Sudan University of Science and Technology

College of Graduate Studies

Measurement of Prothrombin Time, Activated Partial Thromboplastin Time and Platelets Count among Heart disease Patients in Sudan Cardiac Center Khartoum State

قياس زمن البروثرومبين وزمن الثرومبوبلاستين الجزئي المنشط وعدد الصفائح الدموية لدى المصابين بامراض القلب في مركز السودان للقلب ولاية الخرطوم

A dissertation Submitted In partial Fulfillment of the Requirement for Master Degree (M.SC) in Haematology and Immunohaematology

By

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صدق الله العظيم
سورة البقرة
Dedication

To my father and mother

For giving me the hope for life, for love and those give me power supply to all my life.

To my brother and husband

For giving me the chance for choice my live and support me by anything to my study, job, give me hope to tomorrow and future.

To my teachers

For showing me the excitement and joy of hematology.

To my dear friend Huda

To help me and support me in my research.
Acknowledgement

Thank to my supervisor professor Babker Ahmed Mohammed for encouragement, advice, and interest this research.

I would like to acknowledge and thank the staff of the hematology department.

Also I would like to thank the staff of Sudan Cardiac Center, especially staff of hematology lab for their helpful and discussion.
Abstract

Heart diseases are major health problem and greatly affecting the economic and social status of such patients. The objective of this study to measure of prothrombin time, activated partial thromboplastin time and platelets count in heart disease patients compared to control, and compared between heart disease patients them self according to age and gender to observe change which can occur. The study was carried out at the Sudan Cardiac Center, at Khartoum state, Sudan. One hundred blood samples were collected, from 70 heart disease patients and matched by 30 health persons as control. The samples were tested for prothrombin time, activated partial thromboplastin time by manual method and platelets count by sysmex21 Automated Hematology Analyzer. SPSS (version14) was used for statistical analysis. The results showed prolongation in prothrombin time and activated partial thromboplastintime in patients compared with control. The mean of PT in the patients was 30.4±9.7 second and that of control was 13.2±1.9 second. The mean of APTT in the patients was 43.6±8 second and that of control was 32±6.5 second (P value <0.05). Alsono significance change occur in the mean of platelets count in heart disease patients compared to control(P value >0.05). Also no significance change occur in prothrombin time, activated partial thromboplastin time and platelets count between heart disease patients them self according to gender group and different age group (P value >0.05). Therefore its recommended that the patients must be screened always to avoid the complications of thrombosis that cause heart attack and sudden death.
الخلاصة

امراض القلب مشكلة صحية رئيسية ولها تأثير كبير في الحاله الاقتصادي والاجتماعي عند المرضى. لهدف من هذه الدراسة لقياس زمن البروترومين وزمن الثروموبولاستين الجنوبي المنضب وحساب الصفائح الدميه عندمرضي القلب ومقارنتهما مع الضبط وللمقارنة بين مرضى القلب انفسهم بدلاله النوع والالك عوامل التغيير الذي يمكن أن يحدث اجريت هذه الدراسة في مركز السودان للقلب ، ولابه الخرطوم السودان. مانه من عينات الدم جمعت من سبعون مريضا ب المختلف امراض القلب مقابلين بثلاثين من الأصحاء كضبط.

العينات اختبرت زمن البروترومين وزمن الثروموبولاستين الجنوبي المنضب بالطريقة اليدوية، وعدد الصفائح الدميه بالسمكس محلل الدم الاوتوماتيكي وحلل العينات باستخدام الحزمة الإحصائي لعلوم الاجتماعية (14)

نتيجة هذه الدراسة ان هناك اطلال في زمن البروترومين وزمن الثروموبولاستين الجنوبي المنضب عند المرضى حيث وجدت أكثر من المجموعه المقارن بها كضبط حيث وجد متوسط زمن البروترومين عند المرضى (13.9±1.2 ثانية) بينما متوسط زمن الثروموبولاستين الجنوبي المنضب (12.8±2 ثانية). وبدرجة معنويه أقل من 0.05, وكانت لابد وجود تغير ملحوظ في متوسط عدد الصفائح الدميه عند المرضى مقارنة بالإصحاء (بدرجة معنويه أكبر من 0.05). كذلك لابد وجود تغير ملحوظ في متوسط زمن البروترومين زمن الثروموبولاستين الجنوبي المنضب وعدد الصفائح الدميه بين المرضى بدلالة النوع والفئات العمرية المختلفة (بدرجة معنويه أكبر من 0.05). نوصي بان يتم اختبار المرضى دائما وذلك لتجنب مضاعفات النوبة القلبية وموت المفاجي.
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### Chapter one

**Introduction and literature review**

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Abbreviations

APC : Activated Protein C
APTT : Activated Partial Thromboplastin Time
AT : AntiThrombin
BT : Bleeding time
CCDH: cyanotic congenital heart disease
DIC : Disseminated intravascular coagulation
EDTA : Ethylene di adenine tetra acetic acid
EPCR : Endothelial protein C receptor
FDP : Fibrin degradation product
HB : Hemoglobin
HClII : Heparin cofactor II
HiCN :Cynomethemoglobin
HMWH : High molecular weight heparin
IE : Infective endocarditis
LCD : Liquid crystal display
LMWH : Low molecular weight heparin
MI : myocardial infraction
PAI :  Plasminogen activator inhibitor
PC  :  Protein C
PCI :  Protein C inhibitor
PLG :  Plasminogen
PLTS : Platelets
PT  : Prothrombin time
PS  : Protein S
PZ  : Protein Z
RHD : Rheumatic Heart Disease
RBCS : Red blood cells
SK  : Streptokinase
TAFI : Thrombin activatable Fibrinolysis inhibitor
TF  : Tissue Factor
TM  : ThromboModulin
TPA : Tissue plasminogen activator
TT  : Thrombin time
TXA2 : Thromboxane A2
UFH : Un fractionated heparin
UPA : Urinary plasminogen activator
VCAM : Vascular cell adhesion molecule

VWF : Von will brand factor

WBCs : White blood cells

ZPI : Z- dependent protease inhibitor
Chapter one
Introduction and Literature Review
Chapter one

Introduction and Literature Review

1-1. Introduction and background:-

Heamostasis is one of a number of protective processes that have involved in order maintaining a stable physiology. It interacts with other body defence. Such as inflammatory system and immune system. For example of these disseminated intravascular coagulation (DIC) can be initiated by Gram –negativesepticemia.[Hoffbrand et al, 2016].

The heart is blood pump and net of vessels so the study is important. Several biomedical finding have established the effect of cardiovascular disease as arterial hypertension in the coagulation process. [Adaeze et al 2014].

Cardiovascular disease account for about one third of premature deaths in men and one quarter in women and arterial hyper tension is one of the most significant risk factors for cardiovascular disease .[Bernatova.I 2014]

Heart disease is major health problem and greatly affecting the economic and social status of such patients. Globally cardiovascular disease accounts for approximately 17 million deaths a year, nearly one-third of the total.[Chobanian.A.V et al 2003].

Cardiovascular disease develops 7 to 10 years later in women than in men and is still the main cause of the death in women. [Maas and Appelman, 2010].

Coronary artery disease is most common disease, is cause of death in male and female evaluation and treatment of the disease however can differ between male and female [Douglas and Ginsburg, 1996].
Through the world many studies were done in this topic due to the important of the heart in the body.

In study it has been recognized that patients with cyanotic congenital heart disease (CCDH). Show significant bleeding tendency which can be secondary to coagluopathies in these patients. Some coagulation abnormalities, are thrombocytopenia and factor deficiency, fibrinolysis, and disseminated intravascular coagulation (DIC). [Ghasemi et al, 2014]

In other study ,Although significant minority of patients with cyanotic congenital heart disease (CCHD) are thrombocytopenic .The pathogenesis and prevalence have been established .This study was designed to address these tow issue .The conclusion platelets count in CCHD appear to represent a continuum beginning with low platelet counts and ending with thrombocytopenia .[Michael et al,2006] .

Other study platelets have been implicated in the pathogenesis of coronary artery disease ,and number of studies have examined platelets function and coagulation parameters in such patients .But these study designed to examined platelets coagulants activities ,volumes ,and aggregate ratios in patients with chest pain these were find platelets coagulation activities increased activated partial prothrombin time(APTT) in coronary artery disease .There are contribution in factor(seven ,eight ,fibrinogen )and deficiency in antithrombin three.[Kontiro et al,1984].

In other study aim to link between coagulation system and the development of chronic heart failure. Physical stress cause increase in concentration of hormones it is proved that it causes the disorder of the coagulation system an increase of the following factors of plasma (fibrinogen, seven, eight, fibrinopeptidA) thrombin – antithrombin complex, fibrinolysis (D-dimer), endothelium and decrease in E-selectin.[Mongirdine et al, 2010].
Other studies were done in children with congenital heart disease. They were found with increased bleeding time indicating to amicrovascular abnormality or qualitative platelets defect. [Kontras et al, 2014].

Other study they suggest that the association between congestive heart failure and disseminated intra vascular coagulation (DIC) is an under recognized one. Thus the precise role of coagulation factors in congestive heart failure is unknown. [Sarcon et al, 2015].

In other side were study done to clotting characteristic of pulmonary and systemic blood were studied in patients with chronic rheumatic mitral valve disease complicated by arterial fibrillation and other patients with aortic valve disease.

Both group of patients showed difference in patients platelets function between pulmonary and systemic blood patients with mitral valve disease aggregation of platelets was significantly greater in systemic than in pulmonary arterial blood at all time; the converse was true during exercise. In aortic valve disease platelet aggregation was greater in systemic than pulmonary at all time. Only the patients with mitral valve disease patients showed change in blood coagulation during passage through lungs and left heart; statistically significant shortening partial thromboplastin time in systemic compared with pulmonary arterial blood both at rest and during exercise. Similarly the effect of exercise on the various haemostatic factors measured were largely confined to the patients with mitral valve disease in these patients exercise stimulated in increase in factor VIII in pulmonary arterial blood. [Toy et al 1980].
1-2. Literature Review

1-2-1. Normal Haemostasis:

Haemostasis is one of number of protective processes that has involved in order maintaining a stable physiology. It interact with other body defense mechanisms, such as immune system and the inflammatory response. The high blood pressure generated on the arterial side almost instantaneous, but strictly localized procoagulant response in order to compromising blood flow generally. Systemic anticoagulant and clot dissolving component have also evolved to prevent extension of the procoagulant response beyond viciation vascular injury resulting in unwanted thrombus formation. The result haemostatic mechanism is thus a complex mosaic of activating or inhibitory pathways that integrates its five major components (blood vessels, platelets, coagulation, factor and inhibitor, and fibrinolytic element). [Hoffbrand A et al, 2016].

Blood coagulation occurs when the enzyme thrombin is generated and proteolysis soluble plasma fibrinogen forming the insoluble fibrin polymer, or clot. [Hoffbrand and Higgs, 2016].

Haemostasis is process whereby blood coagulation is initiated in tightly regulated fashion, together with the removal (or Fibrinolysis) of the clots parts of vascular remodeling. This process are maintained are the whole organism for its life time. [Hoffbrand et al, 2016].

The whole haemostatic mechanism is integrated in vivo so that thrombin generation is localized, limited and followed by Fibrinolysis.
1-2-2. Blood coagulation process:-

Blood coagulation initiated when exposure of blood to cells expressing tissue factor (TF) on their surface is both necessary and sufficient to initiated blood coagulation in vivo, both in normal hemostasis and pathological situation. Present version of earlien cascade concept for intrinsic and extrinsic pathways of generation of thrombin. [Hoffbrand, et al 2016].

Blood coagulation in vivo involves a biological amplification system in which relatively few initiation substances sequentially activated by proteolysis a cascade of circulating precursor protein (the coagulation factor enzyme), which culminates in the generation of thrombin. [Hoffbrand et al, 2016].

Although the contact system does not appear to have in physiological role in hemostasis it remains available role for understanding a common coagulation tests. Tissue factor (TF) is constitively expressed at biological boundaries such as skin, organ surfaces, vascular adventitia and epithelial, where function as a haemostatic envelop following disruption of vascular integrity, blood is immediately exposed to cells expressing TF, leading to the initiation of blood coagulation. [Hoffbrand et al, 2016].


1-2-3-1. The endothelium:-

Its functions including intracellular transport and maintenance of blood follow. Endothelial cells possess surface receptor for a variety of physiological substances for example thrombin and angiotensin II, once activated, endothelial cells express a variety of intracellular adhesion molecules, some of which are released into the plasma these include Vascular Cell Adhesion Molecules (VCAM), E-selectin,
P-selectin and Von Will Brand Factor (VWF). Which modulate platelet adhesion and vascular permeability. Endothelial cell also have anticoagulant function and fibrinolytic factor. [Hoffbrand et al 2016].

1-2-3-2. The platelet-vessel interaction:-

Platelets (thrombocytes) are cellular fragments of megakaryocyte; the function of the platelet in primary hemostasis is the formation of platelets plug.

Following break in the endothelial lining, there is initial adherence of platelets to exposed connective tissue mediated by VWF. Collagen exposure and thrombin generated through activation of tissue factor produced at site of injury cause adherent platelets to release the granule content and also activate platelet prostaglandin synthesis leading to formation of thromboxane A2 (TXA2). Released ADP causes platelet to swelling and aggregate platelet rolling in direction of blood flow over exposed VWF with activation of GPII\IIIa receptors results in firmer binding. Additional platelets form the circulating blood are drawn to the area of injury. Continuing aggregation promotes the growth of haemostatic plug. The primary haemostatic plug produced by platelets in the first minute or so following injury is usually to provide temporary control of bleeding. [Hoffbrand and Moss, 2016].

1-2-3-3. Von Will Brand Factor (VWF):-

VWF is multimeric glycoprotein that plays an important role in primary heamostasis by promoting platelet adhesion to the subendothelium at sites of vascular injury under high shearrate condition. It also acarrier of factor eight (FVIII) and this association protect FVIII from rapid protolysis. VWF synthesized by endothelial cells, megakaryocytic and platelets. [Hoffbrand et al, 2016].
Table 1-1: The coagulation factor nomenclature with preferred names and synonyms (Hoffbrand and Moss, 2016):

<table>
<thead>
<tr>
<th>Factor number</th>
<th>Descriptive name</th>
<th>Active forms</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Fibrinogen</td>
<td>Fibrin subunit</td>
</tr>
<tr>
<td>II</td>
<td>Prothrombin</td>
<td>Serine protease</td>
</tr>
<tr>
<td>III</td>
<td>Tissue factor</td>
<td>Receptor \ cofactor</td>
</tr>
<tr>
<td>V</td>
<td>Labile factor</td>
<td>Cofactor</td>
</tr>
<tr>
<td>VII</td>
<td>Proconvertin</td>
<td>Serine protease</td>
</tr>
<tr>
<td>VIII</td>
<td>Antihaemophic factor</td>
<td>Cofactor</td>
</tr>
<tr>
<td>IX</td>
<td>Christmas factor</td>
<td>Serine protease</td>
</tr>
<tr>
<td>X</td>
<td>Stuart –power factor</td>
<td>Serine protease</td>
</tr>
<tr>
<td>XI</td>
<td>Plasma thromboplastin - antecedent</td>
<td>Serine protease</td>
</tr>
<tr>
<td>XII</td>
<td>Hageman (contact) factor</td>
<td>Serine protease</td>
</tr>
<tr>
<td>XIII</td>
<td>Fibrin –stiblizing factor</td>
<td>Transglutaminase</td>
</tr>
<tr>
<td></td>
<td>Prekalikrein (Fletcher factor)</td>
<td>Serine protease</td>
</tr>
<tr>
<td></td>
<td>HMWK(fitzgerald factor)</td>
<td>Cofactor</td>
</tr>
</tbody>
</table>
1-2-4. Amplification (intrinsic and extrinsic pathway):-

An updated concept of TF-initiated thrombin generation, including the important feedback reactions of thrombin. Physiological initiator of blood coagulation is exposure of the circulating zymogen FVII to membrane bound TF activation of FVII to the protease FVIIa result in activation of FIX and FX by the TF-FVIIa complex. In the absence of its cofactor FVa, FXa generate only trace amount of thrombin from prothrombin (this extrinsic pathway). This amount insufficient to initiate significant fibrin polymerization but able to back activate FV, FVIII and FXI by limited protolysis in the amplification phase of coagulation, FXIa activate FIXa, which form complex with FVIIIa. This is intrinsic tenase complex (FVIIIa-FXa) that activate sufficient FXa (intrinsic pathway) to form complex with FVa, producing the prothrombinase complex (FVa-FXa). Result in the explosive generation of fibrin clot (common pathway). [Hoffbrand et al, 2016].
Figure 1-1: The intrinsic and extrinsic pathways. [Hoffbrand et al, 2016].
1-2-5. Coagulation factors:-

1-2-5-1. Tissue factor (TF):-

The formation of FVIIa–TF complex as initiator of coagulation in both normal and pathological to coagulation TF is protein contain group of amino acid extra and transmembrane. Vascular adventitial cells, neuralgia, vascular smooth muscle and epidermal cells express TF is initiate clot if leakage out of vessels. Intravascular exposure of TF by any route can result in pathological thrombosis. [Hoffbrand, et al, 2016].

1-2-5-2. Factor VII:-

Plasma FVII bind to TF after vessels trauma or rupture, to form complete initiate coagulation by directly activation of FX. The FVII gene lies adjacent to the FX gene. Is one vitamin k- dependent carboxylase (FX, IX, VII, Prothrombin, PC) the life span of FVII is 3 hours as zymogen, and 2.5 hours as FVIIa. [Hoffbrand et al, 2016].

1-2-5-3. Factor X:-

Its gene and serine protease as FVII. The half life is 36 hours. FX is activated by either FIX a-FVIIa or TF-FVIIa on phospholipids surface in the presence of calcium ion. FXa forms aporphospholipids–bound complex with FVa which efficiently activates prothrombin (prothrombinase complex).[ Hoffbrand et al, 2016].
1-2-5-4. Factor IX:-

Is X-linked gene. Deficiency of FIX result in clinical haemophilia B, the main function of FIX is to participate in the tenase complex (IXa-FVIIIa) is liver specific transcription factor the plasma half life 8 hours. [Hoffbrand et al, 2016].

1-2-5-5. Factor XI:-

Is a zymogen of serine protease that have 4 apple (PAN 1-4) domain and aserine protease domain in each monomer. Activation of FXI is by single cleavage proformed by thrombin. FXa then activate FIX directly in free solution. FXIa activation by the contact protein FXIIa was originally thought to be arelevant step in intrinsic or contact activated coagulation, but it is now considered that the feedback activation of FXI by trace thrombin provides a physiologically relevant route for generation of increased amount of FIXa to assemble tenase during the amplification of the initial TF stimulus. [Hoffbrand et al, 2016].

1-2-5-6. Factor XIII:-

Circulate as a tetramer of 2A-chains and 2B-chains. The B-chain function as a carrier for the A-chains which after activation by thrombin, function as transglutaminase to cross linked fibrin and other proteins in the clot result in a stable structure. [Hoffbrand et al, 2016].

1-2-5-7. Factor VIII:-

Its X chromosome linked gene. Released as a 2-chain molecule. Because of internal homology, the FVIII domain structure can be represented as A1, A2, C1, C2. The B domain is not necessary for procoagulant function so deleted in full activity. FVIII is the essential cofactor activation of FXa by FIXa in the tenase complex. It has no function until protolysed to FVIIIa by thrombin or FXa. [Hoffbrand et al, 2016].
1-2-5-8. Factor V:-

The structure of factor V, like that of FVIII, can be represented as A1-A2-B-A3-C1-C2. In contrast with FVIII the B-domain is required in full procoagulant function. FV also differ from FVIII in that it lack 3 short acidic inter domain peptides implicated in FVIII function.

FV is the cofactor for the activation of prothrombin by FXa. it no functioning until protolysed by thrombin or FXa into Va.[ Hoffbrand et al, 2016].

1-2-5-9. Fibrinogen:-

Its gene cluster is located in chromosome in order Beta, Alfa, Gama, linked by disulfide bond cross-linked.

Polymerization of fibrinogen occurs when thrombin cleaves 2 short negatively charged fibrin peptide A and B from the N-terminal sequences of the alfa and beta chain respectively. This release sequences in fragment E-region (called knob ) that fit in holes in the fragment D-regions. Polymerization then occur spontaneously in staggered half-over lap array. Electron microscopy study still are important in resolve the molecular of fibrillar fibrin formation.[ Hoffbrand et al, 2016].

1-2-5-10. Prothrombin:-

Its sequences similar to that found in other vitamin k dependant protein. FXa complexed with FVa activated prothrombin zymogen to thrombin on a phospholipids surface (prothrombinase). On cleavage of 2 peptide bonds. Fully cleaved thrombin is termed is rapidly released from its site of participate in numerous haemostatic function free in solution; acting as aprocoagulant against many substances including fibrinogen, FV, FVIII, FXI.[ Hoffbrand et al, 2016].
1-2-6. Inhibitor of blood coagulation:-

The thrombin plug must be in the site of injury and must not release to other part of body;

1-2-6-1. Tissue factor pathway inhibitor:-

Is a kunitz type inhibitor; the various serpin found in blood probably play on physiological role in the inhibition of FVIIa in the TF-FVIIa complex. Instead the action of this serine protease cofactor complex is modulated by tissue factor pathway inhibitor (TFPI), which located on the endothelial cell surface, with in platelets, inplasma and monocyte. [Hoffbrand et al, 2016].

1-2-6-2. Serine protease inhibitor:-

Human plasma contain at least 7 type of serine protease inhibitor. Only antithrombin and heparin cofactor II(HCII)assume haemostatic significance. [Hoffbrand et al, 2016].

1-2-6-2-1. Antithrombin:-

AT is synthesized in liver, with a high plasma concentration. Antithrombin (AT) form astable with several serine protease coagulation factors, predominantly thrombin and FXa, but also some extent F (Xa, Xla, XIIIa, Kalikrein). [Hoffbrand et al, 2016].

1-2-6-2-2. Heparin cofactor II:-

It appear to be specific inhibitor of thrombin and have a little or no anti FXa activity the rate of thrombin neutralization by HCIIis increased approximately 1000-fold by heparin ,although because of it lower affinity it require 5-10 times more heparin than AT.[ Hoffbrandet al, 2016].
1-2-6-3. Heparin and heparin like substance:-

Heparin implies asingle compound; it in factor refers to heterogeneous mixture of sulfated polysaccharides.

Unfractionated heparin (UFH) is an extremely heterogenous polymer being composed of between 10-100 saccharide units. Yielding a number of low molecular weight heparin (LMWH) preparation 1-2 units that may inhibit the specific serine protease thrombin. [Hoffbrand et al 2016].

1-2-6-4. Protein Z :-

PZ vitamin k-dependent plasma protein that serves as cofactor for the inhibition of FXa by Z-dependent protease inhibitor (ZPI) a member of the serine super family.

PZ structure similar to those coagulation factors FVII,FIX,FX,and PC .Inhibition of FXa . [Hoffbrand et al, 2016].

1-2-6-5. Alfa 1 –antitrypsin:-

This is aserpin those primary target are pancreatic and leukocyteelasteases. In coagulation the major inhibitory activity is directed against FXIa,and FXa .[Hoffbrand et al, 2016].

1-2-6-6.protease nexin 2:-

This is akunitz type serine protease inhibitor that found in the alfa granules of platelets inhibitor of FXIa. [ Hoffbrand et al, 2016].

1-2-6-7. Alfa 2-Antiplasmin:-

This is the principle inhibitor of the fibrinolytic enzyme plasmin.

1-2-6-8. Esterase inhibitor:-
Is a minor way to the neutralization of FXI a and plasmin.

**1-2-6-9. Alfa2-microglobin:**

Is composed of four identical chain, it binds to coagulation factors at the site away from the active site and make inhibition.

**1-2-6-10. Protein C and protein C pathway:**

PC is vitamin k-dependent serine protease has an identical modular composition to the procoagulant factor FVII, FIX, and FX. In order to exert its anticoagulant effect, PC must first be activated to APC. This by thrombin.

APC interact with protein S bound to the phospholipids surface of activated platelets, enhancing the anticoagulant activity of APC against FVa and FVIIIa.

Protein C pathway inhibits of cofactor FVa and FVIIIa, the activated form of FV, FVIII, enhance the activity of serine protease factors in the tenase and prothrombinase complex.

**1-2-6-11. Thrombomodulin (TM):**

Is an integral transmembrane receptor found on endothelial cells in virtually all body tissues. TM forms a complex with thrombin, preventing binding of the protease to its various procoagulant substrates (Fibrinogen, FV, FVIII, FXIII, and Protease –activated receptor involved in platelet aggregation).

**1-2-6-12. Endothelial protein C receptor:**

EPCR a transmembrane receptor on endothelial cells that binds PC and promotes its activation by the thrombin –TM complex.
1-2-6-13. protein Sand PC inhibitor:-

PS is a single chain vitamin k-dependent glycoprotein chiefly synthesized in the liver by endothelial cells. Its bind to negatively charged phospholipids exposed on the surface of activated platelets.

APC is subject to inhibit by serpin, including APCinhibitor (PCI), PAI-1 and alfa-1 antitrypsin, PCI slowly but progressively blocks the action of APC. [ Hoffbrand et al, 2016 ].

1-2-7. Fibrinolysis:-

That the principle functions of the fibrinolytic system are to ensure that excess fibrin deposition is either prevented or rapid removed and following re-establishment of heamostasis, the fibrin mesh is removed during wound healing. The system of pro fibrinolytic and antifibrinolytic factors that has evolved to meet the requirement to clot formation. [ Hoffbrand et al, 2016].

1-2-7-1.component of the fibrinolyticsystem:-

These include plasminogen (PLG) and plasmin; several endogenous tissue plasma derived or exchange PLG activators, and a number of inhibitor of plasma in or of the PLG activators. Both endogenous and exogenous fibrinolytic factors have been used clinically to treat thrombosis. [Hoffbrand et al, 2016].

1-2-7-2. Plasminogen and plasmin:-

PLG is a single –chain glycoprotein zymogen of serine protease plasmin which carried out the enzymatic degradation of cross linked fibrin.
1-2-7-3.Actoin of plasmin in fibrin and fibrinogen:-

It can hydrolyses a variety of substrate as (FVand FVIII, but its major physiological target are fibrin and fibrinogen) and give heterogenous mixture of small soluble peptides known collecting as fibrin degradation product (FDP).

Digestion of fibrin and fibrinogen give D-fragment, the residue known as Y attacked by plasmin to give fragment E.

Following the thrombin generation and consequent activation of FXIII, intracellular transmidation of the alfa and beta chain by FXIIIa occur and then the action of plasmin yield chacteristic D-dimer, D-dimer –E-fragment and oligomers of fragment Xand Y . However clinically, FDPassay are used to detectDIC, when mixed fibrin fibrinogen degradationproduct appears in the circulation. [Hoffbrand et al, 2016].

1-2-7-4.Plasminogen activators:-

1-2-7-4-1.Tissue plasminogenActivator (TPA):-

TPA is a serine protease secreted by endothelial cells. It is not synthesized by the liver or kidney, but is found in most extra vascular body fluids, including saliva, milk, bile, cerebrospinal fluid and urine.

1-2-7-4-2. Urinary plasminogenActivator (UPA):-

First extracted from urine, is synthesized by tubules and collecting ducts in the kidney and by fibroblast–like cells in the gastrointestinal tract. It is secreted as an inactive zymogen that cleaved by activator in plasma (including kalikriken and plasmin).
1-2-7-4-3. Exogenous plasminogen Activator:-

Derived from non human sources including animals and certain plants and microorganisms known as streptokinase (SK). Is make non enzymatic polypeptide that forms a stable complex with plasminogen. [Hoffbrand et al, 2016].

1-2-8. Inhibitor of Fibrinolysis:-

1-2-8-1. plasminogen activator inhibitor (PAI):-

1-2-8-1-1. Plasminogen activator inhibitor type one:-

PAI-1 is an important fast activity serpin inhibitor of tPA, uPA, and to small extent, plasmin, and secreted by endothelial cells. Also found in platelets alpha granules. It occur in 2 form active functionally complex with tPA.

1-2-8-1-2. Plasminogen activator inhibitor type 2:-

Produce by the placenta and thus contribute to the inhibition of Fibrinolysis that occur during pregnancy. Also synthesized in monocyte, and epidermal cells but not usually found in no pregnant subject. Is more active in inhibition of uPA and tPA. [Hoffbrand et al, 2016].

1-2-8-2. Inhibitor of plasmin:-

1-2-8-2-1. Alfa -2 Antiplasmin:-

Is active predominant plasmin inhibitor. Form a stable complex with plasmin.

1-2-8-2-2. Lipoprotein A:-
The protein portion of the lipoprotein A is termed apo(a). It is synthesized in the liver and circulate in plasma. It can compet with PLG for binding site on fibrinogen or tPA, and may also increase PAI-1 expression.

1-2-8-2-3. Thrombin – activatable Fibrinolysis inhibitor:

In the presence of Thrombomodulin activate carboxy peptidase B, and TAFIa in turin inhibit Fibrinolysis. [Hoffbrand et al, 2016].

1-2-9. Tests of haemostatic functions:

Defective of haemostatic with abnormal bleeding may results from a vascular disorder, thrombocytopenia or platelets function disorder and may be defective in blood coagulation. [Hoffbrand and Moss, 2016].

1-2-9-1. Blood count and blood film examination:

Thrombocytopenia, modern counters measure platelets volume. Also the absolute count of immature platelets correlate increased platelets production. Platelets count may be manually or electronic counting, platelets counting use full in clearing case of defect in haemostatic function due to quantities or qualitative platelets defect. [Hoffbrand and Moss, 2016].

1-2-9-2. Screening tests of blood coagulation:

It provides assessment of the extrinsic and intrinsic system of blood coagulation and also the central conversion of fibrinogen and fibrin. [Hoffbrand and Moss, 2016].
Table 1-2 screening tests used in diagnosis of coagulation disorders [Hoffbrand and Moss, 2016].

<table>
<thead>
<tr>
<th>Screening tests</th>
<th>Abnormalities indicated by prolongation</th>
<th>Most common cause of coagulation disorder</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombin time (TT)</td>
<td>Deficiency or abnormality of fibrinogen or inhibition of thrombin by heparin or FDPs.</td>
<td>DIC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Heparin therapy.</td>
</tr>
<tr>
<td>Prothrombin time (PT)</td>
<td>Deficiency or inhibition of one or more of the following coagulation factors; VII, X, V, II, Fibrinogen.</td>
<td>Liver disease</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Warfarin therapy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>DIC</td>
</tr>
<tr>
<td>Activated partial thromboplastin time (APTT)</td>
<td>Deficiency or inhibition of one or more of the following factors XII, XI, VIII, X, V, II, Fibrinogen.</td>
<td>Hemophilia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Christmas disease (+ condition above)</td>
</tr>
<tr>
<td>Fibrinogen quantitation</td>
<td>Fibrinogen deficiency</td>
<td>DIC and liver disease</td>
</tr>
</tbody>
</table>

1-2-9-2-1. Prothrombin time (PT):

Measure factors VII, X, V, prothrombin and fibrinogen. Tissue thromboplastin (brain extract) or synthetic TF with lipid and calcium is added to citrated plasma. [Hoffbrand and Moss, 2016].
1-2-9-2-2. Activated partial thromboplastin time (APTT):-

Measure factor VIII, IX, XI, and XII in addition to FX, V, Prothrombin and fibrinogen. Three substances—phospholipids, surface activator (kaolin) and calcium added to citrated plasma.

Prolonged PT and APTT because of factor deficiency are corrected by the addition of normal plasma to the test plasma. To know deficiency from presence of inhibitor. [Hoffbrand and Moss, 2016].

1-2-9-2-3. Thrombin time (TT):-

Is sensitive to a deficiency of fibrinogen or inhibitor of thrombin. Diluted bovine thrombin is added to citrated plasma. [Hoffbrand and Moss, 2016].

1-2-9-2-4. Specific assays of coagulation factors:–

Most based on a PT and APTT all factor except are to be measured are presented in substrate plasma. A number of chemical chromometric and immunological methods are available. [Hoffbrand and Moss, 2016].

1-2-9-2-5. Bleeding time (BT):–

Is not a reliable assessment of platelet function as it is sensitive. It was used to identify abnormal platelet function, including the diagnosis of VWF deficiency. It has been replaced by specific platelet aggregation tests, platelet adhesion assay and platelet function analysis. [Hoffbrand and Moss, 2016].
1-2-9-2-6. Test of platelets function:-

Platelets aggregatory measured in full light absorbance in platelets –rich plasma platelets aggregate . [Hoffbrand and Moss, 2016].

1-2-9-2-7. Test of Fibrinolysis:-

As thromboplastogrohy (TEG) or hromboelastmetry (ROTEM) D-dimer is measurement of FDP. [Hoffbrand and Moss, 2016].

1-3. Normal cardiovascular system:-

Cardiovascular system may be considered as being composed of a pump (heart) and plumbing (vessels) that take nutrient to tissue and remove metabolites from them . Metabolites travel by blood, lymphatic return tissue fluid to blood via the thoracic ducts.

The major diseases implicated in the cardiovascular system for this death are atherosclerosis, thrombosis, embolism and infraction. [vardaxis, 2000]
1-3-1. Heart failure :-

It is clinical condition characterized by the inability of heart pump blood with requirement of the metabolic tissues of the body or being able to do so at increased filling pressures. It may be divided into systolic or diastolic failure depending on whether there is abnormality in the cardiac contractility.[Garg and Gupta, 2013].

Figure 1-2; Normal heart anatomy [vardaxis, 2000]
1-3-2. Left ventricle failure:-

Mainly caused by ischemic heart disease, hypertension, aortic or mitral valvular disease and myocardial disease. The feature includes hyper atrophy and fibrosis in the myocardium. Arterial involvement result in the development of arterial fibrillation which is responsible for thrombus or embolic stroke. [Garg and Gupta, 2013].

1-3-3. Sudden cardiac death:-

It is defined as the death of an individual within 1 hour of onset of symptom commonly due to ventricular fibrillation.

In case of coronary vessel occlusion leading to ischemia, there is physiological compensatory vasodilatation resulting in augmentation of coronary blood flow. [Garg and Gupta, 2013].

1-3-4. Stable angina:-

Occur when the myocardial oxygen demand is more than the supply. Is take place when the coronary artery occluded more than 75%. Characterized by the pain on exertion is relieved on taking rest or taking vasodilators. [Garg and Gupta, 2013].

1-3-5. Prinzmetal or variant angina:-

It is an episodic angina due to coronary artery spasm resulting in pain at rest it is characterized by ST segment elevation on the ECG. [Garg and Gupta, 2013].
1-3-6.Unstable or crescentoangina:-

It is induced by atherosclerotic plaque disruption with superimposed partial thrombosis or vasospasm or both of them. The pain occur with increasing frequency and for a longer duration and characteristically precipitated by progressively less exertion.[Garg and Gupta, 2013].

1-3-7.Myocardial infarctions (MI) :-

Table 1-3 type of myocardial infarctions. [Garg and Gupta, 2013].

<table>
<thead>
<tr>
<th>Subendocardial MI</th>
<th>Transmural MI</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Ischemic necrosis limited to (1/3^{rd}) of ventricular wall.</td>
<td>• Ischemic necrosis involves full thickness of ventricular wall.</td>
</tr>
<tr>
<td>• Caused by incomplete coronary artery occlusion.</td>
<td>• Caused by severe coronary atherosclerosis with acute plaque rupture and occlusive thrombus.</td>
</tr>
</tbody>
</table>

1-3-8.Infective endocarditis (IE):-

It is colonization invasion of heart valve and mural endocardium by microbiologic agent leading to formation of bulky, friable vegetation composed of thrombotic debris and organism with destruction of underlying cardiac tissue.[Garg and Gupta, 2013].
1-3-8-1. Morphology:-

The friable, bulky destructive vegetations containing fibrin. When the vegetation erode into myocardium, they can form an abscess, the systemic embolisation can result in septic interact.[Garg andGupta ,2013 ].

1-3-9. Rheumatic Heart Disease (RHD):-

Rheumatic fever is an acute immunologically mediated multisystem inflammatory disease that occur few weeks after an attack of group A,B-hemolytic streptococcal pharyngitis not disease mainly in children between 5-15 years .Only 3% of patients with group A streptococcal pharyngitis develop acute rheumatic fever .[Garg andGupta ,2013 ].

1-3-10. Congenital heart disease:-

About 1 in 200 babies as born have a congenital heart defect .About 5% of cardiac defects are attributed to the chromosomal abnormalities .Or may be to other disease .Defect are variables in severity ,ranging from the trivial and subclinical to the rapidly fatal .There are many types of congenital heart disease ,but only the most common are ;

1-3-10-1. Left to right shunt:-

Arterial septal defect is a connection between right and left arterial due to a hole in the interarterial septum. About 90% congenital heart disease most of this the
occurrence in adult. A complication associated with untreated cases of this disease is the occurrence of paradoxical emboli. [Vardaxis, 2000].

1-3-10-2. Plunonary Stenotic lesions:

This involve narrowing of the pulmonary artery or the pulmonary valve which reduce the amount of blood. So the affected babies appear blue cyanotic this is probably due to embolism of megakaryocyte from the bone marrow. [Vardaxis, 2000].

1-3-10-3. Coarctation of the aorta:

Is the condition in which there is narrowing or blockage of the aorta. Is about 5% of congenital heart disease. There are 2 type;

1-3-10-3-1. Preductal type (infant):

Sever narrowing of segment of the aorta, a patient duct allow blood to enter the systemic circulation from the pulmonary circulation.

1-3-10-3-2. Post ductal type (adult):

More common and involves a shorter segment of the aorta frequently in ring fibrosis occurs in wall of aorta. [Vardaxis, 2000].

1-5. Hypothesis:

Medical report, laboratory investigations and medical record all wide the world clear that the heart disease lead to coagulation disorder and increase especially during major operation suggesting that the decrease of element, crisis, and frequent severe painful and hospital admission have association with coagulation disorders.

We will investigate whether this finding applies in patients with heart disease.
1-6. Rationale:

Heart disease is a major public health concern that has great impact on both individuals and society. Heart disease is also associated with significant mortality.

Recent researches indicate that patients who had heart disease may have ability to stimulate haemostatic disorders coagulation deficiency, platelets dysfunction and thrombocytopenia as results of heart disease. Patients show variable abnormalities in PT, APTT, PLTS Count and some experience no change from the base line value.

1-7. Objectives:-

1-7-1. General objectives:

To Measurement of Prothrombin Time, Activated Partial Thromboplastin Time and Platelets Count among Sudanese Heart disease Patients.

1-7-2. Specific objectives:

To Measure PT, APTT, in heart disease patients compared to control.

To Measure platelet counts in heart disease patients compared to control.

To comparing of PT, APTT and platelets counting in study group according to age group and gender.
Chapter two

Material and methods
Chapter Two

Material and Method

2. Material and method:

2-1. Study design:

A hospital base cross sectional analytical study was conducted for evaluation of haemostatic mechanism in patients with heart disease.

2-2. Study area:

The study conducted in Khartoum state at Sudan cardiac center.

2-3. Study population:

Patients with heart disease investigated for PT, APTT, and PLTS count.

2-4. Sampling:

The frame included all heart disease patients.

2-5. Inclusion criteria:

All patients who had a confirmed diagnosis as heart disease patients.

2-6. Exclusion criteria:

All patients who were not diagnosis as heart disease patients.

2-7. Sample size:

According to design of study, the sample (patients) selected by a simple random sampling method (probability sampling). Seventy samples of patients matched by thirty samples as control.
2-8. **Tool of data collection:**

The data collected by using of laboratory investigation to obtain PT, APTT, PLTS count. Also the interviews used to obtain age, sex, family history, clinical features and using of questionnaire as instrument.

2-9. **Data analysis:**

The data after collection analyzed to obtain the mean standard deviation and the probability (p_ value). between patients and control by using SPSS computer program.

2-10. **Ethical consideration:**

All information that obtained from patients kept as highly confidential and specimens or result not permitted.

The participants provided with information about the study and any risk that may arise especially when collection technique applied.

2-11. **Time line:**

The best of research about 3 month began in 1\4\2016.

2-12. **Sampling:**

Five ml of blood take from patient, 2.5 ml collected in Tri- Sodium citrate anticoagulant container to obtain plasma of patient to PT and APTT testing other 2.5 ml collect in EDTA of platelets count.
2-13. Methodology:

2-13-1. Collection technique:

EDTA container.

Tri-sodium citrate container.

Cotton.

Alcohol (70%).

Syringes.

Tourniquet.

2-13-2. Procedure:

1. Patients’ comfortable sitting, tourniquet applied above elbow and superficial antecubtal for arm vein identified.
2. The skinsterile with 70% ethanol and allowed to dry.
3. Syringe needle inserted correctly into the vein, and 5ml of blood sample take, tourniquet released, needle remove, and 2.5ml into EDTA and other 2.5 ml into 3.2% tri sodium citrate to separate to plasma. [Lewiset al 2012]
2-13-3. Platelets count:

By sysmex 21 Automated Hematology Analyzer.

2-13-3-1. Reagent and material:

   1. Stromatolyser.
   2. Detergent.

2-13-3-2. Principle of sysmex 21 Automated Hematological Analyzer:

Measurement of blood cells (red blood cells, white blood cells, and platelets) and hemoglobin concentration obtained by aspiration of small volume of EDTA blood by sample probe and mixed isotonic diluents in nebulizer diluted mixture aspiration delivered to RBCs aperture bath for providing information about RBCs and platelets based on cell sizes, particles of 2 to 20 femtoliter counted as platelets, above 36 femtoliter counted as Red blood cells. Some portion of aspirated mixture induced into white blood cells bath in hemolytic reagent (Stromatolyser) was added automatically to measure hemoglobin concentration in build colorimeter, based on cynomethemoglobin method (HiCN).

Blood cells counted and size information generated in triplicate pulses according to electronic conductivity, and translated into digital number using in build calculator programmed and designed for that RBCs, WBCs counts. Hence three values were directly measured (RBC, WBC, Hb) and displayed on (LCD). Other values of red cell indices, platelets counts, leukocyte
differential and absolute count calculated from given information and automated constructed histogram, the result printed out according to the setting mode. [Bendetteet al 1995].

2-13-4. PT and APTT estimation:
By manual method
2-13-4-1. Reagent and material:
1. Patient and control platelets poor plasma (ppp).
2. Thromboplastin.
2. Kaolin; 5 g/l.
3. Phospholipid; 0.35-0.4 iu/ml.
4. Cacl2 0.25 mol/l.

2-13-4-1-1. Preparation of plasma:
2.5 ml of citrated anti coagulated venous blood samples were collected (9 part blood to 1 part anti coagulant). Blood was thoroughly mixed with the anticoagulant. Samples were centrifuged at 3000 rpm for 15 minutes to obtain platelet –poor plasma (PPP). Plasma was separated from cells into eppendorf tube and tested.

2-13-4-2. Principle and method

Pro thrombin Time:
Principle:
The pro thrombin time measures the clotting time of re calcified plasma in the presence of an optimal concentration of tissue extract (thromboplastin). and indicate the overall efficiency of the extrinsic clotting system.
Method:
Deliver 0.1 ml of plasma into glass tube placed in water bath and add 0.1 ml of thromboplastin. Wait 1-3 minutes to allow the mixture to warm. Then add 0.1 ml of warmed CaCl2 and start stop watch. And record the time of clotting. Must be duplicated.

Normal value:
10-12 seconds.

Activated partial thromboplastin time:

Principle:
The test measures the clotting time of plasma after the activation of contact factors and the addition of phospholipid and CaCl2, but without added tissue thromboplastin. So it indicates the overall efficiency of the intrinsic pathway.

Method:
Mix equal volume of kaolin and phospholipid and leave in glass tube in water bath at 37°C. Add to plasma then add 0.1 ml from CaCl2. Mix content and start the stop watch and the time of clot record as APTT time.

Normal Range:
26-40 seconds.

Statistical analysis
Statistical analysis was performed by using SPSS computer program version 14, the value were expressed as mean ± Std. Devising by using Independent T-test, frequency and graph to get mean ages and distribution between gender.
Chapter three

Results
Chapter three

Results

3. Results:

100 venous blood sample were collected, 70 sample collected from heart disease patients were recognized according to age 32 patients (45.7%) between 1-30 years, 23 patients (32.9%) between 31-60 years and 15 patients (21.4%) more than +60 years. And 30 sample collected from healthy person matched as control and also recognized according to age 13 control (43.3%) between 1-30 years, 13 control (43.3%) between 31-60 and 4 control (13.3%) more than 60 years. Also recognized according to number about 35 patients is male (50%), and 35 patient is female (50%), and the control 15 male (50%), and 15 female (50%).

3-1. Comparison of PT, APTT level and PLTs count between study group and control group.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Mean ± STD</th>
<th>P.value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Study group</td>
<td>control group</td>
</tr>
<tr>
<td>PT by second</td>
<td>30.4± 9.7</td>
<td>13.2±1.9</td>
</tr>
<tr>
<td>APTT by second</td>
<td>43.6± 8</td>
<td>32±6.5</td>
</tr>
<tr>
<td>PLTs count thousands per cumm</td>
<td>258±97.7</td>
<td>221.4±82</td>
</tr>
</tbody>
</table>
3-2. Age group in study group:

<table>
<thead>
<tr>
<th>Group</th>
<th>Range</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group1</td>
<td>1-30 years</td>
<td>32</td>
</tr>
<tr>
<td>Group2</td>
<td>31-60 years</td>
<td>23</td>
</tr>
<tr>
<td>Group3</td>
<td>More than 60 years</td>
<td>15</td>
</tr>
</tbody>
</table>

3-3. Comparison of PT, APTT level and PLTs count between (group1, group2 and group3) in study group.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Mean±STD</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>group1</td>
<td>group 2</td>
</tr>
<tr>
<td>PT by second</td>
<td>30.7±10.4</td>
<td>31±10.4</td>
</tr>
<tr>
<td>APTT by second</td>
<td>43.7±8.7</td>
<td>45±7.4</td>
</tr>
<tr>
<td>PLTs count thousand per cumm</td>
<td>255±101</td>
<td>285±107</td>
</tr>
</tbody>
</table>

3-4. Comparison of PT, APTT level and PLTs count between male group and female group in study group.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Mean ±STD</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>PT by second</td>
<td>29±9.4</td>
<td>36±3.5</td>
</tr>
<tr>
<td>APTT by second</td>
<td>44±7.2</td>
<td>43.2±8.8</td>
</tr>
<tr>
<td>PLTs count thousand per cumm</td>
<td>312.3±184.4</td>
<td>221±61.6</td>
</tr>
</tbody>
</table>
Figure 3-1: The percentage of male and female in study group compared to control.
Figure 3-2: The percentage of age group in study group compared to control.
Chapter four

Discussion, conclusion and Recommendation
Chapter four

Discussion, Conclusion and Recommendation

4-1. Discussion

The result of this study show there was increased in prothrombin time (PT) were increased than control (p < 0.05). The PT in our study which agree with that reported in [Adaeze et al 2014], previous study.

Also our study show the significance increased in activated partial thromboplastin time (APTT) was increased than control (p < 0.05). The APTT in our study which agree with that reported in [Adaeze et al 2014] previous study.

This also agrees with study [Ghasemi et al 2014] in Iran. Were study done in cyanotic congenital heart disease (CCHD) were fund the patients have factor deficiency this cause increase of PT and APTT.

were find platelets coagulation activities increased activated partial prothrombin time (APTT) in coronary artery disease. There are contribution in factor (seven, eight, fibrinogen) and deficiency in antithrombin three. [Kontiro et al 1984]. Also platelet count in our study no significance change between patients and control were no significance decrease or increase than control (p > 0.05). These may due to small sample size.

The PLTs count in our study agrees with. Were this fund minority of heart disease patients with thrombocytopenia. The conclusion platelets count in CCHD appears to represent a continuum beginning with low platelet counts and ending with thrombocytopenia. [Michael et al 2006].
When compared between patients according to the age group we found no significance change between them in PT, APTT (p > 0.05). Where there are no significance change in PLTs count in patients according to age group (p > 0.05).

Also we found no significance change in PT, APTT and PLTs count in study group associated to gender (male \ female) (p > 0.05).

We observed the equal percentage of male and female in study group.

Also observed the presence of different age group in study group.
4-2. Conclusion

The study showed that ;- 

1-The mean of PT in the patients 30.4±9.7 second, were in control 13.2±1.9 second.

2-The mean of APTT in the patients 43.6±8 second, were in control 32±6.5 second.

3-The platelets count in patients 258±97.7 thousand cells per cumm, were in control 221±82 thousand cells per cumm. Were no significance decrease between patients and control platelets count

4- No significance change in PT ,APTT and platelets count in study group according to age group.

5- No significance change PT, APTT and platelets count in male and female study group.
4-3. Recommendation

-Coagulation screening should be done as routine test for all patients with heart disease and must be check monthly to patients to prevent heart attack that leads to sudden death.

-CBC also must be done monthly to avoid complication of thrombocytopenia.
Chapter five

References
Chapter five

References


GhasemiA, HorriM, Salah Y (2014); Coagulation Abnormalities in Pediatric Patients with Congenital Heart disease. International Journal of pediatric 2(2.2);14.

Hoffbrand A, Higgs D, Mehta D (2016); Post Graduate Hematology seventh edition; 676-698.


Appendix 1

Sudan University of Sciences and Technology

Collage of Medical Laboratory sciences

Hematology Department

Data sheet

Name: ................................................................................................................. No: ( )

Gender: Male; ( ) Female; ( )

Age: ......................................................................................................................

Investigation:

PT: ............................................................................................................. second.

APTT: ............................................................................................................. second.

PLTS Count: .............................................................................. c\cmm

Date: ......................................................... Sig:
Appendix 2

sysmex 21 Automated Hematology Analyzer