERREIRA, D. A., MOHAN, N. M., MARTINS, M. & FERNANDES, A. R. J. F. I. M. 2018. Nano-strategies to fight multidrug resistant bacteria—"A Battle of the Titans". 9**,** 1441.
BARTLETT, J. G., GILBERT, D. N. & SPELLBERG, B. 2013. Seven ways to preserve the miracle of antibiotics. *Clinical Infectious Diseases,* 56**,** 1445-1450.
BASHI, A. M., HADDAWI, S. M., MEZAAL, M. A. J. A. J. F. S. & ENGINEERING 2013. Layered double hydroxides nanohybrid intercalation with folic acid used as delivery system and their controlled release properties. 38**,** 1663-1680.
BAZZI, A. M., RABAAN, A. A., FAWARAH, M. M., AL-TAWFIQ, J. A. J. J. O. I. & HEALTH, P. 2017. Direct identification and susceptibility testing of positive blood cultures using high speed cold centrifugation and Vitek II system. 10**,** 299-307.
BEJIQI, R., RETKOCERI, R., MALOKU, A., MUSTAFA, A., BEJIQI, H. & BEJIQI, R. 2019. The diagnostic and clinical approach to pediatric myocarditis: a review of the current literature. *Open access Macedonian journal of medical sciences,* 7**,** 162.
BENJAMIN, E., MUNTNER, P., ALONSO, A. J. H. D. & CIRCULATION, S. S. U. A. R. F. T. A. H. A. 2019. Lic VS on behalf of the AHAC on E and PSC and SSS. 139**,** e1-e473.
BENNADI, D. 2013. Self-medication: A current challenge. *Journal of basic and clinical pharmacy,* 5**,** 19.
BERKLEY, J. A. 2021. Bacterial Infections and Nutrition: A Primer. *Nutrition and Infectious Diseases.* Springer.
BERMUDES, A. C. G., DE CARVALHO, W. B., ZAMBERLAN, P., MURAMOTO, G., MARANHÃO, R. C. & DELGADO, A. F. J. N. 2018. Changes in lipid metabolism in pediatric patients with severe sepsis and septic shock. 47**,** 104-109.
BESSIÈRE, F., KHENIFER, S., DUBOURG, J., DURIEU, I. & LEGA, J.-C. J. I. C. M. 2013. Prognostic value of troponins in sepsis: a meta-analysis. 39**,** 1181-1189.

BHANDARI, B. & CUNNINGHAM, J. J. C. 2020. The Role of Brain Natriuretic Peptide as a Prognostic Marker for Sepsis. 12.

BIANCO, A., PAPADOPOLI, R., MASCARO, V., PILEGGI, C. & PAVIA, M. 2018. Antibiotic prescriptions to adults with acute respiratory tract infections by Italian general practitioners. *Infection and drug resistance*, 11**,** 2199.

BOAMAH, V. E., AGYARE, C., ODOI, H., ADU, F., GBEDEMA, S. Y., DALSGAARD, A. J. I. & RESISTANCE, D. 2017. Prevalence and antibiotic resistance of coagulase-negative Staphylococci isolated from poultry farms in three regions of Ghana. 10**,** 175.

BOJANIĆ, L., MARKOVIĆ-PEKOVIĆ, V., ŠKRBIĆ, R., STOJAKOVIĆ, N., ĐERMANOVIĆ, M., BOJANIĆ, J., FÜRST, J., KURDI, A. B. & GODMAN, B. 2018. Recent initiatives in the Republic of Srpska to enhance appropriate use of antibiotics in ambulatory care; their influence and implications. *Frontiers in pharmacology*, 9**,** 442.

BONARES, M. J., VAISMAN, A. & SHARKAWY, A. J. I. 2016. Prosthetic vascular graft infection and prosthetic joint infection caused by Pseudomonas stutzeri. 6**,** 106-108.

BOYLES, T., EICK, B., NAICKER, V., RAWOOT, N., RAUBENHEIMER, P. & MENDELSON, M. 2017. Sustained reduction in antibiotic consumption in a South African public sector hospital: Four-year outcomes from the Groote Schuur Hospital antibiotic stewardship programme. *South African medical journal*, 107**,** 115-118.

BOZKURT, B., COLVIN, M., COOK, J., COOPER, L. T., DESWAL, A., FONAROW, G. C., FRANCIS, G. S., LENIHAN, D., LEWIS, E. F. & MCNAMARA, D. M. 2016. Current diagnostic and treatment strategies for specific dilated cardiomyopathies: a scientific statement from the American Heart Association. *Circulation*, 134**,** e579-e646.

BRACAMONTE-BARAN, W., ČIHÁKOVÁ, D. J. T. I. O. C. H. & PATHOLOGY 2017. Cardiac autoimmunity: myocarditis. 187-221.

BREIDTHARDT, T., WEIDMANN, Z. M., TWERENBOLD, R., GANTENBEIN, C., STALLONE, F., RENTSCH, K., RUBINI GIMENEZ, M., KOZHUHAROV, N., SABTI, Z. & BREITENBÜCHER, D. J. E. J. O. H. F. 2017. Impact of haemoconcentration during acute heart failure therapy on mortality and its relationship with worsening renal function. 19**,** 226-236.

BUJAK, K., WASILEWSKI, J., OSADNIK, T., JONCZYK, S., KOŁODZIEJSKA, A., GIERLOTKA, M. & GĄSIOR, M. J. D. M. 2015. The prognostic role of red blood cell distribution width in coronary artery disease: a review of the pathophysiology. 2015.

BUMPENSIL, W. & KANITSAP, N. 2018. Study of hematologic change among patients with sepsis at internal medicine wards.

BURT SOLORZANO, C. M., KNUDSEN, K. L., ANDERSON, A. D., HUTCHENS, E. G., COLLINS, J. S., PATRIE, J. T., MARSHALL, J. C., MCCARTNEY, C. R. J. T. J. O. C. E. & METABOLISM 2018. Insulin resistance, hyperinsulinemia, and LH: relative roles in peripubertal obesity-associated hyperandrogenemia. 103**,** 2571-2582.

CAFORIO, A. L., PANKUWEIT, S., ARBUSTINI, E., BASSO, C., GIMENO-BLANES, J., FELIX, S. B., FU, M., HELIÖ, T., HEYMANS, S. & JAHNS, R. 2013. Current state of knowledge on aetiology, diagnosis, management, and therapy of myocarditis: a position statement of the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases. *European heart journal,* 34**,** 2636-2648.

CAI, A., LI, X., ZHONG, Q., LI, M., WANG, R., LIANG, Y., CHEN, W., HUANG, T., LI, X. & ZHOU, Y. J. M. 2016. Associations of high HDL cholesterol level with all-cause mortality in patients with heart failure complicating coronary heart disease. 95.

CARBONE, S., LAVIE, C. J. & ARENA, R. Obesity and heart failure: focus on the obesity paradox. Mayo Clinic Proceedings, 2017. Elsevier, 266-279.

CARE, G. O. A. D. A. J. D. 2015. Standards of medical care in diabetes–2015: summary of revisions. 38**,** S4.

CARUBELLI, V., BONADEI, I., CASTRINI, A. I., GORGA, E., RAVERA, A., LOMBARDI, C. & METRA, M. J. J. O. C. M. 2017. Prognostic value of the absolute lymphocyte count in patients admitted for acute heart failure. 18**,** 859-865.

CEDIEL, G., CODINA, P., SPITALERI, G., DOMINGO, M., SANTIAGO-VACAS, E., LUPÓN, J. & BAYES-GENIS, A. 2021. Gender-Related Differences in Heart Failure Biomarkers. *Frontiers in Cardiovascular Medicine,* 7.

CEDIEL, G., CODINA, P., SPITALERI, G., DOMINGO, M., SANTIAGO-VACAS, E., LUPÓN, J. & BAYES-GENIS, A. J. F. I. C. M. 2020. Gender-related differences in heart failure biomarkers. 7.

CHAMBERS, H. F. & BAYER, A. S. 2020. Native-valve infective endocarditis. *New England Journal of Medicine,* 383**,** 567-576.

CHANG, S.-A. 2017. Tuberculous and infectious pericarditis. *Cardiol Clin,* 35**,** 615-622.

CHARACH, G., ARGOV, O., NOCHOMOVITZ, H., ROGOWSKI, O., CHARACH, L. & GROSSKOPF, I. J. Q. A. I. J. O. M. 2018. A

longitudinal 20 years of follow up showed a decrease in the survival of heart failure patients who maintained low LDL cholesterol levels. 111**,** 319-325.

CHARPENTIER, J., LUYT, C.-E., FULLA, Y., VINSONNEAU, C., CARIOU, A., GRABAR, S., DHAINAUT, J.-F., MIRA, J.-P. & CHICHE, J.-D. J. C. C. M. 2004. Brain natriuretic peptide: A marker of myocardial dysfunction and prognosis during severe sepsis. 32**,** 660-665.

CHATTERJEE, K. & MASSIE, B. J. J. O. C. F. 2007. Systolic and diastolic heart failure: differences and similarities. 13**,** 569-576.

CHATTERJEE, N. A., CHAE, C. U., KIM, E., MOORTHY, M. V., CONEN, D., SANDHU, R. K., COOK, N. R., LEE, I.-M. & ALBERT, C. M. J. J. H. F. 2017. Modifiable risk factors for incident heart failure in atrial fibrillation. 5**,** 552-560.

CHEN, H., DING, X., LI, J., WU, Z., WANG, Y., HE, H., YANG, Z., WU, J., WANG, Y. & XIE, D. J. M. 2018. White blood cell count: an independent predictor of coronary heart disease risk in middle-aged and elderly population with hyperuricemia. 97.

CHIABRANDO, J. G., BONAVENTURA, A., VECCHIÉ, A., WOHLFORD, G. F., MAURO, A. G., JORDAN, J. H., GRIZZARD, J. D., MONTECUCCO, F., BERROCAL, D. H. & BRUCATO, A. 2020. Management of acute and recurrent pericarditis: JACC state-of-the-art review. *Journal of the American College of Cardiology,* 75**,** 76-92.

CHIHA, J., MITCHELL, P., GOPINATH, B., PLANT, A. J., KOVOOR, P., THIAGALINGAM, A. J. I. H. & VASCULATURE 2015. Gender differences in the severity and extent of coronary artery disease. 8**,** 161-166.

CHOI, H.-M., PARK, M.-S. & YOUN, J.-C. J. T. K. J. O. I. M. 2019. Update on heart failure management and future directions. 34**,** 11.

CHOUIHED, T., ROSSIGNOL, P., BASSAND, A., DUARTE, K., KOBAYASHI, M., JAEGER, D., SADOUNE, S., BUESSLER, A., NACE, L. & GIACOMIN, G. J. C. R. I. C. 2019. Diagnostic and prognostic value of plasma volume status at emergency department admission in dyspneic patients: results from the PARADISE cohort. 108**,** 563-573.

CLELAND, J. G., CARUBELLI, V., CASTIELLO, T., YASSIN, A., PELLICORI, P. & ANTONY, R. J. H. F. R. 2012. Renal dysfunction in acute and chronic heart failure: prevalence, incidence and prognosis. 17**,** 133-149.

COLLABORATION, C. T. T. 2015. Efficacy and safety of LDL-lowering therapy among men and women: meta-analysis of individual data from 174,000 participants in 27 randomised trials.

CONTROL, C. F. D. & PREVENTION 2013. Office of Infectious Disease. *Antibiotic resistance threats in the United States*.

COOPER JR, L. T., KEREN, A., SLIWA, K., MATSUMORI, A. & MENSAH, G. A. 2014. The global burden of myocarditis: part 1: a systematic literature review for the Global Burden of Diseases, Injuries, and Risk Factors 2010 study. *Global Heart,* 9**,** 121-129.

COSTA, N. A., POLEGATO, B. F., PEREIRA, A. G., DA SILVA BASTOS, R. V., DE PAIVA, S. A. R., GUT, A. L., BALBI, A. L., PONCE, D., ZORNOFF, L. A. M. & AZEVEDO, P. S. 2019. Evaluation of peptidylarginine deiminase 4 concentration and PADI4 polymorphisms in sepsis-induced acute kidney injury.

CROFTS, T. S., GASPARRINI, A. J. & DANTAS, G. J. N. R. M. 2017. Next-generation approaches to understand and combat the antibiotic resistome. 15**,** 422-434.

CUI, J., LIANG, Z., MO, Z., ZHANG, J. J. A. R. & CONTROL, I. 2019. The species distribution, antimicrobial resistance and risk factors for poor outcome of coagulase-negative staphylococci bacteraemia in China. 8**,** 1-10.

DAGASSO, G., CONLEY, J., PARFITT, E., PASQUILL, K., STEELE, L. & LAUPLAND, K. 2018. Risk factors associated with bloodstream infections in end-stage renal disease patients: a population-based study. *Infectious Diseases,* 50**,** 831-836.

DAMMAN, K. & TESTANI, J. M. J. E. H. J. 2015. The kidney in heart failure: an update. 36**,** 1437-1444.

DAVEY, P., PAGLIARI, C. & HAYES, A. 2002. The patient's role in the spread and control of bacterial resistance to antibiotics. *Clinical Microbiology and Infection,* 8**,** 43-68.

DE BLASI, R. A., CARDELLI, P., COSTANTE, A., SANDRI, M., MERCIERI, M. & ARCIONI, R. J. I. C. M. 2013. Immature platelet fraction in predicting sepsis in critically ill patients. 39**,** 636-643.

DENTALI, F., SIRONI, A. P., AGENO, W., BONFANTI, C., CRESTANI, S., FRATTINI, F., STEIDL, L. & FRANCHINI, M. Relationship between ABO blood group and hemorrhage: a systematic literature review and meta-analysis. Seminars in thrombosis and hemostasis, 2013. Thieme Medical Publishers, 072-082.

DOCAN, A., GRECU, I., CREŢU, M., ANTACHE, A. & DEDIU, L. J. L. Ș.-U. D. Ș. A. Ș. M. V., SERIA ZOOTEHNIE 2017. Haematological and

serum biochemical changes associated with bacteriological infection in Acipenser gueldenstaedtii reared in intensive condition. 67**,** 104-109.
DREES, M., KANAPATHIPPILLAI, N. & ZUBROW, M. T. J. T. A. J. O. M. 2012. Bandemia with normal white blood cell counts associated with infection. 125**,** 1124. e9-1124. e15.
DUNN, J., ZHANG, Q., WEEKS, M. R., LI, J., LIAO, S. & LI, F. 2017. Indigenous HIV prevention beliefs and practices among low-earning Chinese sex workers as context for introducing female condoms and other novel prevention options. *Qualitative health research,* 27**,** 1302-1315.
DUPUY, A.-M., PHILIPPART, F., PÉAN, Y., LASOCKI, S., CHARLES, P.-E., CHALUMEAU, M., CLAESSENS, Y.-E., QUENOT, J.-P., GRAS-LE GUEN, C. & RUIZ, S. 2013. Role of biomarkers in the management of antibiotic therapy: an expert panel review: I–currently available biomarkers for clinical use in acute infections. *Annals of intensive care,* 3**,** 1-8.
EGEBLAD, H., WIERUP, P. & LAURSEN, A. L. 2005. Salmonella-infected left ventricular thrombus. *European heart journal,* 26**,** 2549-2549.
EGGERS, K. M. & LINDAHL, B. J. C. C. 2017. Application of cardiac troponin in cardiovascular diseases other than acute coronary syndrome. 63**,** 223-235.
EGOROV, N. S. 1985. *Antibiotics: A scientific approach*, Mir publishers.
EGWUATU, T. F. 2019 ANTIBIOTICS SENSITIVITY PATTERN OF MICROBES ISOLATED FROM BLOOD TONICS.
EHIGIATOR, O., AZODO, C. C., EHIZELE, A. O., EZEJA, E. B., EHIGIATOR, L. & MADUKWE, I. U. 2013. Self-medication practices among dental, midwifery and nursing students. *European Journal of General Dentistry,* 2**,** 54.
FADINI, G. P., AVOGARO, A., DEGLI ESPOSTI, L., RUSSO, P., SARAGONI, S., BUDA, S., ROSANO, G., PECORELLI, S., PANI, L. & JOURNAL, O. H.-D. N. J. E. H. 2015. Risk of hospitalization for heart failure in patients with type 2 diabetes newly treated with DPP-4 inhibitors or other oral glucose-lowering medications: a retrospective registry study on 127,555 patients from the Nationwide OsMed Health-DB Database. 36**,** 2454-2462.
FADWA, A. O., ALKOBLAN, D. K., MATEEN, A. & ALBARAG, A. M. J. S. J. O. B. S. 2021. Synergistic effects of zinc oxide nanoparticles and various antibiotics combination against Pseudomonas aeruginosa clinically isolated bacterial strains. 28**,** 928-935.

FALAGAS, M. E., VOULOUMANOU, E. K., SAMONIS, G. & VARDAKAS, K. Z. J. C. M. R. 2016. Fosfomycin. 29**,** 321-347.
FARKAS, J. D. J. J. O. T. D. 2020. The complete blood count to diagnose septic shock. 12**,** S16.
FATAHI-BAFGHI, M. 2019. Antibiotic resistance genes in the Actinobacteria phylum. *European Journal of Clinical Microbiology & Infectious Diseases,* 38**,** 1599-1624.
FELTZ DE FARIA, L. 2020. Análise do papel da neuraminidase na resposta fagocítica de neutrófilos humanos estimulados com LPS.
FOUNOU, L. L., FOUNOU, R. C. & ESSACK, S. Y. 2016. Antibiotic resistance in the food chain: a developing country-perspective. *Frontiers in microbiology*, 7**,** 1881.
FRYDRYCH, L. M., BIAN, G., O'LONE, D. E., WARD, P. A. & DELANO, M. J. J. J. O. L. B. 2018. Obesity and type 2 diabetes mellitus drive immune dysfunction, infection development, and sepsis mortality. 104**,** 525-534.
GAJDÁCS, M. 2019. The concept of an ideal antibiotic: implications for drug design. *Molecules,* 24**,** 892.
GAJDÁCS, M., PAULIK, E. & SZABÓ, A. 2020. Knowledge, attitude and practice of community pharmacists regarding antibiotic use and infectious diseases: a cross-sectional survey in Hungary (KAPPhA-HU). *Antibiotics,* 9**,** 41.
GALAR, A., WEIL, A. A., DUDZINSKI, D. M., MUÑOZ, P. & SIEDNER, M. J. 2019. Methicillin-resistant Staphylococcus aureus prosthetic valve endocarditis: pathophysiology, epidemiology, clinical presentation, diagnosis, and management. *Clinical microbiology reviews,* 32**,** e00041-18.
GANDHI, P. S. & GAMIT, B. N. 2019. The role of platelet indices in ischemic heart disease: a hospital based case control type of study.
GAO, Y., LI, Y., YU, X., GUO, S., JI, X., SUN, T., LAN, C., LAVERGNE, V., GHANNOUM, M. & LI, L. J. P. O. 2014. The impact of various platelet indices as prognostic markers of septic shock. 9**,** e103761.
GAO, Z., WANG, L., ZHOU, L. & ZHANG, J. 2016. HEp-2 cell image classification with deep convolutional neural networks. *IEEE journal of biomedical and health informatics,* 21**,** 416-428.
GARCIA, M., MULVAGH, S. L., BAIREY MERZ, C. N., BURING, J. E. & MANSON, J. E. J. C. R. 2016. Cardiovascular disease in women: clinical perspectives. 118**,** 1273-1293.

GIEDRAITIENĖ, A., VITKAUSKIENĖ, A., NAGINIENĖ, R. & PAVILONIS, A. 2011. Antibiotic resistance mechanisms of clinically important bacteria. *Medicina,* 47**,** 19.

GIULIANO, C., PATEL, C. R. & KALE-PRADHAN, P. B. 2019. A guide to bacterial culture identification and results interpretation. *Pharmacy and Therapeutics,* 44**,** 192.

GOLKAR, Z., BAGASRA, O. & PACE, D. G. 2014. Bacteriophage therapy: a potential solution for the antibiotic resistance crisis. *The Journal of Infection in Developing Countries,* 8**,** 129-136.

GONG, F. F., JELINEK, M. V., CASTRO, J. M., COLLER, J. M., MCGRADY, M., BOFFA, U., SHIEL, L., LIEW, D., WOLFE, R. & STEWART, S. J. O. H. 2018. Risk factors for incident heart failure with preserved or reduced ejection fraction, and valvular heart failure, in a community-based cohort. 5**,** e000782.

GOPALKRISHNA, S., AHMED, A. L., ANDREW, J. M. & PRABHAKARA, R. N. J. P. R. 2020. Emerging roles of neutrophil-borne S100A8/A9 in cardiovascular inflammation. 105212.

GRIMALDI, D., PODGLAJEN, I., AUBERT, A., BUU-HOÏ, A., DIEBOLD, B. & MAINARDI, J.-L. J. J. O. C. M. 2009. Case of indolent endocarditis due to Pseudomonas stutzeri with genetic evidence of relapse after 4 years. 47**,** 503-504.

GROOT, H. E., VILLEGAS SIERRA, L. E., SAID, M. A., LIPSIC, E., KARPER, J. C., VAN DER HARST, P. J. A., THROMBOSIS, & BIOLOGY, V. 2020. Genetically determined ABO blood group and its associations with health and disease. 40**,** 830-838.

GROUP, J. J. W. 2011. Guidelines for Diagnosis and Treatment of Myocarditis (JCS 2009)–Digest Version–. *Circulation Journal***,** 1102021098-1102021098.

GROUP, S. R. 2015. A randomized trial of intensive versus standard blood-pressure control. *New England Journal of Medicine,* 373**,** 2103-2116.

GUJYTĖ, G., MONGIRDIENĖ, A. & LAUKAITIENĖ, J. Correlation of Inflammation, Lipidogram and Clinical Read-ings in Chronic Heart Failure Patients. Presented at the 1st International Electronic Conference on Medicine, 2021. 30.

GUO, R., LI, K., QIN, J., NIU, S. & HONG, W. 2020. Development of polycationic micelles as an efficient delivery system of antibiotics for overcoming the biological barriers to reverse multidrug resistance in Escherichia coli. *Nanoscale,* 12**,** 11251-11266.

GUPTA, N., RAI, D. B., JANGID, A. K. & KULHARI, H. J. M. I. M. 2019. Use of nanotechnology in antimicrobial therapy. 46**,** 143-172.

GUTEMA, G. B., GADISA, D. A., KIDANEMARIAM, Z. A., BERHE, D. F., BERHE, A. H., HADERA, M. G., HAILU, G. S. & ABRHA, N. G. 2011. Self-medication practices among health sciences students: the case of Mekelle University. *Journal of Applied Pharmaceutical Science,* 1**,** 183.

HA, J., HONG, S. K., HAN, G. H., KIM, M., YONG, D. & LEE, K. J. A. O. L. M. 2018. Same-day identification and antimicrobial susceptibility testing of bacteria in positive blood culture broths using short-term incubation on solid medium with the MicroFlex LT, Vitek-MS, and Vitek2 systems. 38**,** 235-241.

HABIB, G., LANCELLOTTI, P., ANTUNES, M. J., BONGIORNI, M. G., CASALTA, J.-P., DEL ZOTTI, F., DULGHERU, R., EL KHOURY, G., ERBA, P. A. & IUNG, B. 2015. 2015 ESC guidelines for the management of infective endocarditis: the task force for the management of infective endocarditis of the European Society of Cardiology (ESC) endorsed by: European Association for Cardio-Thoracic Surgery (EACTS), the European Association of Nuclear Medicine (EANM). *European heart journal,* 36**,** 3075-3128.

HADDADIN, R. N., ALSOUS, M., WAZAIFY, M. & TAHAINEH, L. 2019. Evaluation of antibiotic dispensing practice in community pharmacies in Jordan: A cross sectional study. *PloS one,* 14**,** e0216115.

HAJOULI, S. & LUDHWANI, D. 2020. Heart failure and ejection fraction.

HALABI, Z., MOCADIE, M., EL ZEIN, S., KANJ, S. S. J. J. O. I. & HEALTH, P. 2019. Pseudomonas stutzeri prosthetic valve endocarditis: A case report and review of the literature. 12**,** 434-437.

HALLDIN, A.-K., LISSNER, L., LERNFELT, B. & BJÖRKELUND, C. J. B. O. 2020. Cholesterol and triglyceride levels in midlife and risk of heart failure in women, a longitudinal study: the prospective population study of women in Gothenburg. 10**,** e036709.

HALLE, M., BINZENHÖFER, L., MAHRHOLDT, H., SCHINDLER, M. J., ESEFELD, K. & TSCHÖPE, C. 2020. Myocarditis in athletes: a clinical perspective. *European journal of preventive cardiology***,** 2047487320909670.

HAMZEH, N., GHADIMI, F., FARZANEH, R. & HOSSEINI, S. K. J. T. J. O. T. U. H. C. 2017. Obesity, heart failure, and obesity paradox. 12**,** 1.

HASEGAWA, D., NISHIDA, K., KAWAJI, T., HARA, Y., SHIMOMURA, Y., MORIYAMA, K., NIIMI, D., KURIYAMA, N., SHINTANI, A. & KOMURA, H. J. D. 2020. Impact of blood type O on mortality of sepsis patients: a multicenter retrospective observational study. 10**,** 826.

HASHEMPOUR-BALTORK, F., HOSSEINI, H., SHOJAEE-ALIABADI, S., TORBATI, M., ALIZADEH, A. M. & ALIZADEH, M. 2019. Drug resistance and the prevention strategies in food borne bacteria: An update review. *Advanced pharmaceutical bulletin,* 9**,** 335.

HAZRATI, E., NOORIFARD, M., AFSAHI, M., ROHI, A., RAFIEI, M. J. J. O. A. P. E., RESEARCH & JAN-MAR 2018. The relationship between lipid profile and CRP in severe sepsis with patient prognosis. 8.

HELAL, R. & ABOU-ELWAFA, H. 2017. Self-medication in university students from the city of Mansoura, Egypt. *Journal of environmental and public health,* 2017.

HEMKENS, L. G. & BUCHER, H. C. 2014. HIV infection and cardiovascular disease. *European heart journal,* 35**,** 1373-1381.

HITZEROTH, J., BECKETT, N. & NTULI, P. J. S. A. M. J. 2016. An approach to a patient with infective endocarditis: CME. 106**,** 145-150.

HOGAS, S., BILHA, S. C., BRANISTEANU, D., HOGAS, M., GAIPOV, A., KANBAY, M. & COVIC, A. 2017. Potential novel biomarkers of cardiovascular dysfunction and disease: cardiotrophin-1, adipokines and galectin-3. *Archives of medical science: AMS,* 13**,** 897.

HOIT, B. & OH, J. K. 2016. Etiology of pericardial diseases.

HOMBACH, M., MAURER, F. P., PFIFFNER, T., BÖTTGER, E. C. & FURRER, R. 2015. Standardization of operator-dependent variables affecting precision and accuracy of the disk diffusion method for antibiotic susceptibility testing. *Journal of clinical microbiology,* 53**,** 3864-3869.

HOVLAND, A., MUNDAL, L. J., IGLAND, J., VEIERØD, M. B., HOLVEN, K. B., BOGSRUD, M. P., TELL, G. S., LEREN, T. P. & RETTERSTØL, K. J. A. 2017. Increased risk of heart failure and atrial fibrillation in heterozygous familial hypercholesterolemia. 266**,** 69-73.

HUHAND, Y. & KWON, J. 2011. Nanoantibiotics': anewparadigmfortreatinginfectiousdis-easesusingnanomaterialsintheantibioticsresistantera. JournalofControlledRelease.

IBANEZ, B., JAMES, S., AGEWALL, S., ANTUNES, M. J., BUCCIARELLI-DUCCI, C., BUENO, H., CAFORIO, A. L., CREA, F., GOUDEVENOS, J. A. & HALVORSEN, S. 2018. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). *European heart journal,* 39**,** 119-177.

IBRAHIM, N. & JANUZZI, J. L. J. E. R. O. C. T. 2015. The potential role of natriuretic peptides and other biomarkers in heart failure diagnosis, prognosis and management. 13**,** 1017-1030.

INAMDAR, A. A. & INAMDAR, A. C. 2016. Heart failure: diagnosis, management and utilization. *Journal of clinical medicine,* 5**,** 62.

IOANNOU, P., MAVRIKAKI, V. & KOFTERIDIS, D. P. J. J. O. C. 2021. Infective endocarditis by Acinetobacter species: A systematic review. 33**,** 203-215.

JORGENSEN, J. H. & TURNIDGE, J. D. 2015. Susceptibility test methods: dilution and disk diffusion methods. *Manual of clinical microbiology***,** 1253-1273.

JOSEPH, C. 2020. Modern Biomarkers those are effective in diagnosing neonatal sepsis (Early and Late).

JUJO, K., MINAMI, Y., HARUKI, S., MATSUE, Y., SHIMAZAKI, K., KADOWAKI, H., ISHIDA, I., KAMBAYASHI, K., ARASHI, H. & SEKIGUCHI, H. J. E. H. F. 2017. Persistent high blood urea nitrogen level is associated with increased risk of cardiovascular events in patients with acute heart failure. 4**,** 545-553.

KAKIHANA, Y., ITO, T., NAKAHARA, M., YAMAGUCHI, K. & YASUDA, T. 2016. Sepsis-induced myocardial dysfunction: pathophysiology and management. *Journal of intensive care,* 4**,** 1-10.

KAYA, H., YıLDıRıML ı, M. K., KURT, R., BETON, O. & YILMAZ, M. B. J. A. C. S. 2017. Mean platelet volume as a predictor of heart failure-related hospitalizations in stable heart failure outpatients with sinus rhythm. 33**,** 292.

KEYZER, J. M., HOFFMANN, J. J., RINGOIR, L., NABBE, K. C., WIDDERSHOVEN, J. W., POP, V. J. J. C. C. & MEDICINE, L. 2014. Age-and gender-specific brain natriuretic peptide (BNP) reference ranges in primary care. 52**,** 1341-1346.

KHADEMI, F., VAEZ, H., MOMTAZI-BOROJENI, A. A., MAJNOONI, A., BANACH, M. & SAHEBKAR, A. J. A. O. M. S. A. 2019. Bacterial infections are associated with cardiovascular disease in Iran: a meta-analysis. 15**,** 902.

KHODE, V., SINDHUR, J., KANBUR, D., RUIKAR, K. & NALLULWAR, S. J. J. O. C. D. R. 2012. Mean platelet volume and other platelet volume indices in patients with stable coronary artery disease and acute myocardial infarction: A case control study. 3**,** 272-275.

KIM, J. H., LIM, S., PARK, K. S., JANG, H. C. & CHOI, S. H. 2017. Total and differential WBC counts are related with coronary artery

atherosclerosis and increase the risk for cardiovascular disease in Koreans. *PloS one,* 12**,** e0180332.

KIM, W. & KIM, E. J. 2018. Heart failure as a risk factor for stroke. *Journal of stroke,* 20**,** 33.

KISHIMOTO, S., MARUHASHI, T., KAJIKAWA, M., MATSUI, S., HASHIMOTO, H., TAKAEKO, Y., HARADA, T., YAMAJI, T., HAN, Y. & KIHARA, Y. J. S. R. 2020. Hematocrit, hemoglobin and red blood cells are associated with vascular function and vascular structure in men. 10**,** 1-9.

KLEBER, M., KOZHUHAROV, N., SABTI, Z., GLATZ, B., ISENREICH, R., WUSSLER, D., NOWAK, A., TWERENBOLD, R., BADERTSCHER, P. & PUELACHER, C. J. I. J. O. C. 2019. Relative hypochromia and mortality in acute heart failure. 286**,** 104-110.

KOLEKAR, T., YADAV, H., BANDGAR, S. & DESHMUKH, P. J. I. S. R. J. 2011. Synthesis by sol–gel method and characterization of ZnO nanoparticles. 1**,** 1-4.

KONG, D.-X., XIAO, Y.-X., ZHANG, Z.-X. & LIU, Y.-B. J. P. J. O. M. S. 2020. Study on the Correlation between Metabolism, Insulin Sensitivity and progressive weight loss change in Type-2 Diabetes. 36**,** 1523.

KOZDAG, G., ERTAS, G., EMRE, E., AKAY, Y., CELIKYURT, U., SAHIN, T., GORUR, G., KARAUZUM, K., YILMAZ, I. & URAL, D. J. T. H. I. J. 2013. Low serum triglyceride levels as predictors of cardiac death in heart failure patients. 40**,** 521.

KREITMANN, L., MONTAIGNE, D., LAUNAY, D., MORELL-DUBOIS, S., MAILLARD, H., LAMBERT, M., HACHULLA, E. & SOBANSKI, V. J. J. O. C. M. 2020. Clinical characteristics and outcome of patients with infective endocarditis diagnosed in a department of internal medicine. 9**,** 864.

KSIĄŻCZYK, M., KUCZKOWSKI, M., DUDEK, B., KORZEKWA, K., TOBIASZ, A., KORZENIOWSKA-KOWAL, A., PALUCH, E., WIELICZKO, A. & BUGLA-PŁOSKOŃSKA, G. J. C. M. 2016. Application of routine diagnostic procedure, VITEK 2 compact, MALDI-TOF MS, and PCR assays in identification procedure of bacterial strain with ambiguous phenotype. 72**,** 570-582.

LAHMIDI, I., CHARMAKE III, D., ELOUAFI, N. & BAZID, Z. J. C. 2020. Acinetobacter Baumannii Native Valve Infective Endocarditis: A Case Report. 12.

LAM, C. S., ARNOTT, C., BEALE, A. L., CHANDRAMOULI, C., HILFIKER-KLEINER, D., KAYE, D. M., KY, B., SANTEMA, B. T.,

SLIWA, K. & VOORS, A. A. 2019. Sex differences in heart failure. *European heart journal,* 40**,** 3859-3868c.
LAVIE, C. J., SHARMA, A., ALPERT, M. A., DE SCHUTTER, A., LOPEZ-JIMENEZ, F., MILANI, R. V. & VENTURA, H. O. J. P. I. C. D. 2016. Update on obesity and obesity paradox in heart failure. 58**,** 393-400.
LEE, C. S. & AULD, J. 2015. Heart Failure: A Primer. *Critical Care Nursing Clinics,* 27**,** 413-425.
LEE, N.-Y., KO, W.-C. & HSUEH, P.-R. J. F. I. P. 2019. Nanoparticles in the treatment of infections caused by multidrug-resistant organisms. 10**,** 1153.
LEONG, K., KANE, J. M. & JOY, B. F. 2018. Acquired Cardiac Disease in the Pediatric Intensive Care Unit. *Pediatric annals,* 47**,** e280-e285.
LI, B., LU, J., PENG, D.-Z., ZHANG, X.-Y. & YOU, Z. J. M. 2020a. Elevated platelet distribution width predicts poor prognosis in hilar cholangiocarcinoma. 99.
LI, B. & WEBSTER, T. J. 2018. Bacteria antibiotic resistance: New challenges and opportunities for implant-associated orthopedic infections. *Journal of Orthopaedic Research®,* 36**,** 22-32.
LI, H., HASTINGS, M. H., RHEE, J., TRAGER, L. E., ROH, J. D. & ROSENZWEIG, A. J. C. R. 2020b. Targeting age-related pathways in heart failure. 126**,** 533-551.
LI, H., LUO, Y.-F., WILLIAMS, B. J., BLACKWELL, T. S. & XIE, C.-M. 2012. Structure and function of OprD protein in Pseudomonas aeruginosa: from antibiotic resistance to novel therapies. *International Journal of Medical Microbiology,* 302**,** 63-68.
LI, T., LIU, C., LU, J., GAURAV, G. K. & CHEN, W. 2020c. Determination of how tetracycline influences nitrogen removal performance, community structure, and functional genes of biofilm systems. *Journal of the Taiwan Institute of Chemical Engineers,* 106**,** 99-109.
LINDENFELD, J., ALBERT, N. M., BOEHMER, J. P., COLLINS, S. P., EZEKOWITZ, J. A., GIVERTZ, M. M., KATZ, S. D., KLAPHOLZ, M., MOSER, D. K. & ROGERS, J. G. 2010. HFSA 2010 comprehensive heart failure practice guideline. *Journal of cardiac failure,* 16**,** e1-194.
LIPPI, G., TURCATO, G., CERVELLIN, G. & SANCHIS-GOMAR, F. J. W. J. O. C. 2018. Red blood cell distribution width in heart failure: a narrative review. 10**,** 6.
LIVERTOX, N. J. B. N. I. O. D., DIGESTIVE & DISEASES, K. 2012. Clinical and Research Information on Drug-Induced Liver Injury.

LOCKHART, P. B., BRENNAN, M. T., SASSER, H. C., FOX, P. C., PASTER, B. J. & BAHRANI-MOUGEOT, F. K. 2008. Bacteremia associated with toothbrushing and dental extraction. *Circulation,* 117**,** 3118-3125.

MAGGIONI, A. P., DAHLSTRÖM, U., FILIPPATOS, G., CHIONCEL, O., LEIRO, M. C., DROZDZ, J., FRUHWALD, F., GULLESTAD, L., LOGEART, D. & FABBRI, G. 2013. EURObservational Research Programme: regional differences and 1-year follow-up results of the Heart Failure Pilot Survey (ESC-HF Pilot). *European journal of heart failure,* 15**,** 808-817.

MAGKOS, F., FRATERRIGO, G., YOSHINO, J., LUECKING, C., KIRBACH, K., KELLY, S. C., DE LAS FUENTES, L., HE, S., OKUNADE, A. L. & PATTERSON, B. W. J. C. M. 2016. Effects of moderate and subsequent progressive weight loss on metabolic function and adipose tissue biology in humans with obesity. 23**,** 591-601.

MAGNUSSEN, C., NIIRANEN, T. J., OJEDA, F. M., GIANFAGNA, F., BLANKENBERG, S., VARTIAINEN, E., SANS, S., PASTERKAMP, G., HUGHES, M. & COSTANZO, S. 2019. Sex-specific epidemiology of heart failure risk and mortality in Europe: results from the BiomarCaRE Consortium. *JACC: Heart Failure,* 7**,** 204-213.

MAHAPATRA, S. & HEFFNER, A. C. 2017. Septic shock.

MAISEL, A. S., DURAN, J. M. & WETTERSTEN, N. J. H. F. C. 2018. Natriuretic peptides in heart failure: atrial and B-type natriuretic peptides. 14**,** 13-25.

MAJUMDER, B., JAIN, H., CHATTERJEE, S. & DAS, T. K. J. N. J. O. C. 2018. Study of platelet count and platelet volume indices in the spectrum of coronary artery diseases and its clinicopathological correlation. 15**,** 63.

MALARKODI, C., RAJESHKUMAR, S., PAULKUMAR, K., VANAJA, M., GNANAJOBITHA, G., ANNADURAI, G. J. B. C. & APPLICATIONS 2014. Biosynthesis and antimicrobial activity of semiconductor nanoparticles against oral pathogens. 2014.

MALIK, A., BRITO, D. & CHHABRA, L. 2020. Congestive Heart Failure (CHF). *StatPearls [Internet]*. StatPearls Publishing.

MAMAS, M. A., SPERRIN, M., WATSON, M. C., COUTTS, A., WILDE, K., BURTON, C., KADAM, U. T., KWOK, C. S., CLARK, A. B. & MURCHIE, P. 2017. Do patients have worse outcomes in heart failure than in cancer? A primary care-based cohort study with 10-year follow-up in Scotland. *European journal of heart failure,* 19**,** 1095-1104.

MARÇULA, M., DE SOUZA BUTO, M. F., MADALOSO, B. A., NUNES, R. A. B., CUOCO, M. A. R., DE PAULA, R. S., YAMADA, A. T., SANDOVAL, M. C., BOTTER, D. A. & MANSUR, A. J. J. I. J. O. C. 2015. Lymphocyte count and prognosis in patients with heart failure. 188**,** 60-62.

MASSON, S., CAIRONI, P., FANIZZA, C., CARRER, S., CARICATO, A., FASSINI, P., VAGO, T., ROMERO, M., TOGNONI, G. & GATTINONI, L. J. C. C. M. 2016. Sequential N-terminal pro-B-type natriuretic peptide and high-sensitivity cardiac troponin measurements during albumin replacement in patients with severe sepsis or septic shock. 44**,** 707-716.

MATSUE, Y., VAN DER MEER, P., DAMMAN, K., METRA, M., O'CONNOR, C. M., PONIKOWSKI, P., TEERLINK, J. R., COTTER, G., DAVISON, B. & CLELAND, J. G. J. H. 2017. Blood urea nitrogen-to-creatinine ratio in the general population and in patients with acute heart failure. 103**,** 407-413.

MATUSIAK, A., CHAŁUBIŃSKI, M., BRONCEL, M., RECHCIŃSKI, T., RUDNICKA, K., MISZCZYK, E., WALENCKA, M., STRAPAGIEL, D., GAJEWSKI, A. & CHMIELA, M. 2016. Putative consequences of exposure to Helicobacter pylori infection in patients with coronary heart disease in terms of humoral immune response and inflammation. *Archives of medical science: AMS,* 12**,** 45.

MCEVOY, J. W., CHEN, Y., RAWLINGS, A., HOOGEVEEN, R. C., BALLANTYNE, C. M., BLUMENTHAL, R. S., CORESH, J. & SELVIN, E. J. J. O. T. A. C. O. C. 2016. Diastolic blood pressure, subclinical myocardial damage, and cardiac events: implications for blood pressure control. 68**,** 1713-1722.

MCINTYRE, V., BUTANY, J., BOLES, D. & SHAO, T. 2017. Recurrent infective endocarditis causing heart valve failure: A case report. *Human Pathology: Case Reports,* 10**,** 39-42.

MCNEIL, A. 2007. The trouble with troponin. *Heart, Lung and Circulation*, 16**,** S13-S16.

MEISNER, M. 2005. Biomarkers of sepsis: clinically useful? *Current opinion in critical care,* 11**,** 473-480.

MENSAH, S., KOUDANDÉ, O., SANDERS, P., LAURENTIE, M., MENSAH, G. & ABIOLA, F. 2014. Antimicrobial residues in foods of animal origin in Africa: public health risks. *Rev Sci Tech,* 33**,** 987-96.

MERSICH, A. ADVANCED BLOOD-PRESSURE MEASUREMENT AT HOME. 12TH PHD MINI-SYMPOSIUM, 2005. 26.

MESQUITA, E. T. J. A. B. D. C. 2018. Infections in heart failure-impact on mortality. 110**,** 371-372.

MICHAEL, C. A., DOMINEY-HOWES, D. & LABBATE, M. 2014. The antimicrobial resistance crisis: causes, consequences, and management. *Frontiers in public health,* 2**,** 145.

MOHAN, N., GEDELA, V. P., VOONA, M. K. & KOLLI, V. K. Diagnostic Role of RDW & PDW as Early Markers of Sepsis in Chemotherapy Induced Febrile Neutropenia.

MOJADIDI, M. K., GALEAS, J. N., GOODMAN-MEZA, D., ESHTEHARDI, P., MSAOUEL, P., KELESIDIS, I., ZAMAN, M. O., WINOKER, J. S., ROBERTS, S. C., CHRISTIA, P. J. H., LUNG & CIRCULATION 2016. Thrombocytopaenia as a prognostic indicator in heart failure with reduced ejection fraction. 25**,** 568-575.

MONSERRAT-MARTINEZ, A., GAMBIN, Y. & SIERECKI, E. 2019. Thinking outside the bug: molecular targets and strategies to overcome antibiotic resistance. *International journal of molecular sciences,* 20**,** 1255.

MORKA, K., BYSTROŃ, J., BANIA, J., KORZENIOWSKA-KOWAL, A., KORZEKWA, K., GUZ-REGNER, K. & BUGLA-PŁOSKOŃSKA, G. J. B. M. 2018. Identification of Yersinia enterocolitica isolates from humans, pigs and wild boars by MALDI TOF MS. 18**,** 1-10.

MOZAFFARIAN, D., BENJAMIN, E. J., GO, A. S., ARNETT, D. K., BLAHA, M. J., CUSHMAN, M., DAS, S. R., DE FERRANTI, S., DESPRÉS, J.-P. & FULLERTON, H. J. 2016. Heart disease and stroke statistics—2016 update: a report from the American Heart Association. *circulation,* 133**,** e38-e360.

MOZOS, I. J. B. R. I. 2015. Mechanisms linking red blood cell disorders and cardiovascular diseases. 2015.

MUJAHID, A. & DICKERT, F. L. J. S. 2016. Blood group typing: from classical strategies to the application of synthetic antibodies generated by molecular imprinting. 16**,** 51.

MUKHERJEE, A., SADIQ, I. M., PRATHNA, T., CHANDRASEKARAN, N. J. S. A. M. P. C. C. R. & ADVANCES, T. 2011. Antimicrobial activity of aluminium oxide nanoparticles for potential clinical applications. 1**,** 245-251.

MURPHY, W. G. J. B. R. 2014. The sex difference in haemoglobin levels in adults—mechanisms, causes, and consequences. 28**,** 41-47.

MUZAMMIL, S., HAYAT, S., FAKHAR-E-ALAM, M., ASLAM, B., SIDDIQUE, M. H., NISAR, M. A., SAQALEIN, M., ATIF, M.,

SARWAR, A. & KHURSHID, A. J. F. B. 2018. Nanoantibiotics: Future nanotechnologies to combat antibiotic resistance. 10**,** 352-374.
NAJAFI, F., DOBSON, A. J., HOBBS, M. & JAMROZIK, K. J. E. J. O. H. F. 2007. Temporal trends in the frequency and longer-term outcome of heart failure complicating myocardial infarction. 9**,** 879-885.
NAKAGOMI, A., SEINO, Y., NOMA, S., KOHASHI, K., KOSUGI, M., KATO, K., KUSAMA, Y., ATARASHI, H. & SHIMIZU, W. J. I. M. 2014. Relationships between the serum cholesterol levels, production of monocyte proinflammatory cytokines and long-term prognosis in patients with chronic heart failure. 53**,** 2415-2424.
NIELSEN, J. C., GERDES, J. C. & VARMA, N. 2015. Infected cardiac-implantable electronic devices: prevention, diagnosis, and treatment. *European heart journal,* 36**,** 2484-2490.
NTUSI, N., AUBIN, L., OLIVER, S., WHITELAW, A. & MENDELSON, M. J. S. A. M. J. 2010. Guideline for the optimal use of blood cultures: guideline. 100**,** 839-843.
NUNES, M. C. P., GUIMARÃES-JÚNIOR, M. H., PINTO, P. H. O. M., COELHO, R. M. P., BARROS, T. L. S., MAIA, N. D. P. A. F., MADUREIRA, D. A., REIS, R. C. P., COSTA, P. H. N. & BRÁULIO, R. J. I. J. O. I. D. 2018. Outcomes of infective endocarditis in the current era: early predictors of a poor prognosis. 68**,** 102-107.
O'NEILL, J. 2016. Review on antimicrobial resistance: tackling drug-resistant infections globally: final report and recommendations. *Review on antimicrobial resistance: tackling drug-resistant infections globally: final report and recommendations.*
OKAMOTO, R., ALI, Y., HASHIZUME, R., SUZUKI, N. & ITO, M. J. I. J. O. M. S. 2019. BNP as a major player in the heart-kidney connection. 20**,** 3581.
OKUNO, K., NAITO, Y., ASAKURA, M., SUGAHARA, M., ANDO, T., YASUMURA, S., NAGAI, T., SAITO, Y., YOSHIKAWA, T., MASUYAMA, T. J. H. & VESSELS 2019. Effective blood hemoglobin level to predict prognosis in heart failure with preserved left ventricular ejection fraction: results of the Japanese heart failure syndrome with preserved ejection fraction registry. 34**,** 1168-1177.
OLMOS, C., VILACOSTA, I., FERNANDEZ, C., LOPEZ, J., SARRIA, C., FERRERA, C., REVILLA, A., SILVA, J., VIVAS, D. & GONZALEZ, I. 2013. Contemporary epidemiology and prognosis of septic shock in infective endocarditis. *European heart journal,* 34**,** 1999-2006.
ORG/CLINICAL_BREAKPOINTS, E. C. O. A. S. T. J. E. H. E. 2020. Clinical breakpointsbreakpoints and guidance.

OSEMENE, K. & LAMIKANRA, A. 2012. A study of the prevalence of self-medication practice among university students in Southwestern Nigeria. *Tropical Journal of Pharmaceutical Research,* 11**,** 683-689.

PAGE-SHIPP, L., LEWIS, J. J., VELEN, K., SENOGE, S., ZISHIRI, E., POPANE, F., CHIHOTA, V. N., CLARK, D., CHURCHYARD, G. J. & CHARALAMBOUS, S. 2018. Household point of care CD4 testing and isoniazid preventive therapy initiation in a household TB contact tracing programme in two districts of South Africa. *PloS one,* 13**,** e0192089.

PAL, S., TAK, Y. K., SONG, J. M. J. A. & MICROBIOLOGY, E. 2007. Does the antibacterial activity of silver nanoparticles depend on the shape of the nanoparticle? A study of the gram-negative bacterium Escherichia coli. 73**,** 1712-1720.

PANDEY, A., CORNWELL, W. K., WILLIS, B., NEELAND, I. J., GAO, A., LEONARD, D., DEFINA, L. & BERRY, J. D. J. J. H. F. 2017. Body mass index and cardiorespiratory fitness in mid-life and risk of heart failure hospitalization in older age: findings from the Cooper Center Longitudinal Study. 5**,** 367-374.

PARADIS, J.-M., FRIED, J., NAZIF, T., KIRTANE, A., HARJAI, K., KHALIQUE, O., GRUBB, K., GEORGE, I., HAHN, R. & WILLIAMS, M. J. E. H. J. 2014. Aortic stenosis and coronary artery disease: what do we know? What don't we know? A comprehensive review of the literature with proposed treatment algorithms. 35**,** 2069-2082.

PARK, S. H., HA, S. O., CHO, Y.-U., PARK, C.-J., JANG, S. & HONG, S.-B. J. A. O. L. M. 2016. Immature platelet fraction in septic patients: clinical relevance of immature platelet fraction is limited to the sensitive and accurate discrimination of septic patients from non-septic patients, not to the discrimination of sepsis severity. 36**,** 1-8.

PÉREZ-LLARENA, F. J. & BOU, G. 2016. Proteomics as a tool for studying bacterial virulence and antimicrobial resistance. *Frontiers in microbiology,* 7**,** 410.

PÉREZ, J., CONTRERAS-MORENO, F. J., MARCOS-TORRES, F. J., MORALEDA-MUÑOZ, A., MUÑOZ-DORADO, J. J. C. & JOURNAL, S. B. 2020. The antibiotic crisis: How bacterial predators can help.

PHILLIPS, H. R., O'CONNOR, C. M. & ROGERS, J. 2007. Revascularization for heart failure. *American heart journal,* 153**,** 65-73.

PONIKOWSKI, P., ANKER, S. D., ALHABIB, K. F., COWIE, M. R., FORCE, T. L., HU, S., JAARSMA, T., KRUM, H., RASTOGI, V. & ROHDE, L. E. 2014. Heart failure: preventing disease and death worldwide. *ESC heart failure,* 1**,** 4-25.

PONIKOWSKI, P., VOORS, A. A., ANKER, S. D., BUENO, H., CLELAND, J. G., COATS, A. J., FALK, V., GONZÁLEZ-JUANATEY, J. R., HARJOLA, V.-P. & JANKOWSKA, E. A. 2016. ESC Scientific Document Group. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur Heart J,* 37**,** 2129-2200.

POTTER, L. R., YODER, A. R., FLORA, D. R., ANTOS, L. K., DICKEY, D. M. J. C. G., EFFECTORS & IMPLICATIONS, T. 2009. Natriuretic peptides: their structures, receptors, physiologic functions and therapeutic applications. 341-366.

PRASHANTH, K., VASANTH, T., SARANATHAN, R., MAKKI, A. R. & PAGAL, S. 2012. Antibiotic resistance, biofilms and quorum sensing in Acinetobacter species. *Antibiotic resistant bacteria: a continuous challenge in the new millennium***,** 179-212.

PULIDO, M. R., GARCÍA-QUINTANILLA, M., MARTÍN-PEÑA, R., CISNEROS, J. M. & MCCONNELL, M. J. 2013. Progress on the development of rapid methods for antimicrobial susceptibility testing. *Journal of Antimicrobial Chemotherapy,* 68**,** 2710-2717.

PUREK, L., LAULE-KILIAN, K., CHRIST, A., KLIMA, T., PFISTERER, M. E., PERRUCHOUD, A. P. & MUELLER, C. 2006. Coronary artery disease and outcome in acute congestive heart failure. *Heart,* 92**,** 598-602.

RAJIAH, P. 2011. Cardiac MRI: part 2, pericardial diseases. *American Journal of Roentgenology,* 197**,** W621-W634.

RASHID, M., SULAIMAN, N., MUSTAFA, M., KHATUN, S. & BARI, B. S. The classification of EEG signal using different machine learning techniques for BCI application. International Conference on Robot Intelligence Technology and Applications, 2018. Springer, 207-221.

RECHCIŃSKI, T., JASIŃSKA, A., FORYŚ, J., KRZEMIŃSKA-PAKUŁA, M., WIERZBOWSKA-DRABIK, K., PLEWKA, M., PERUGA, J. Z. & KASPRZAK, J. D. J. C. J. 2013. Prognostic value of platelet indices after acute myocardial infarction treated with primary percutaneous coronary intervention. 20**,** 491-498.

RELLER, L. B., WEINSTEIN, M., JORGENSEN, J. H. & FERRARO, M. J. 2009. Antimicrobial susceptibility testing: a review of general principles and contemporary practices. *Clinical infectious diseases,* 49**,** 1749-1755.

REN, Z., MO, X., CHEN, H. & PENG, J. J. B. I. D. 2019. A changing profile of infective endocarditis at a tertiary hospital in China: a retrospective study from 2001 to 2018. 19**,** 1-10.

REVILLA, A., LÓPEZ, J., VILACOSTA, I., VILLACORTA, E., ROLLÁN, M. J., ECHEVARRÍA, J. R., CARRASCAL, Y., DI STEFANO, S., FULQUET, E. & RODRÍGUEZ, E. 2007. Clinical and prognostic profile of patients with infective endocarditis who need urgent surgery. *European heart journal,* 28**,** 65-71.

ROBERTS, E., LUDMAN, A. J., DWORZYNSKI, K., AL-MOHAMMAD, A., COWIE, M. R., MCMURRAY, J. J. & MANT, J. 2015. The diagnostic accuracy of the natriuretic peptides in heart failure: systematic review and diagnostic meta-analysis in the acute care setting. *Bmj,* 350.

RODGERS, J. L., JONES, J., BOLLEDDU, S. I., VANTHENAPALLI, S., RODGERS, L. E., SHAH, K., KARIA, K., PANGULURI, S. K. J. J. O. C. D. & DISEASE 2019. Cardiovascular risks associated with gender and aging. 6**,** 19.

RUPPAR, T. M., COOPER, P. S., MEHR, D. R., DELGADO, J. M. & DUNBAR-JACOB, J. M. J. J. O. T. A. H. A. 2016. Medication adherence interventions improve heart failure mortality and readmission rates: systematic review and meta-analysis of controlled trials. 5**,** e002606.

SALVAGNO, G. L., SANCHIS-GOMAR, F., PICANZA, A. & LIPPI, G. J. C. R. I. C. L. S. 2015. Red blood cell distribution width: a simple parameter with multiple clinical applications. 52**,** 86-105.

SANTAJIT, S. & INDRAWATTANA, N. 2016. Mechanisms of antimicrobial resistance in ESKAPE pathogens. *BioMed research international,* 2016.

SASIKUMAR, C., KUMAR, V. N., MOHANA, S. & YASODHA, S. 2016. Enhanced Antagonistic Bacterial Activity of Meropenem with Bioattuned Nanodriblet against Listeria monocytogeneses. *Research Journal of Pharmacy and Technology,* 9**,** 1043-1054.

SATO, M., INAI, K., OGISO, M., KUDO, Y., NISHIMURA, T., MORI, H., HARADA, G., ASAGAI, S., SHIMADA, E. & ISHIDO, M. J. E. H. J. 2020a. Platelet volume indices correlate to severity of heart failure and

have prognostic value for both cardiac and thrombotic events in patients with congenital heart disease. 41**,** ehaa946. 2208.

SATO, Y., YOSHIHISA, A., WATANABE, K., HOTSUKI, Y., KIMISHIMA, Y., YOKOKAWA, T., MISAKA, T., SATO, T., KANESHIRO, T. & OIKAWA, M. J. P. O. 2020b. Association between platelet distribution width and prognosis in patients with heart failure. 15**,** e0244608.

SAVARESE, G. & LUND, L. H. 2017. Global public health burden of heart failure. *Cardiac failure review,* 3**,** 7.

SCHELLACK, N., BENJAMIN, D., BRINK, A., DUSE, A., FAURE, K., GOFF, D., MENDELSON, M., MEYER, J., MIOT, J. & PEROVIC, O. 2017. A situational analysis of current antimicrobial governance, regulation, and utilization in South Africa. *International journal of infectious diseases,* 64**,** 100-106.

SEIGEL, T. A., COCCHI, M. N., SALCICCIOLI, J., SHAPIRO, N. I., HOWELL, M., TANG, A. & DONNINO, M. W. J. T. J. O. E. M. 2012. Inadequacy of temperature and white blood cell count in predicting bacteremia in patients with suspected infection. 42**,** 254-259.

SHAH, A. D., DENAXAS, S., NICHOLAS, O., HINGORANI, A. D. & HEMINGWAY, H. J. J. O. T. A. C. O. C. 2017. Neutrophil counts and initial presentation of 12 cardiovascular diseases: a CALIBER cohort study. 69**,** 1160-1169.

SHAIKH, S. A., JAIN, T., SANDHU, G., LATHA, N. & JAYARAM, B. 2007. From drug target to leads-sketching a physicochemical pathway for lead molecule design in silico. *Current pharmaceutical design,* 13**,** 3454-3470.

SHARMA, A., OOMMEN, S., TOPNO, I. & SAYA, R. P. 2015. Perceptions and practices of self-medication in healthcare and nonhealthcare university students in South India. *Journal of basic and clinical physiology and pharmacology,* 26**,** 633-640.

SHEYIN, O., DAVIES, O., DUAN, W., PEREZ, X. J. H. & LUNG 2015. The prognostic significance of troponin elevation in patients with sepsis: a meta-analysis. 44**,** 75-81.

SHRESTHA, L. B., BHATTARAI, N. R., KHANAL, B. J. I. & RESISTANCE, D. 2018. Comparative evaluation of methods for the detection of biofilm formation in coagulase-negative staphylococci and correlation with antibiogram. 11**,** 607.

SIMON, L., GAUVIN, F., AMRE, D. K., SAINT-LOUIS, P. & LACROIX, J. 2004. Serum procalcitonin and C-reactive protein levels as markers

of bacterial infection: a systematic review and meta-analysis. *Clinical infectious diseases,* 39**,** 206-217.

SINGER, M., DEUTSCHMAN, C. S., SEYMOUR, C. W., SHANKAR-HARI, M., ANNANE, D., BAUER, M., BELLOMO, R., BERNARD, G. R., CHICHE, J.-D. & COOPERSMITH, C. M. 2016. The third international consensus definitions for sepsis and septic shock (Sepsis-3). *Jama,* 315**,** 801-810.

SINGHAL, P., LUK, A. & BUTANY, J. 2013. Bioprosthetic heart valves: impact of implantation on biomaterials. *International Scholarly Research Notices,* 2013.

SOEHNLEIN, O., STEFFENS, S., HIDALGO, A. & WEBER, C. J. N. R. I. 2017. Neutrophils as protagonists and targets in chronic inflammation. 17**,** 248-261.

SOUTHON, S. B., BERES, S. B., KACHROO, P., SAAVEDRA, M. O., ERLENDSDÓTTIR, H., HARALDSSON, G., YERRAMILLI, P., PRUITT, L., ZHU, L. & MUSSER, J. M. 2020. Population genomic molecular epidemiological study of macrolide-resistant Streptococcus pyogenes in Iceland, 1995 to 2016: identification of a large clonal population with a pbp2x mutation conferring reduced in vitro β-lactam susceptibility. *Journal of clinical microbiology,* 58**,** e00638-20.

SPINAR, J., JARKOVSKY, J., SPINAROVA, L., MEBAZAA, A., GAYAT, E., VITOVEC, J., LINHART, A., WIDIMSKY, P., MIKLIK, R. & ZEMAN, K. 2016. AHEAD score—long-term risk classification in acute heart failure. *International journal of cardiology,* 202**,** 21-26.

STEENMAN, M. & LANDE, G. J. B. R. 2017. Cardiac aging and heart disease in humans. 9**,** 131-137.

STUDENT, P. & MIRELA, P. HEMATOLOGICAL CHANGES IN HEART FAILURE.

SUD, M., WANG, X., AUSTIN, P. C., LIPSCOMBE, L. L., NEWTON, G. E., TU, J. V., VASAN, R. S. & LEE, D. S. J. E. H. J. 2015. Presentation blood glucose and death, hospitalization, and future diabetes risk in patients with acute heart failure syndromes. 36**,** 924-931.

SULEIMAN, S. A., ONAOLAPO, J. A. & OLAYINKA, B. O. 2020. Molecular detection of chloramphenicol-florfenicol resistance (cfr) genes among linezolid resistant MRSA isolates in Sokoto State, Nigeria. *Journal of Health & Biological Sciences,* 8**,** 1-6.

SUNDSTRÖM, J., BRUZE, G., OTTOSSON, J., MARCUS, C., NÄSLUND, I. & NEOVIUS, M. J. C. 2017. Weight loss and heart failure: a nationwide study of gastric bypass surgery versus intensive lifestyle treatment. 135**,** 1577-1585.

SYAL, K., MO, M., YU, H., IRIYA, R., JING, W., GUODONG, S., WANG, S., GRYS, T. E., HAYDEL, S. E. & TAO, N. 2017. Current and emerging techniques for antibiotic susceptibility tests. *Theranostics,* 7**,** 1795.

TAMELYTĖ, E., VAIČEKAUSKIENĖ, G., DAGYS, A., LAPINSKAS, T. & JANKAUSKAITĖ, L. 2019. Early blood biomarkers to improve sepsis/bacteremia diagnostics in pediatric emergency settings. *Medicina,* 55**,** 99.

TAN, J., TAY, J., HEDRICK, J. & YANG, Y. Y. 2020. Synthetic macromolecules as therapeutics that overcome resistance in cancer and microbial infection. *Biomaterials,* 252**,** 120078.

TEKLAY, G., TEKLU, T., LEGESSE, B., TEDLA, K. & KLINKENBERG, E. 2016. Barriers in the implementation of isoniazid preventive therapy for people living with HIV in Northern Ethiopia: a mixed quantitative and qualitative study. *BMC public health,* 16**,** 1-9.

TER MAATEN, J. M., VALENTE, M. A., DAMMAN, K., CLELAND, J. G., GIVERTZ, M. M., METRA, M., O'CONNOR, C. M., TEERLINK, J. R., PONIKOWSKI, P. & BLOOMFIELD, D. M. J. C. H. F. 2016. Combining diuretic response and hemoconcentration to predict rehospitalization after admission for acute heart failure. 9**,** e002845.

TEWARI, R., DUDEJA, M., DAS, A. K., NANDY, S. J. J. O. C. & JCDR, D. R. 2013. Kocuria kristinae in catheter associated urinary tract infection: a case report. 7**,** 1692.

THAPA, S. & SAPKOTA, L. B. J. I. J. O. P. 2019. Changing trend of neonatal septicemia and antibiotic susceptibility pattern of isolates in Nepal. 2019.

TJ, C. J. L. 2016. Prendergast BD. Infectiveendocarditis. 27**,** 10021.

TKACZYSZYN, M., COMÍN-COLET, J., VOORS, A. A., VAN VELDHUISEN, D. J., ENJUANES, C., MOLINER-BORJA, P., ROZENTRYT, P., POLOŃSKI, L., BANASIAK, W. & PONIKOWSKI, P. J. E. J. O. H. F. 2018. Iron deficiency and red cell indices in patients with heart failure. 20**,** 114-122.

TROUGHTON, R. W., ASHER, C. R. & KLEIN, A. L. 2004. Pericarditis. *The Lancet,* 363**,** 717-727.

TSIMPLOULIS, A., LAM, P. H., ARUNDEL, C., SINGH, S. N., MORGAN, C. J., FASELIS, C., DEEDWANIA, P., BUTLER, J., ARONOW, W. S. & YANCY, C. W. J. J. C. 2018. Systolic blood pressure and outcomes in patients with heart failure with preserved ejection fraction. 3**,** 288-297.

TSUJIMOTO, T. & KAJIO, H. J. I. J. O. C. 2018. Low diastolic blood pressure and adverse outcomes in heart failure with preserved ejection fraction. 263**,** 69-74.

TUNUGUNTLA, H., JEEWA, A. & DENFIELD, S. W. 2019. Acute myocarditis and pericarditis in children. *Pediatrics in review,* 40**,** 14-25.

UEDA, T., KAWAKAMI, R., HORII, M., SUGAWARA, Y., MATSUMOTO, T., OKADA, S., NISHIDA, T., SOEDA, T., OKAYAMA, S. & SOMEKAWA, S. J. C. J. 2013. High mean corpuscular volume is a new indicator of prognosis in acute decompensated heart failure. CJ-13-0718.

VADUGANATHAN, M., GREENE, S. J., FONAROW, G. C., VOORS, A. A., BUTLER, J. & GHEORGHIADE, M. J. T. A. J. O. M. 2014. Hemoconcentration-guided diuresis in heart failure. 127**,** 1154-1159.

VAGDATLI, E., GOUNARI, E., LAZARIDOU, E., KATSIBOURLIA, E., TSIKOPOULOU, F. & LABRIANOU, I. J. H. 2010. Platelet distribution width: a simple, practical and specific marker of activation of coagulation. 14**,** 28.

VALENTOVA, M., VON HAEHLING, S., BAUDITZ, J., DOEHNER, W., EBNER, N., BEKFANI, T., ELSNER, S., SLIZIUK, V., SCHERBAKOV, N. & MURÍN, J. J. E. H. J. 2016. Intestinal congestion and right ventricular dysfunction: a link with appetite loss, inflammation, and cachexia in chronic heart failure. 37**,** 1684-1691.

VALLABHAJOSYULA, S., SAKHUJA, A., GESKE, J. B., KUMAR, M., POTERUCHA, J. T., KASHYAP, R., KASHANI, K., JAFFE, A. S. & JENTZER, J. C. J. J. O. T. A. H. A. 2017. Role of admission Troponin-T and serial Troponin-T testing in predicting outcomes in severe sepsis and septic shock. 6**,** e005930.

VAN BELKUM, A., BACHMANN, T. T., LÜDKE, G., LISBY, J. G., KAHLMETER, G., MOHESS, A., BECKER, K., HAYS, J. P., WOODFORD, N. & MITSAKAKIS, K. 2019. Developmental roadmap for antimicrobial susceptibility testing systems. *Nature Reviews Microbiology,* 17**,** 51-62.

VAN VELDHUISEN, D. J., ANKER, S. D., PONIKOWSKI, P. & MACDOUGALL, I. C. J. N. R. C. 2011. Anemia and iron deficiency in heart failure: mechanisms and therapeutic approaches. 8**,** 485-493.

VAN WEZENBEEK, J., RAVINDRA, K., CARBONE, S., TRANKLE, C. R., KADARIYA, D., BUCKLEY, L. F., DEL BUONO, M., BILLINGSLEY, H., VISCUSI, M. & WOHLFORD, G. F. J. F. I. C. M. 2018. C-reactive protein and N-terminal pro-brain natriuretic

peptide levels correlate with impaired cardiorespiratory fitness in patients with heart failure across a wide range of ejection fraction. 5**,** 178.

VARBO, A., NORDESTGAARD, B. G. J. A., THROMBOSIS, & BIOLOGY, V. 2018. Nonfasting triglycerides, low-density lipoprotein cholesterol, and heart failure risk: two cohort studies of 113 554 individuals. 38**,** 464-472.

VELOSO, T. R., CHAOUCH, A., ROGER, T., GIDDEY, M., VOUILLAMOZ, J., MAJCHERCZYK, P., QUE, Y.-A., ROUSSON, V., MOREILLON, P. & ENTENZA, J. M. 2013. Use of a human-like low-grade bacteremia model of experimental endocarditis to study the role of Staphylococcus aureus adhesins and platelet aggregation in early endocarditis. *Infection and immunity,* 81**,** 697-703.

VIRANI, S. S., ALONSO, A., BENJAMIN, E. J., BITTENCOURT, M. S., CALLAWAY, C. W., CARSON, A. P., CHAMBERLAIN, A. M., CHANG, A. R., CHENG, S. & DELLING, F. N. J. C. 2020. Heart disease and stroke statistics—2020 update: a report from the American Heart Association. 141**,** e139-e596.

VOICU, G., OPREA, O., VASILE, B., ANDRONESCU, E. J. D. J. O. N. & BIOSTRUCTURES 2013. ANTIBACTERIAL ACTIVITY OF ZINC OXIDE-GENTAMICIN HYBRID MATERIAL. 8.

VOS, T., ALLEN, C., ARORA, M., BARBER, R. M., BHUTTA, Z. A., BROWN, A., CARTER, A., CASEY, D. C., CHARLSON, F. J. & CHEN, A. Z. 2016. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. *The lancet,* 388**,** 1545-1602.

WALDUM, B., WESTHEIM, A. S., SANDVIK, L., FLØNÆS, B., GRUNDTVIG, M., GULLESTAD, L., HOLE, T. & OS, I. J. J. O. T. A. C. O. C. 2012. Baseline anemia is not a predictor of all-cause mortality in outpatients with advanced heart failure or severe renal dysfunction: results from the norwegian heart failure registry. 59**,** 371-378.

WANG, H., YANG, G., ZHAO, J. & WANG, M. J. J. O. I. M. R. 2020. Association between mean corpuscular volume and severity of coronary artery disease in the Northern Chinese population: a cross-sectional study. 48**,** 0300060519896713.

WATANABE, K., SATO, Y., YOSHIHISA, A., ICHIJO, Y., HOTSUKI, Y., KIMISHIMA, Y., YOKOKAWA, T., MISAKA, T., SATO, T. & OIKAWA, M. J. C. 2020. Platelet Distribution Width is Associated

With Adverse Prognosis in Patients With Heart Failure. 142**,** A13332-A13332.
WEISSIG, V., PETTINGER, T. K. & MURDOCK, N. J. I. J. O. N. 2014. Nanopharmaceuticals (part 1): products on the market. 9**,** 4357.
WERDAN, K., DIETZ, S., LÖFFLER, B., NIEMANN, S., BUSHNAQ, H., SILBER, R.-E., PETERS, G. & MÜLLER-WERDAN, U. 2014. Mechanisms of infective endocarditis: pathogen–host interaction and risk states. *Nature Reviews Cardiology,* 11**,** 35-50.
WIDMER, E., QUE, Y.-A., ENTENZA, J. M. & MOREILLON, P. 2006. New concepts in the pathophysiology of infective endocarditis. *Current infectious disease reports,* 8**,** 271-279.
WILLIAMS, M. R., STEDTFELD, R. D., GUO, X. & HASHSHAM, S. A. 2016. Antimicrobial resistance in the environment. *Water Environment Research,* 88**,** 1951-1967.
WOGAYEHU, B., ADINEW, A. & ASFAW, M. 2020. Knowledge on dispensed medications and its determinants among patients attending outpatient pharmacy at Chencha Primary Level Hospital, Southwest Ethiopia. *Integrated Pharmacy Research & Practice,* 9**,** 161.
WONG, C. C., NG, A. C., KRITHARIDES, L., SINDONE, A. P. J. H., LUNG & CIRCULATION 2016. Iron deficiency in heart failure: looking beyond anaemia. 25**,** 209-216.
WONG, D., NIELSEN, T. B., BONOMO, R. A., PANTAPALANGKOOR, P., LUNA, B. & SPELLBERG, B. J. C. M. R. 2017. Clinical and pathophysiological overview of Acinetobacter infections: a century of challenges. 30**,** 409-447.
WOUDSTRA, L., BIESBROEK, P. S., EMMENS, R. W., HEYMANS, S., JUFFERMANS, L. J., VAN ROSSUM, A. C., NIESSEN, H. W. & KRIJNEN, P. A. J. I. J. O. C. 2017. Lymphocytic myocarditis occurs with myocardial infarction and coincides with increased inflammation, hemorrhage and instability in coronary artery atherosclerotic plaques. 232**,** 53-62.
YAMAGUCHI, S., ABE, M., ARAKAKI, T., ARASAKI, O. & SHIMABUKURO, M. J. C. J. 2018. Incremental Prognostic Value of Platelet Count in Patients With Acute Heart Failure—A Retrospective Observational Study—. CJ-18-0961.
YAN, Q., CHEN, S. J. E. & MEDICINE, T. 2020. Hemoconcentration is a valuable predictor of prognosis in patients with acute heart failure. 19**,** 2792-2798.
YANCY, C. W., JESSUP, M., BOZKURT, B., BUTLER, J., CASEY, D. E., DRAZNER, M. H., FONAROW, G. C., GERACI, S. A., HORWICH,

T. & JANUZZI, J. L. 2013. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Journal of the American College of Cardiology,* 62**,** e147-e239.

YANG, Z., QDAISAT, A., HU, Z., WAGAR, E. A., REYES-GIBBY, C., MENG, Q. H. & YEUNG, S.-C. J. J. P. O. 2016. Cardiac troponin is a predictor of septic shock mortality in cancer patients in an emergency department: a retrospective cohort study. 11**,** e0153492.

YIN, Z., YU, B., LIU, W. & LAN, K. J. O. 2017. Blood transfusion and mortality in myocardial infarction: An updated meta-analysis. 8**,** 102254.

YOUNG, D. J. A. O. C. B. 1997. Effects of drugs on clinical laboratory tests. 34**,** 579-581.

YUSUF, S., RANGARAJAN, S., TEO, K., ISLAM, S., LI, W., LIU, L., BO, J., LOU, Q., LU, F. & LIU, T. 2014. Cardiovascular risk and events in 17 low-, middle-, and high-income countries. *New England Journal of Medicine,* 371**,** 818-827.

ZAHARIE, M., CÂRSTEA, D., CÂRSTEA, A. & ZAHARIE, S. 2017. Prevalence of erythrocyte changes in patients with heart failure. *Current health sciences journal,* 43**,** 263.

ZHANG, H. B., CHEN, J., LAN, Q. F., MA, X. J., ZHANG, S. Y. J. E. & MEDICINE, T. 2016. Diagnostic values of red cell distribution width, platelet distribution width and neutrophil-lymphocyte count ratio for sepsis. 12**,** 2215-2219.

ZHANG, L., PORNPATTANANANGKUL, D., HU, C.-M. & HUANG, C.-M. J. C. M. C. 2010. Development of nanoparticles for antimicrobial drug delivery. 17**,** 585-594.

ZHAO, Q., LI, J., YANG, J. & LI, R. J. M. 2017. Association of total cholesterol and HDL-C levels and outcome in coronary heart disease patients with heart failure. 96.

ZHOU, H., XU, T., HUANG, Y., ZHAN, Q., HUANG, X., ZENG, Q. & XU, D. J. B. C. D. 2017. The top tertile of hematocrit change during hospitalization is associated with lower risk of mortality in acute heart failure patients. 17**,** 1-8.

ZIAEIAN, B. & FONAROW, G. C. 2016. Epidemiology and aetiology of heart failure. *Nature Reviews Cardiology,* 13**,** 368-378.

Appendix

Appendix 1: Diagnostic results of biochemical tests for Gram positive bacteria isolated from heart failure patients

Tests	*Staphylococcus hominis* ssp hominis (1)	*Staphylococcus hominis* ssp hominis (2)	*Staphylococcus hominis* ssp hominis (3)	*Staphylococcus hominis* ssp hominis (4)	*Staphylococcus hominis* ssp hominis (5)	*Staphylococcus haemolayticus* (1)	*Staphylococcus haemolayticus* (2)	*Staphylococcus sciuri* (1)	*Staphylococcus sciuri* (2)	*Staphylocoous lentus*	*Gardnerella vaginalis*	*Kocuria kristinae*
AMY	-	-	-	-	-	-	-	-	+	+	-	-
PIPLC	-	-	-	-	-	-	-	-	-	-	-	-
d XYL	-	-	-	-	-	-	-	-	+	-	-	-
ADH1	-	+	-	-	-	+	+	+	+	-	-	+
BGAL	-	-	-	-	-	-	-	+	-	-	-	-
AGLU	-	+	-	-	+	-	-	-	+	-	+	-
APPA	-	-	-	-	-	-	-	-	-	-	-	-
CDEX	-	-	-	-	-	-	-	-	-	-	-	-
AspA	-	-	-	-	-	-	-	-	-	-	-	-
BGAR	-	-	-	-	-	-	-	-	-	-	+	-
AMAN	-	-	-	-	-	-	-	+	-	-	-	-
PHOS	-	-	-	-	-	-	-	-	-	-	-	-
LeuA	-	-	-	-	-	-	-	-	-	-	-	+
ProA	-	-	-	-	-	-	-	-	-	-	-	+
BGURr	-	-	-	-	-	-	-	-	+	-	-	-
AGAL	-	-	-	-	-	-	-	+	-	-	-	-
PyrA	-	+	-	-	-	+	+	-	-	-	-	-
BGUR	-	-	-	-	-	-	-	-	+	-	-	-
AAAl	-	-	-	-	-	-	-	-	-	-	-	+
TyrA	-	-	-	-	-	-	-	-	-	-	-	-
dSOR	-	-	-	-	-	-	-	-	-	-	-	-
URE	-	+	-	+	+	-	-	-	-	-	-	-
POLYB	-	-	-	-	-	-	-	-	+	-	-	-
dGAL	-	+	-	-	-	-	+	-	-	-	-	-
dRIB	-	-	-	-	-	+	+	+	+	+	-	-
ILATk	-	+	-	-	-	-	+	+	+	-	-	+
LAC	+	+	-	-	-	-	+	-	-	-	-	-
NAG	-	-	-	+	-	-	+	-	+	+	-	-
dMAL	+	+	+	+	+	+	+	+	+		-	-
BACI	-	+	-	-	-	-	+	+	+	+	-	-
NOVO	-	+	-	-	-	-	-	-	+	-	-	-
NC6.5	+	+	+	+	+	+	+	+	+	-	+	-
dMAN	-	-	-	-	-	-	+	+	+	+	-	-
dMNE	-	-	-	-	-	-	-	+	+	+	-	+
MBdG	-	-	-	-	-	-	-	+	+	+	-	-
PUL	-	-	-	-	-	-	-	-	-	-	+	-
dRAF	-	-	-	-	-	-	-	-	+	-	-	-
O129R	+	+	+	+		+	+	-	+	-	-	+
SAL	-	-	-	-	-	-	-	+	+	+	-	-
SAC	+	+	+	+	+	+	+	+	+	+	-	-
dTRE	+	+	-	+	+	+	+	+	+	+	-	+
ADH2s	-	-	-	-	-	+	-	-	-	-	-	-
OPTO	+	+	+	+	+	+	+	+	+	+	-	-

Appendix 2: Diagnostic results of biochemical tests for Gram negative bacteria isolated from heart failure patients

Tests	*Pseudomonas stutzer* (1)	*Pseudomonas stutzer* (2)	*Pseudomonas stutzer* (3)	*Acinetobacter baumanii*
BGAL	-	-	-	-
APPA	-	-	-	-
PHOS	-	-	-	-
ProA	+	+	+	-
AGAL	-	-	-	-
PyrA	-	-	-	-
BGUR	-	-	-	-
TyrA	+	+	+	+
URE	-	-	-	-
ILATk	-	-	-	+
Dmal	-	-	-	-
Dman	-	-	-	-
Dmne	-	--	-	+
O129R	-	-	-	+
SAC	-	-	-	-
Dtre	-	-	-	-
ADO	-	-	-	-
IARL	-	-	-	-
Dcel	-	-	-	+
H2S	-	-	-	-
BNAG	-	-	-	-
AGLTp	-	-	-	-
Dglu	+	+	+	+
GGT	+	+	+	-
OFF		-	-	-
BGLU	-	-	-	-
BXYL	-	-	-	-
BAIap	-	-	-	-
LIP	-	-	-	-
PLE	-	-	-	-
Dtag	-	-	-	-
CIT	-	-	-	+
MNT	-	-	+	+
5KG	-	-	-	-
AGLU	+	-	-	-
SUCT	+	-	-	+
NAGA	-	-	-	-
GIyA	-	-	-	-
ODG	-	-	-	-
LDC	-	-	-	-
IHISa	-	-	-	-
CMT	-	-	-	+
GGAA	-	-	-	-
IMLTa	+	-	-	-
ELLM	-	-	-	-
ILATa	-	-	-	-

الخلاصة

تهدف الدراسه الحاليه الى تحديد الانواع البكتيريه الاكثر شيوعا لمرضى الفشل القلبي، ودراسه علاقتها بعوامل الخطوره لفشل القلب وتحديد حساسيتها للمضادات الحيويه

أجريت الدراسة في الفترة من تشرين الأول 2020 إلى أيار 2021 في مدينة الإمام الحسين الطبية في كربلاء. تم اخذ 10 مل من عينة الدم الوريدي ل 71 مريض بالفشل القلبي بعد دخولهم إلى وحدة العناية المركزة والمراقبة و يقابلها نفس العدد من الاصحاء. اجريت عدة تحاليل مثل تحاليل القلب (BNP, Troponin , CRP) وصورة الدهون (TC, TG, HDL, LDL) واختبارات وظائف الكلى (Urea, Creatinine) ، و بعض المعايير العامة مثل (العمر ، الوزن ، الجنس) ، والمعايير الفسيولوجية (فصائل الدم ، صوره الدم ، ضغط الدم الانقباضي ، ضغط الدم الانبساطي والجلوكوز) ، الاختبارات الميكروبية (تشخيص البكتريا ،اختبارات الحساسية للمضادات الحيويه) ودراسة النانويه (XRD، FTIR، AFM، SEM) ودراسه الفعاليه التثبيطيه للمضاد الميروبنيم الحرو النانوي (Nano-Meropenem, Free- Meropene).

كانت نتائج هذه الدراسه بالنسبه للمرضى بالفشل القلبي للمعايير المدروسه هي

CRP (46.013 mg/l)، BNP (218.84 ng/dl)، تروبونين (لمرضى الفشل القلبي بدون الالتهابات البكتيريه) (924.526 ng/ml) و (لمرضى الفشل القلبي مع الالتهابات البكتيريه) (383.97 ng/ml) TG، (138.61 mg/dl) HDL ، (44.323 mg/dl) LDL ، (113.249 mg/dl) TC، (160.423 mg/dl) ، الكرياتنين (1.343 mg/dl) ، اليوريا (62.658 mg/dl) RDW SD، (49.253 fl) RDW CV، (49.253%) NEUT، (70.129%) LYM، (20.329%) MCHC، (لمرضى الفشل القلبي مع الالتهابات البكتيرية) (31.393 g/dl) HgB، (12.804 g/dl) WBC ، (12.67010^3/ µl) و الكلوكوز (202.336 mg/dl). وفصيلة الدم الاكثر شيوعا عند مرضى فشل القلب هي O ، اما البكتريا الأكثر شيوعًا في مرضى الفشل القلبي *Staphylococcus hominis ssp hominis* . كما اظهرت معظم العزلات البكتيريه مقاومه تجاه المضاد الميروبنيم. كما اشارت النتائج الى ان هنالك علاقه ارتباط بين بعض معايير المدروسه للمرضى مثل علاقه الارتباط الطردي بين RBC مع كل من HGB و HCT ، حيث كان ارتباط طرديا (0.728 و 0.792) ، على التوالي. كما كان هناك ارتباط في HGB

مع HCT وبين MCV مع MCH حيث كان هناك ارتباط طرديا أيضًا (0.893 و 0.890) على التوالي. يمكن أيضًا رؤية ارتباط بين PDW و MPV و P-LCR حيث كان ارتباطًا طرديا (0.733 و 0.737) ، على التوالي أيضًا. في نفس الوقت كان هناك ارتباط بين MPV و P-LCR حيث كان طرديا (0.503). شوهد الارتباط أيضًا بين TC وكلا من HDL و LDL ، حيث كان ارتباطًا طرديا (0.661 و 0.937) ، على التوالي. وبين LDL و HDL حيث كان ارتباط طردي (0.534). كان هناك ارتباط بين اليوريا والكرياتينين حيث كان هناك ارتباط طردي (0.548). أخيرًا ، كان هناك ارتباط بين DBP و SBP ، حيث كان ارتباطًا طرديا (0.709). في فشل القلب مع العدوى البكتيرية كانت هناك بعض معاملات الارتباط المختلفة مثل MCHC مع MCH ، حيث كان الارتباط طرديا (0.733). وبين PLT مع RBC و HGB و HCT ، حيث كان ارتباط طردي (0.625 و 0.574 و 0.575) على التوالي. كما كان هناك ارتباط في NEUT مع كل من WBC و LYM ، حيث كان هناك ارتباط طردي وعكسي (0.969 و -0.555) على التوالي. كان هناك ارتباط بين PDW و RDW ، حيث كان طرديا (0.622). كان هناك ارتباط بين PCT مع RBC و HGB مع HCT ، حيث كان هناك ارتباط طرديا (0.654 و 0591 و 0.574) على التوالي. كما لوحظ الارتباط بين العمر و BNP ، حيث كان هناك ارتباط عكسيا (- 0.527). كما كان هناك ارتباط بين CRP وكلا من TG والكرياتينين ، حيث كان هناك ارتباط طرديا (0.731 ، 0.894). بينما كان هناك ارتباط بين CRP مع HDL، LDL ، واليوريا حيث كان هناك ارتباطات عكسيه و طرديه (- 0.505 ، - 0.505 ، 0.664) على التوالي. كان هناك ارتباط بين الكرياتينين و TG والارتباط بين الجلوكوز والوزن ، حيث كان هناك ارتباط طرديا (0.763 ، 0.593) على التوالي.

يمكن الاستنتاج بان أكثر الأنواع البكتيرية شيوعًا لدى مرضى الفشل القلبي هي بكتريا *Staphylococcus hominis ssp hominis* و ان معظم البكتريا المعزوله كانت مقاومًه لمضاد الميروبنيم.

وزارة التعليم العالي والبحث العلمي
جامعة كربلاء
كلية العلوم الطبية التطبيقية
قسم التحليلات المرضية

دراسة تأثير الالتهابات البكتيرية على بعض العوامل الفسيولوجية والكيموحيويه لمرضى الفشل القلبي في محافظة كربلاء

رسالة مقدمة

الى مجلس كلية العلوم الطبية التطبيقية - جامعة كربلاء

وهي جزء من متطلبات نيل شهادة الماجستير في التحليلات المرضية

مقدمة من قبل

زينب ناسي عارف

بكالوريوس تحليلات مرضية / 2018 كلية العلوم التطبيقية - جامعة كربلاء

بأشراف

ألاستاذ المساعد
د . علاء عبد الحسين الدعمي

الطبيب الاختصاص
د . احمد قاسم الحيدري

(محرم) 1443

(اغسطس) 2021