بسم الله الرحمن الرحيم

Sudan University of Science and Technology

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Assessment of Erythrocyte Sedimentation Rate, C - reactive protein and Red Cell Distribution Width among Myocardial Infarction Patients in Khartoum State

تقييم معدل ترسيب كريات الدم احمراء وبروتينات سي النشطة و عرض توزيع كريات الدم الحمراء لدى مرضى الذبحة القلبية

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قال الله تعالى:

﴿قَالُوا سُبْحَانَكَ لَا عِلْمَ لَنَا إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنتَ الْعَلِيمُ الْحَكِيمُ﴾

صدق الله العظيم

سورة البقرة – الآية (32).

Dedication

To the Candle of My Life (My Mother)

To My Father

To My Sisters and My Brothers

To All of My Family

To My Colleagues and Friends

I Dedicate This Work

Acknowledgments

All my thanks are in the name of Allah, the most Gracious and the most Merciful.

In this instance, I extend my thanks, deep sincere gratitude and honest appreciation to my supervisor Dr. Lina Babiker Mergani and Dr. Suhair Ahmed.
Department of Hematology, Sudan University of Science and Technology, for this kindness, good guidance, valuable direction that has kept me on the track.

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Abstract

Myocardial infarction (MI), commonly known as a heart attack, occurs when blood flow decrease or stop to part of the heart, causing damage to heart muscle**.** ESR and CRP are inflammatory biomarker which are elevated in inflammatory condition and also elevated in chronic diseases such as Cardiac diseases.RDW value increased indicate there are Anisocytosis in RBC and there is association between RDW and increase risk of cardiac diseases.

This study is aimed to detect that there is relation between ESR, RDW, CRP levels and the morbidity and mortality in MI patients.

This is analytical case control study conducted during the period of March 2019 to September 2019 in Khartoum state in Sudan Heart Center, A total of 70 subjects were included ,30 myocardial infract patients and 40 healthy individual from both sexes . A structured questionnaire was prepared which included general information and laboratory investigations; Verbal consent was obtained from each subject before evolvement in the study.

The results showed Significant increased in mean level of ESR between case and control group (*p .value* = 0.00) , and there was significant increased in mean level of CRP between case and control group (*p .value* = 0.00) ,and there was significant increased in mean level of RDW between case and control group (*p .value* = 0.00) .

Results showed that there was no significant increased in the mean of ESR in myocardial infract patients males compared to females (p. *value* 0.2), and the mean of CRP between males and females (p. *value* 0.6).and the mean of RDW between males and females (p .*value* 0.9).

According to age groups (20-50)and (51-80) there was no significant difference in the mean of ESR (p .*value* 0.3) , CRP (p .*value* 0.3) and RDW (p. value 0.1) in myocardial infarct patients.

ملخص الدراسة

الذبحة القلبية هي حاله مرضية تحدث نتيجة لنقصان تدفق الدم لعضلات القلب او انعدام تام لتدفق الدم ف تلك العضلات مما يؤدي الى موتها وذلك يتسبب ف ضمور عضلة القلب و خلل وظيفي. معدل ترسيب كريات الدم الحمراء وبروتينات سي النشطة هي مؤشرات التهابية والتي ترتفع في حالات التهاب و ايضا ف حالات الامراض المزمنة مثل امراض القلب . ارتفاع قيمة عرض توزيع كريات الدم الحمراء يدل على اختلاف في حجم كريات الدم الحمراء و ايضا هنالك علاقة بين ارتفاع قيمة عرض توزيع كريات الدم الحمراء وزيادة الخطورة لدى مرضى القلب. أجريت هذه الدراسة لإثبات ان هنالك علاقة بين ارتفاع معدل ترسيب كريات الدم الحمراء وبروتينات سي النشطة ،عرض توزيع كريات الدم الحمراء ومعدل وفيات لدى الاشخاص المصابون بالذبحة القلبية. أجريت هذه الدراسة التحليلية خلال الفترة من مارس 2019 الى سبتمبر 2017 في ولاية الخرطوم بمركز السودان للقلب و لتحديد قيمة معدل ترسيب كريات الدم الحمراء ، وقيمة بروتينات سي النشطة وقيمة متوسط حجم كريات الدم الحمراء بين ثلاثين من مرضى الذبحة القلبية وأربعين من المعادلين الطبيعيين من الجنسين. جمعت البيانات الخاصة بمرضى القلب و المعادلين الطبيعيين من خلال استبيانا وأشتمل على معلومات عامة وعلى التحاليل المعملية بعد اخذ اقرار الموافقة .

اوضحت الدراسة انه يوجد زيادة هامة في متوسط قيمة معدل ترسيب كريات الدم الحمراء(0.00 P.*value*) ويوجد زيادة هامة في متوسط قيمة بروتينات سي النشطة (0.00P.*value*) وزيادة هامة في متوسط قيمة عرض توزيع كريات الدم الحمراء بين المرضى والمعادلين الطبيعيين.

اوضحت الدراسة انه لا توجد زيادة مهمة في متوسط قيمة معدل ترسيب كريات الدم الحمراء) 0.2 (P.*value*ويوجد اختلاف في متوسط قيمة بروتينات سي النشطة (P.*value* 0.6) ولا توجد زيادة مهمة متوسط قيمة متوسط حجم كريات الدم الحمراء (0.9 *value*. p) في الذكور المصابين بمرض الذبحة القلبية مقارنة مع الاناث المصابين. وأيضا لا يوجد اختلاف مهم في متوسط قيمة معدل ترسيب كريات الدم الحمراء (P.*value* 0.3)ومتوسط قيمة بروتينات سي النشطة (P.*value* 0.3) ومتوسط قيمة متوسط حجم كريات الدم الحمراء 0.1) (P.*value*بين مرضى ارتفاع ضغط الدم وفقا للاختلاف في العمر .

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List of Abbreviations

Abbreviations	Full Name
CABG	Coronary artery bypass surgery
CDK	Cycline dependent kinase
CKMB	Creatine kinase MB
CRP	C reactive protein
CT scan	Computerized tomography scan
ECG	Electro cardiograph
ESR	Erythrocyte sedimentation rate
Hs CRP	High sensitive C reactive protein
LDL	Low density lipoprotein
MCV	Mean cell volume
MI	Myocardial infarction
NSTEMI	Non ST myocardial infraction
PCI	Percutaneous intervention
RDW	Red cell distribution width
STEMI	ST elevation myocardial infraction
Us CRP	Ultra-sensitive C reactive protein

Chapter 1

Introduction and Literature Review

Chapter 1

Introduction and Literature Review

1.1General introduction

Myocardial infarction (MI), commonly known as a heart attack, occurs when blood flow decrease or stop to part of the heart, causing damage to heart muscle. The most common symptom is chest pain or discomfort which may travel into the shoulder arm, back, neck or jaw .Often it occurs in the center or left side of the chest and lasts for more than a few minutes.(Hazinski ,2015). Myocardial infarction may cause heart failure, an irregular heartbeat, cardiogenic shock or cardiac arrest. (Nolan, 2015).

Most MIs occur due to coronary artery disease. Risk factor include high blood pressure ,smoking, diabetes, lack of exercise ,obesity ,high blood cholesterol, poor diet, and excessive alcohol intake among others (Mehta,2015).The complete blockage of a coronary artery caused by rupture of an atherosclerotic plaque is usually the underlying mechanism of an MI(Nolan ,2015). MIs are less commonly caused by coronary artery spasms, which may be due to cocaine, significant emotional stress, and extreme cold, among others (Aickin ,2015).

A number of tests are useful to help with diagnosis , including electrocardiogram (ECG), blood tests ,and coronary angiography .(Bahanji,2013).An ECG ,which is a recording of the heart ′s electrical activity.(Steg,*et al.*2012)

Commonly used blood tests as troponin and less often creatine kinase MB. (Bahanji,2013).

An appropriate immediate treatment of an MI is time critical (Nicki ,*et al*2010) . Aspirin is for a suspected MI. Supplemental oxygen is recommended in those with low oxygen levels or shortness of breath. (O′Connor, Bardy , and Brooks,2010).In ST elevation myocardial infarction (STEMI),treatments to restore blood flow to the heart , and include

percutaneous coronary intervention (PCI),where the arteries are pushed open and may be stented or thrombolysis , where the blockage is removed using medications. (Steg,*et al.*2012)

People who have a non- ST elevation myocardial infarction (NSTEMI) are often managed with the blood thinner heparin , with the additional use of PCI in those at high risk(O′Connor, Bardy , and Brooks,2010). In people with blockages of multiple coronary arteries and diabetes, coronary artery bypass surgery (CABG) may be recommended rather than angioplasty (Bahanji, 2013).

After an MI, life style modifications, along with long term of treatment with aspirin, beta blockers, and stains are typically recommended. (Steg, *et al.*2012).

An erythrocyte sedimentation rate (ESR) is a type of blood test that measure how quickly erythrocytes settle at bottom of a test tube that contains a blood sample. Normally, red cell settle relative slowly .a faster –than- normal rate may indicate inflammation in the body inflammation is part the immune system response system. It cans a reaction to infection or injury. Also may be a sign of chronic disease ,an a immune disorder ,or other medical condition .The high level of ESR is associated with inflammatory condition ,such as, infection, rheumatoid arthritis ,vascular disease ,heart disease ,renal disease and certain cancers . (Deice and Lwis,2011).

C-reactive protein is a substance produced by liver in the response to inflammation. High levels can indicate there is inflammation in arteries of the heart, which can mean a higher risk of heart attack. (Judith, 2017).

Red cell distribution width (RDW) is a measure of the range of variation of red blood cell in volume that is reported as part of a standard complete blood count. Usually red blood cells are a standard size of about 6-8 µm in diameter .Certain disorders, however, cause a significant variation in cell size. Higher RDW values indicate greater variation in size above the normal reference range of RDW in human red blood cells which is 11.5-14.5 %(Carl and Sherrie ,2013).

1.2 Literature review

1.2.1 Overview on Myocardial Infraction

Myocardial infarction (MI), commonly known as a heart attack, occurs when blood flow decrease or stop to part of the heart, causing damage to heart muscle (Hazinski ,2015). The most common symptom is chest pain or discomfort which may travel into the shoulder arm, back, neck or jaw (Hazinski ,2015).often it occurs in the center or left side of the chest and lasts for more than a few minute s, the discomfort may occasionally feel like heartburn. Other symptoms may include shortness of breath, nausea, feeling faint, a cold sweat, or feeling tired .(Hazinski ,2015).

Myocardial infarction may cause heart failure, an irregular heartbeat, Cardiogenic shock or cardiac arrest.(Nolan ,2015).

Most MIs occur due to coronary artery disease. Risk factor include high blood pressure, smoking, diabetes, lake of exercise, obesity, high blood cholesterol, poor diet, and excessive alcohol intake among others (Mehta,2015).

The complete blockage of a coronary artery caused by rupture of an atherosclerotic plaque is usually the underlying mechanism of an MI (Nolan ,2015). MIs are less commonly caused by coronary artery spasms, which may be due to cocaine, significant emotional stress, and extreme cold, among others (Aickin ,2015).

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1.2.2 Types

Myocardial infarctions are generally clinically classified into ST elevation MI(STEMI) and non ST elevation MI(STEMI) .These are based on changes to an ECG. STEMIs make up about 35%-40% of myocardial infractions (Mu and Rich ,2016). A more explicit classification system, based on international

consensus in 2012, also exists. This classifies myocardial infarctions into five types:

1. Spontaneous MI related to plaque erosion and| or rupture, fissuring ,or dissection.
2. MI related to ischemia ,such as form increased oxygen demand or decreased supply , e.g., coronary artery spasm, coronary embolism, anemia, arrhythmias , high blood pressure or low blood pressure.
3. Sudden unexpected cardiac death ,including cardiac arrest, where symptoms may suggest MI, an ECG may be taken with suggestive changes ,or a blood clot is found in a coronary artery by angiography and \or at be obtained ,or at a time before the appearance of cardiac biomarkers in the blood
4. Associated with coronary angioplasty or stents.

- Associated with percutaneous coronary intervention (PCI).
- Associated with stent thrombosis as documented by angiography or at autopsy

5. Associated with spontaneous coronary artery dissection in young, fit women.(Mu and Rich ,2016)

1.2.3 Risk Factors

The most prominent risk factors for myocardial infarction are older age, actively smoking, high blood pressure , diabetes mellitus, and total cholesterol and high density lipoprotein levels (O ′gara , Kushner and Asheim Fang ,2013)**.**

Many risk factor are shared with coronary artery disease, the primary cause of myocardial infarction ,with other risk factors including male sex, low levels of physical activity, a past family history ,obesity, and alcohol use(O ′gara , Kushner and Asheim Fang ,2013)

Many risk factors for myocardial infarction are potentially modifiable, with the most important being tobacco smoking , smoking appears to be the cause of about 36% and obesity the cause of 20% of coronary artery disease. Lack of physical activity has been linked to 7-12% of cases. Less common causes

include stress-related causes such as job stress which accounts for about 3% of cases ,and chronic high stress levels (Nyberg , Batty , Fransson ,2012).

1.2.3.1 Diet and risk of myocardial infarction

There is evidence about the importance of saturated fat in the development of myocardial infarctions. Eating polyunsaturated fats has been shown in studies to be associated with a decreased risk of myocardial infarction (Nyberg , Batty and Fransson ,2012). While other studies find a little evidence that reducing dietary saturated fat or increasing polyunsaturated fat intake affects heart attack risk(Lee, Shiroma and Lobelo,2012).

Dietary cholesterol does not appear to have a significant effect on blood cholesterol and thus recommendations about its consumption may not be needed. Acute and prolonged intake of high quantities of alcoholic drinks (3-4or more daily) increases the risk of heart attack .(Lee, Shiroma and Lobelo ,2012)

1.2.3.2 Genetics

Family history of ischemic heart disease or MI, particularly if one has a male first degree relative (father, brother) who had a myocardial infarction before age55 years ,or a female first relative (mother, sister)

Genome wide association studies have found 27 genetic variants that are associated with an increased risk of myocardial infarction .(Steptoe and Kimivaki ,2012).

The strongest association of MI has been found in chromosome 9 on short arm *p* at locus 21, which contains genes CDKN2A and 2B, although the single nucleotide polymorphisms that are implicated are within a non- coding region(Hooper ,Martin and Davey smith ,2015).

1.2.3.3 Other Risk Factors

The risk of having a myocardial infarction increases with older age, low physical activity, and low socioeconomic status (Hooper Martin and Davey smith ,2015).Heart attacks appear to occur more commonly in the morning hours, especially between 6AM and noon. Evidence suggests that heart

attacks are at least three times more likely to occur in the morning than in the late evening.(Steptoe and Kimivaki ,2012).

Women who use combined oral contraceptive pills have a modestly increased risk of myocardial infarction , especially in the presence of other risk factors. The use of non steroidal anti inflammatory drugs (NSAIDs), even for as short as a week, increases risk factor(Chowdhory and Warnakula 2014).

Short time exposure to air pollution such as carbon monoxide ,nitrogen dioxide, and sulfur dioxide (but not ozone) have been associated with MI.(De Souza and Mente , 2015).

A number of acute and chronic infections including Chlamydophila pneumonia, influenza, Helicobacter pylori ,and Prophyromonas gingival is among others have been linked to atherosclerosis and myocardial infarction (Krenz and Korthuis , 2012).

Calcium deposits in the coronary arteries can be detected with CT scans, Calcium seen in coronary arteries can provide predictive information beyond that of classical risk factors. High blood levels of the amino acid homocysteine is associated with premature atherosclerosis (Culic ,2007).

1.2.4Mechanism of Myocardial Infarction Development

The most common cause of myocardial infarction is the rupture of an atherosclerotic plaque on an artery supplying heart muscle(Shaw and Tofler ,2009). Plaque can became unstable ,rupture, and additionally promote the formation of a blood clot that blocks the artery; this can occur in minutes. Blockage of an artery can lead to tissue death in tissue being supplied by that artery(Janszky and Ljung ,2008).

Atherosclerotic plaques are often present for decades before they result in symptom .The gradual build up of cholesterol and fibrous tissue in plaques in the wall of the coronary arteries or other arteries , typically over decades, is termed atherosclerosis(Janszky and Ljung ,2008).

Atherosclerosis is characterized by progressive inflammation of the walls of arteries (Shaw and Tofler ,2009).Inflammatory cells, particularly macrophages ,moves into e affected arterial walls, Over time ,they became

laden with cholesterol products, particularly LDL, and became foam cells .A cholesterol core forms as foam cells die .In response to growth factors secreted by macrophages ,smooth muscle and other cells move into the plaque and act to stabilize it. A stable plaque may have a thick fibrous cap with calcification If there is ongoing inflammation, the cap may be thin or ulcerate. Exposed to the pressure associated with blood flow , plaques, especially those with a thin lining ,may rupture and trigger the information of blood clot (thrombus) (Shaw and Tofler ,2009).The cholesterol crystal have been associated with plaque rupture through mechanical injury and inflammation(Shaw and Tofler ,2009).

A myocardial infarction may result from a heart with a limited blood supply subject to increased oxygen demands, such as in fever, a fast heart rate, and hyperthyroidism, too few red blood cells in the bloodstream or low blood pressure. Damage or failure of procedures such as percutaneous coronary intervention or coronary artery bypass grafts may cause a myocardial infarction. Spasm of coronary arteries, such as prinzmetal's angina may cause blockage (Roach , Helmerhorst and Lijfering ,2015).

If impaired blood flow to the heart lasts long enough , it triggers a process called the ischemic cascade ;the heart cells in the territory of blocked coronary artery die (infarction) ,chiefly through necrosis ,and don't grow back .A collagen scar forms in their place(Roach , Helmerhorst and Lijfering ,2015). When an artery is blocked, cells lack oxygen, needed to produce ATP in mitochondria. ATP is required for the maintenance of electrolyte balance, particularly through the Na/K ATPase .This lead to an affected cells (Roach , Helmerhorst and Lijfering ,2015).

Cells in the area with the worst blood supply, just below the inner surface of the heart (endocardium), are most susceptible to damage. Ischemia first affects this region, the sub endocardial region, and tissue begins to die within 15-30 minutes of loose of blood supply (Bally *et al*,2017).

The dead tissue is surrounded by a zone of potentially reversible ischemia that progresses to became a full thickness transmural infarct (Bally *et al*,2017).

The position ,size and extent of an infarct depends on the affected artery , totality of the blockage ,duration of the blockage, the presence of collateral blood vessels ,oxygen demand ,and success of interventional procedure (Bally *et al*,2017).

Tissue death and myocardial scarring alter the normal conduction pathways of the heart, and weaken affected areas. The size and location puts a person at risk of abnormal heart rhythms (arrhythmias) or heart block, aneurysm of the heart ventricles, inflammation of heart wall following infarction, and rupture of the heart wall that can have catastrophic consequences (Bally *et al*,2017).

1.2.5 Diagnosis

An acute myocardial infarction, according to current consensus**,** is and at least one of the following:

- Symptoms relating to ischemia
- Changes on an electrocardiogram(ECG),
- Change in the motion of the heart wall on the imaging.
- Demonstration of a thrombus on angiogram or at autopsy.

1.2.5.1 Cardiac biomarkers

There are a number of different biomarkers used to determine the presence of cardiac muscle damage. Troponins, measured through a blood test, are considered to be the best, and are preferred because they have greater sensitivity and specificity for measuring injury to the heart muscle than other tests.(Janoudi ,Shamon and Abela ,2016).

A rise in troponin occurs within 2-3 hours of injury to the heart muscle, and peaks within 1-2 days. The level of the troponine ,as will as a change over time, are useful in measuring and diagnosing or excluding myocardial infarctions ,and the diagnostic accuracy of troponin testing is improving over time. One high sensitivity cardiac troponin is able to rule out a heart attack as long as the ECG is normal (Janoudi ,Shamon and Abela ,2016).

Other tests, such as CK-MB or myoglobin, are discouraged.CK-MB is not as specific as troponins for acute myocardial injury , and may be elevated with

past cardiac surgery, inflammation or electrical cardioversion; is rises within 4-8 hours and returns to normal within 2-3 days(Buja ,2005).

1.2.5.2 Electrocardiogram

Electrocardiogram (ECGs) are a series of leads placed on a person′s chest that measure electrical activity associated with contraction of heart muscle .The taking of an ECG is an important part in workup of an MI. and ECGs are often not just taken once, but may be repeated over minutes to hours, or in response to changes in sign and symptoms (Buja l,2005).

ECG readouts product a waveform with different labelled features. In addition to a rise in biomarkers, a rise in the ST segment, changes in the shape or flipping of T waves, new Q waves, or anew left bundle branch block can be used to diagnose an MI (Kutty , Jones and Moorjanin,2013).In addition ,ST elevation can be used to diagnose an ST segment myocardial infarction (STEMI). Arise must be new in V2 and V3≥2mm(0,2mV) for males or ≥1.5 mm(0.15mV)for leads.ST elevation is associated with infarction, and may be preceded by changes indicating ischemia, such as ST depression or inversion of the T waves(Buja ,2005).Abnormalities can help differentiate the location of an infarct ,based on the leads that are affected by changes, Early STEMIs may be preceded by peaked T waves .Other ECG abnormalities relating to complications of acute myocardial infarctions may also be evident, such as atrial or ventricular fibrillation (Buja ,2005).

1.2.5.3 Imaging

Noninvasive imaging plays an important role in the diagnosis and characterisation of myocardial infarction (Kutty , Jones and Moorjanin,2013). Test such as chest as X-rays can used to explore and exclude alternate causes of person′s symptoms. Test such as stress echocardiography and myocardial perfusion imaging can confirm diagnosis when a person′s history, physical examination (including cardiac examination) ECG, and cardiac biomarkers suggest the likelihood of problem (Kutty , Jones and Moorjanin,2013).

Echocardiography , an ultrasound scan of the heart ,is able to visualize the heart ,its size ,shape ,and any abnormal motion of the heart walls as they beat

that may indicate a myocardial infarction .the flow of blood can be imaged, and contrast dyes may be given to improve image .(Nyberg , Batty , Fransson ,2012).

Other scans using radioactive contrast include SPECT CT-scans using thallium, sestamibi (MIBI scans)or tetrofosmin ; or a PET scan using Fludeoxyglucose or rubidium-82.These nuclear medicine scans can visualize the perfusion of heart muscle. SPECT may also be used to determine viability of tissue, and whether areas of ischemia are inducible (Nyberg , Batty , Fransson ,2012).

Medical societies and professional guidelines recommend that the physician confirm a person is at high risk for myocardial infarction before conducting imaging tests to make a diagnosis, such as tests are unlikely to change management and result increased costs, patients who have a normal ECG and who are able to exercise, for example do not merit routine imaging (Nolan ,2015).

1.2.6 Differential diagnosis

There are many causes of chest pain, which can originate from heart, lungs, gastrointestinal tract, aorta, and other muscles, bone and nerves surrounding the chest. In addition to myocardial infarction, other causes include angina, insufficient blood supply (ischemia) to the heart muscles without evidence of cell death. Rare sever differential diagnoses include aortic dissection, esophageal rupture, tension pneumothorax, and pericardial effusion causing cardiac tamponade (Nolan, 2015) .The chest pain in an MI may mimic heartburn. Causes of sudden -onset breathlessness generally involve the lungs or heart -including pulmonary edema ,pneumonia ,allergic reactions and asthma .and pulmonary embolus ,acute respiratory distress syndrome and metabolic acidosis (Nolan ,2015).

1.2.7 Prognosis

The prognosis after myocardial infarction varies greatly depending on the extent and location of the affected heart muscle, and the development and management of complications, prognosis is worse with older age, and social isolation(Bahanji,2013).Anterior infarcts, persistent ventricular tachycardia or fibrillation ,development of heart blocks, and left ventricular impairment are all associated with poorer prognosis(Bahanji,2013) .Without treatment ,about a quarter of those affected by MI die within minutes, and about forty percent within the first month (Kutty , Jones and Moorjanin,2013).

Morbidity and mortality from myocardial infarction has however improved over the years due to earlier and better treatment (Kutty , Jones and Moorjanin,2013).

1.2.8 Complications

Complication may occur immediately following the myocardial infarction or may take time to develop. Disturbance of heart rhythms ,including atrial fibrillation, ventricular tachycardia and fibrillation and heart block can arise as a result of ischemia, cardiac scarring ,and infarct location.(Kutty , Jones and Moorjanin,2013).

Stroke is also risk, either as a result of clots transmitted from the heart during PCI, as a result of bleeding following anticoagulation, or as a result of disturbances in the heart's ability to pump effectively as a result of the infarction (Mehta,2015).

Regurgitation of blood through the mitral valve is possible, particularly if the infarction causes dysfunction of the papillary muscle (Mehta,2015). Cardiogenic shock as a result of the heart being unable to adequately pump blood may develop, dependent on infarct size, and is the most likely to occur within the days following an acute myocardial infarction. Cardiogenic shock is the largest cause of in hospital mortality. Rupture of the ventricular dividing wall or left ventricular wall may occur within the initial weeks (Mehta,2015).

Heart failure may develop as a long term consequence, with an impaired ability of heart muscle to pump, scarring, and increase in size of the existing

muscle. Aneurysm of left ventricle myocardium develops in about 10%of MI and is itself a risk factor for heart failure ventricular arrhythmia and the development of clots. Risk factors for complications and death including age, hemodynamic parameters (such as heart failure, cardiac arrest on admission, systolic blood pressure) ST-segment deviation, diabetes, serum creatinine, peripheral vascular disease and elevation of cardiac markers (Kutty , Jones and Moorjanin,2013).

1.2.9 Erythrocyte Sedimentation Rate (ESR)

An erythrocyte sedimentation rate is a type of blood test that measures how quickly erythrocytes settle at the bottom of a test tube that contains a blood sample. Normally red blood cells settle relatively slowly. A faster-than-normal rate may indicate inflammation in the body. Inflammation is part of your immune response system. It can be a reaction to an infection or injury .inflammation may also be a sign of a chronic disease, an immune disorder, or other medical condition (Turgeon,2012).

1.2.9.1 significant of Erythrocyte Sedimentation Rate

An ESR test can help determine if you have a condition that causes inflammation, these include arthritis, vasculitis or inflammatory bowel disease. An ESR may also be used to monitor an existing condition (Turgeon, 2012).

1.2.9.2 The Result of ESR

If the result of ESR is high it may be related to an inflammatory condition, such as:

- Infection
- Rheumatoid arthritis
- Vascular disease
- Inflammatory bowel disease
- Heart disease
- Kidney disease
- Certain cancers

Sometimes the ESR can be lower than normal. A low ESR may indicate a blood disorder such as:

- Polycythemia
- Sickle cell anemia
- Leukocytosis, an abnormal increase in white blood cells

If results are not in the normal range, it doesn't necessarily mean have a medical condition that requires treatment. a moderate ESR may indicate pregnancy, menstruation ,or anemia ,rather than an inflammatory disease . Certain medicines and supplements can also affect the results. these include oral contraceptives, aspirin, cortisone and vitamin A(Hoff brand ,2007).

1.2.10 C - reactive protein

C-reactive protein is a substance produced by liver in response to inflammation, other name is highly -sensitivity C- reactive protein (hs-CRP) and ultra-sensitive C-reactive protein (us CRP).(Judith ,2017).

A high level of CRP in the blood is the a marker of inflammation, it can be caused by a wide variety of conditions, from infection to cancer .High CRP levels can also indicate that there's inflammation A heart attack .C-reactive protein is measure in milligrams of CRP per liter of blood(mg\L). in general ,a low C-reactive protein is better than a high one ,because is indicates less inflammation in the body.(Judith ,2017).

According to Cleveland Clinic, a reading of less than 1 mg/L indicates you're at low risk of cardiovascular disease. A reading between 1and 2.9 mg/L means you're at intermediate risk. a reading of greater than 3mg/L indicates you're at high risk of cardiovascular disease. (Judith, 2017).

A reading above 10mg/L may signal a need for further testing to determine the cause of such significant inflammation in your body. This specifically high reading may indicate:

- Bone infection or osteomyelitis.
- An autoimmune arthritis flare-up
- Tuberculosis.
- Lupus, connective tissue disease or other autoimmune disease.

- Pneumonia or other significant disease.

1.2.11 Red cell distribution width

Red cell distribution width is a measure of the range of variation of red blood cell in volume that is reported as part of a standard complete blood count. Usually red blood cells are a standard size of about 6-8 µm in diameter certain disorders, however, cause a significant variation in cell size. Higher RDW values indicate greater variation in size normal reference range of RDW in human red blood cells is 11.5-14.5%(Carl and Sherrie ,2013).

If anemia is observed , RDW test result s are often used together with mean corpusclar volume (MCV) result to determine the possible causes of anemia .It is mainly used to differentiate an anemia of mixed causes from an anemia of single cause(Carl and Sherrie ,2013).

1.3 Previous studies

In study conducted in India in Tertiary cardiac center to evaluate some inflammatory marker among myocardial infarction patients. A total of 175 (male and female), 175 healthy individual selected as control group. The results obtained from patients showed that the means of RDW were ≥15.5% ,CRP≥1µg\ml , and ESR ≥10 m m/h, also the results showed significant increase in the means of patients in the RDW (p=0.003) ,ESR(0.004) and CRP(0.001) In both sex(Aunge,2013).

And other cohort study conducted in university hospital of Verona to evaluate some inflammatory marker among myocardial infarction patients ,3845 patients were selected ,the result obtained showed that there is strong graded increase of RDW,ESR and CRP(P.value 0.001), and these results are independently to age and sex(Giuseppe,2009).

1.4 Rationale and Objectives

1.4.1 Rationale

About 15.9 million myocardial infarctions occurred in 2015. More than 3 million people had an ST elevation MI and more than 4 million had an NSTMI.

STEMIs occur about twice as often in men as women. In the developed world the risk of death in those who had an STEMI is about 10%.

Recently studies indicate that the high level of C - reactive protein, ESR and RDW is increase mortality and morbidity in patient with myocardial infarction.

Red blood cell distribution width (RDW) is a traditional hematological index used to explore the etiology of anemia. During past years, association between RDW and non-hematological diseases has attracted much attention. Accumulated evidence has revealed that RDW is elevated in various autoimmune diseases and associates with disease activity or complications. The higher risk of cardiac problems in patients with autoimmune rheumatic diseases has been attributed to traditional cardiovascular risk factors as well as chronic systemic inflammation. It has been postulated that increased red blood cell distribution width (RDW) reflects underlying chronic inflammation which contributes to the increased risk of cardiac diseases. It has been reported that increased RDW is strongly and independently associated with the risk of cardiovascular morbidity and mortality in patients with a history of MI. RDW positively correlates with inflammatory markers, C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) even after excluding anemia. Recently studies indicate that the high level of C-Reactive protein, ESR and RDW is associated with increased mortality and morbidity in patient s with myocardial infarction.RDW ,ESR and CRP must be investigated as monitor in MI patients do decrease risk of mortality.

1.4.2 Objectives

1.4.2.1General objective

To assess the ESR, C - reactive protein and Red Cell Distribution Width among Myocardial Infarction Patients in Khartoum State.

1.4.2.2 Specific objectives

- To measure Erythrocyte Sedimentation Rate, C - reactive protein among case and control group.
- To detect the red cell distribution width from the assayed complete blood count from case and control groups
- To compare the mean concentration of ESR, CRP and RDW between case and control groups.
- To correlate ESR, CRP and RDW results with demographic data, sex and gender.

Chapter Two

Materials and Methods

2. Materials & Methods

2.1Study Design

This was analytical case control study.

2.2 Study Area and Duration

This study was conducted in Sudan Heart center during March 2019 to December 2019.

2.3 Study Population

Patients who fulfilled the clinical diagnosis of myocardial infarction with high troponin level of either sex.

2.3.1 Inclusion Criteria

Case include both sex with myocardial infarction, control included apparently healthy individuals.

2.3.2 Exclusion Criteria

Individual with infection, other cases of inflammation, renal disorder, rheumatic arthritis.

2.4 Sample Size

A total 70 subjects were include, 30 patients with MI and 40 healthy people.

2.5 Sample Collection

For this study patient with myocardial infarction was selected as case group compared with apparently healthy individuals. 6ml of venous blood collected in EDTA, heparin and sodium citrate containers by a disposable plastic syringe from each subject.

2.6Methdology

2.6.1 Erythrocyte Sedimentation Rate (ESR)

Westergren Method

The erythrocyte sedimentation rate (ESR), measures the rate of settling of erythrocytes in diluted human plasma. This phenomenon depends on an enter relationship of variables, such as the plasma protein composition, the concentration of erythrocytes, and the shape of erythrocytes. The ESR value is determined by measuring the distance from the surface meniscus to the top of

the erythrocyte sedimented in a special tube that is placed perpendicular in a rack for 1 hour .the clinical value of this procedure is in the diagnosis and monitoring of inflammatory or infectious states.

2.7.1.2 Procedure

2ml of blood was collected under aseptic condition. Blood was aspirated into a bubble -free blood into a clean and dry Westergren pipette. Filled to the zero mark. Pipette was Placed into the vertical rack at 20C˚to 25C˚ in an area free from vibrations, drafts, and direct sun light .After 60 minutes, the distance was read in millimeters from the bottom of the plasma meniscus to the top of the sedimented erythrocytes. The value was recorded as millimeters in 1 hour.

1.7.2 C-Reactive protein

Full automated mindary 480

Is fully automated chemistry machine that depend on the absorbance and turbid metric method to estimate the parameters, the principle of absorbance and turbid metric is based on the scattering or absorption of light by solid or colloidal particles suspended in solution. When light is passed through the suspension, part of incident radiant energy is dissipated by absorption, reflection and reaction while reminder is transmitted.

2.7.2.1 Principle of Red Cell Distribution width

There are two transducer chambers one used to count WBCs and Hb

Together and other used to count RBCs and platelets.

Apportion of blood is separated aspirated whole blood and mixed with diluents in pre-rest ratio, a defined amount of this dilution is sent to detection chamber and passed through a small opening known as aperture. There are also electrodes on each side of aperture – and direct current pass through these electrodes. The direct current resistances between the electrodes changes as the blood suspension pass through aperture. This resistance causes an electrical pulse change proportional to the size of blood cell. These electrical data are converted into graphical displays of volume distribution curves, or histograms.

2.7.3.3 Procedure of Complete Blood Count

The instrument was checked up for the sufficient of the solutions (all pack stromatolyser), also checked electric power supply machine has full battery and earthed connected then power key was pressed on.

Sample was mixed well and entered to probe then the start switch was pressed, when LCD screen was displayed analyzing the sample removed. 30sec and then the results were printed out.

2.8 Ethical Consideration

The consent of selected individuals to the study was taken after being informed verbally their simple language about the objectives of the study, then their approval was taken.

2.9 Data Analysis

The collected data was processed by using a computer based statistical program SPSS (Statistical Package for Social Science) Version (20), T test and P *value* was obtained (P *value* $\leq$ 0.05 was considered statistically significant).

Chapter Three

Results

3. Results

Table (3.1): Frequency of age and sex among study group

This table shows the frequency between the demographic data and study groups.

Variable		**Case**	**Control**
Age	**<**40 years	4	3
	40-60years	17	28
	>60years	9	9
Sex	Male	14	23
	Female	16	17
Total		30	40

Table (3.2): Mean and Standard deviation of ESR, RDW and CRP among case and control group.

This table the mean and standard deviation of ESR,CRP and RDW among case and control group , there is significant increase in ESR, CRP and RDW among myocardial infarction patients compare with control group.

Parameters	Case		Control		P.value
	Mean	STD	Mean	STD	
ESR(mm\h)	27.3	16.0	9.8	4.0	0.00
CRP(µg\l)	30.0	27.2	4.6	5.5	0.00
RDW(%)	52.8	7.1	44.3	5.2	0.00
Total	30		40		-

Table (3.3):

This table shows the comparison between mean of ESR and sex (male and female). And there is insignificant increase in ESR in correlation in male and female.

Case		**ESR**	**P.value**
Sex	**Male**	**37.1**	**0.2**
	Female	**30.9**	

Table (3.4):

This table shows the comparison between mean of CRP and sex (male and female). And there is insignificant increase in CRP in correlation in male and female.

Case		**CRP**	**P.value**
Sex	**Male**	**42.4**	**0.6**
	Female	**38.0**	

Table (3.5):

This table shows the comparison between mean of RDW and sex (male and female). And there is insignificant increase in RDW in correlation in male and female.

Case		**RDW**	**P.value**
Sex	**Male**	**56.0**	**0.9**
	Female	**55.9**	

Table (3.6):

This table shows the comparison between mean of ESR and age groups, and there is insignificant increase in ESR in correlation in age groups.

Case		**ESR**	**P.value**
Age	**20-50**	**25**	**0.38**
	51-80	**40**	

Table (3.7):

This table shows the comparison between mean of CRP and age groups, and there is insignificant increase in CRP in correlation in age groups.

Case		**CRP**	**P.value**
Age	**20-50**	**50**	**0.3**
	51-80	**40**	

Table (3.8):

This table shows the comparison between mean of RDW and age groups, and there is insignificant increase in RDW in correlation in age groups.

Case		**RDW**	**P.value**
Age	**20-50**	**45**	**0.14**
	51-80	**48**	

Chapter Four

Discussion, Conclusion and Recommendations

4. Discussion, Conclusion and Recommendations

4.1 Discussion

Myocardial infarction is one of the most common disease effects through the world, because of association of mortality and morbidity and the cost of society. Myocardial infarction may cause heart failure, an irregular heartbeat, Cardiogenic shock or cardiac arrest.(Nolan ,2015).

Blood pressure, smoking, diabetes, lake of exercise, obesity, high blood cholesterol, poor diet, and excessive alcohol intake among others (Mehta,2015).

Our study show significant increase in ESR (p. value 0.00),

CRP(p. value 0.00) and RDW (p. value0.00)among myocardial patients when compared with control group.

Study that conducted in London by Lippi was agree with our study which show there is significant increase in `ESR(P.value 0.02) ,(P.value 0.03)and RDW result (P.value 0.00).

Other study was conducted in India by vashistha was not agree with our study in the result of RDW that show there in no significant difference (P.value 0.1).

We observed that there is no significant difference in the mean of ESR (p. value 0.2), CRP (p. value0.6) and RDW(p. value 0.9)in myocardial patients males and females . According to the age groups, our study show that there is no significant difference in the mean of ESR (p .value 0.38), RDW (p. value 0.30) and CRP (p. value 0.14) in myocardial patients.

4.2 Conclusion

1. The result of ESR, CRP and RDW is high in myocardial patients and normal in control group.
2. The result of ESR, RDW and CRP is not affected by genders and age.

4.3 Recommendation

Increase the sample size and another study should be done investigation of mortality and morbidity in myocardial patients.

Focus on the result of CBC mainly the RDW because is correlated with the mortality of myocardial infarct patient and the result of CRP also.

These parameters must be investigated as monitor in patients with MI.

Chapter Five

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5.References

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Appendixes


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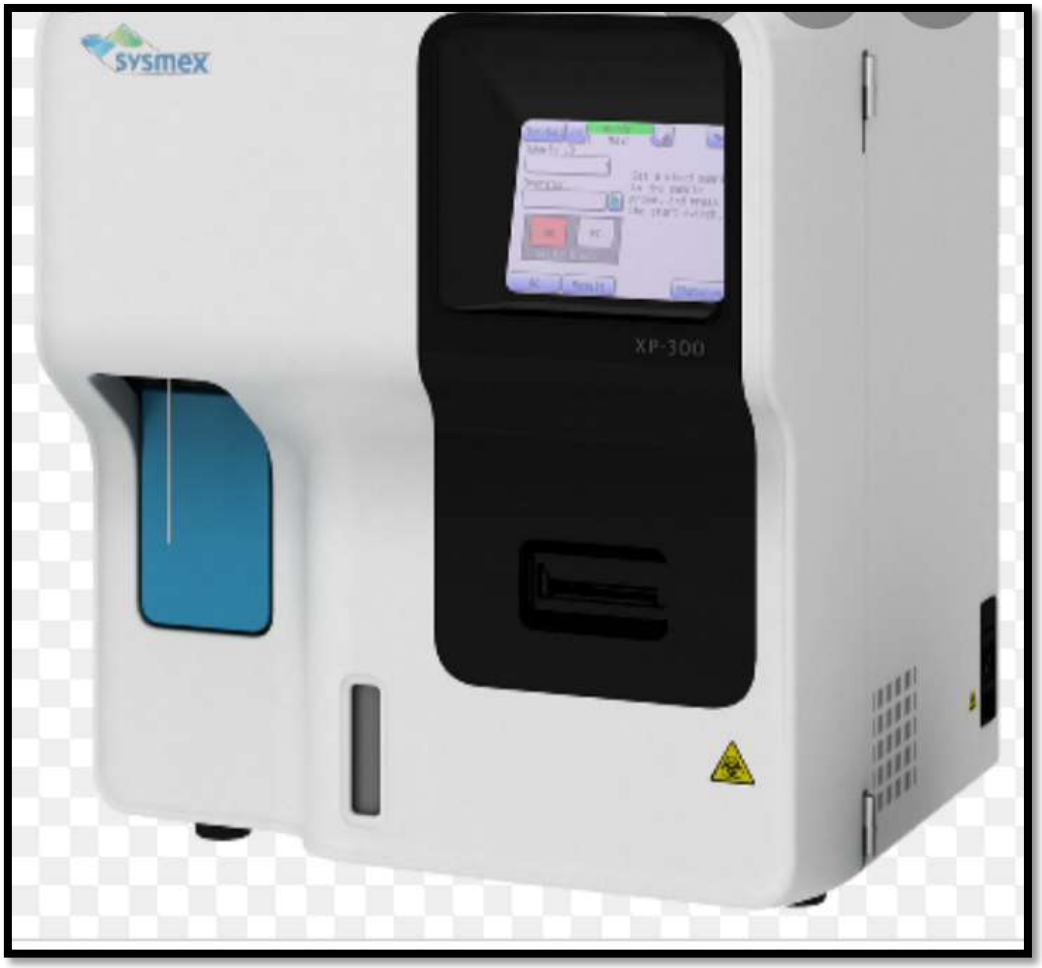
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