Tuijin Jishu/Journal of Propulsion Technology
ISSN: 1001-4055
Vol. 44 No. 5 (2023)

Thickening Profile Analysis: A Novel Approach to Understanding Hemostasis

Somia A. Nassar [1,2] , Adwa S.Almutairi [1] , Monerah M.Almuqrin[1], Sara F. Alquhiz [1], Ahmed Hjazi [1] , Humood Al Shmrany [1] , Sultan f Alqahtani [3], Munirah saad aldossari [4], Haifa Saad aldosseri [5], Abdulkarim S. Binshaya [1]

[1] Department of Medical Laboratory Sciences, College of Applied medical sciences, Prince Sattam bin Abdulaziz University, Alkharj, 11942, Saudi Arabia.

[2] Professor, Department of Parasitology & Animal Diseases, National Research Centre, Bohouth St., Dokki, Giza, 12622, Egypt

[3] Laboratory Department, Aliman General Hospital, Riyadh, 13782, Saudi Arabia

[4] Diabetic Center, Al Adiriyah Hospital, Riyadh, Saudi Arabia

[5]Department of Medical Imaging, King Saud Medical City, Riyadh, Saudi Arabia.

*Corresponding Author:

Abdulkarim S.Binshaya
Department of Medical Laboratory Sciences, College of Applied medical sciences, Prince Sattam bin Abdulaziz University, Alkharj, 11942, Saudi Arabia.
Abd.ALDOSARI@psau.edu.sa

Abstract

Background: Hemostasis is a sequence of enzymatic processes that result in the creation of a clot at the site of the injury. This is done with blood platelets and fibrin to regulate and stop additional bleeding. When the wound heals, the plug gradually remodels and dissolves as the injured area returns to its natural state. The protective mechanism against hemorrhage is controlled by the hemostatic cascade. Bleeding symptoms in the patient can often prompt laboratory evaluation for bleeding disorders. To screen for hemostatic disorders and distinguish between congenital and acquired disorders, physicians should obtain a detailed personal and family hemostatic history. They should also perform a thorough physical examination. Activated partial thromboplastin time (APTT) and prothrombin time (PT) are screening assays indicated for the initial assessment of hemostasis disorders. Although these assays have been described for several decades, recent improvements in coagulation automated analyzers now available in most clinical laboratories have led to their widespread use. Evaluation of hemostasis by evaluating and recording coagulation profile tests (PT & APTTs) of patients, including prolonged and shortened PT and/or APTTs according to age and sex.

Materials and Method: This study was carried out in the medical laboratory department - King Khaled Hospital and included 1884 patients whose ages ranged from 20 to over 60 years old. Different hospital clinics requested coagulation profile tests (PT and APTT) for all patients. Samples were tested during the first quarter of 2023 (January to March) recording the results of PT and APTT and distribution of results according to sex and age using the Stagogroupe - STA R Max®

Results: Prolongation and shortening of PT and/ or APTT were observed in 628 patients representing 33% of the total collected data in 1884. Of these patients, 284 were female (45.2%) and 344 were male (54.8%). According to age and sex, the majority of abnormalities were over 60 years of age for both genders, reaching 268 (42.7%). In both genders, there were 20 patients with high PT, representing 3.18 % of the overall abnormal results. According to age, the highest incidence was between 40-50 years for both genders and the total were 35% of total cases, (20%) females and (15%) males. Total patients with shortened PT were 120 (19.1%) of the

total abnormal results (628) at an age over 60 years old. There were 42 patients (35%) with low PT, 15 female (12.5%) and 27 male (22.5%). Patients with prolonged PT according to age and gender were 357 (56.4%) out of the non-normal (628). At age over 60 there were 173 (48%) patients, 84 females (23.5%), and 89 males (25%). There were 35 patients out of 628 with short APTT representing 5.6%; at the age of 30-40 years, the total number was (37%), with 14.3% females and 22.9% males. Regarding prolongation of both PT and APTT, the total results were 84 (13.4%), at age over 60 the total cases were (48.8%); females were (23.8%) while males (25%). Results of the shortened PTT and APTT totaled (1.9%) out of 628. At age 50-60, the total was (25%), females were 8.33 percent, and males were 16.2%.
Conclusions: According to the findings of this study, the results of prolongation and shortening of PT and/or APTT are age and risk-factor-related. These results increase the incidence of bleeding and thrombosis so laboratory testing should be pursued especially without an obvious explanation for the disturbances of the PT or APTT. The most susceptible age groups were over 50 years due to their greater exposure to coagulopathies and other risk factors.

Keywords: Hemostasis, Activated partial thromboplastin time (APTT), prothrombin time (PT)

1. Introduction

The hemostatic system is responsible for maintaining blood in a fluid state, preventing coagulation or the formation of thrombi, and halting blood loss, known as hemorrhage [1][2]. Haemostasis is a precisely regulated process that ensures normal blood flow and prevents excessive blood loss following vascular injury [3]. Normal blood clotting relies on several components, including functional platelets, intact endothelium, and normal coagulation proteins [4]. Hemostasis is a series of enzymatic processes leading to the formation of a clot at the injury site. This involves blood platelets and fibrin to control and halt further bleeding. As the wound heals, the clot gradually undergoes remodeling and dissolves, restoring the injured area to its natural state. The hemostatic cascade governs the protective mechanism against hemorrhage, with natural substances in the blood preventing clot formation through the conversion of plasminogen to plasmin and promoting fibrinolysis [5].

Physiologically, the formation of clots in response to injury is regulated by various anticoagulant proteins and factors. These same factors also serve to prevent abnormal clotting, such as thrombosis. Bleeding disorders are typically identified in patients with a personal and/or family history of bleeding and laboratory abnormalities indicating inherited or acquired bleeding disorders [6]. Immediate and targeted assessment of a patient's coagulation status is crucial in various emergency situations. Therefore, global plasma-based coagulation tests are commonly used to assess the risk of thromboembolism and bleeding in patients requiring immediate medical attention. Examples of conventional coagulation tests (CCTs) include prothrombin time (PT) and activated partial thromboplastin time (APTT), initially designed to evaluate individuals with isolated clotting factor deficiencies or those on anticoagulant therapy. Similarly, other widely used coagulation tests, like platelet counts, D-dimers, or fibrinogen levels, have been adapted to assess coagulation status in various specific clinical scenarios [7]. Coagulation testing is indispensable for diagnosing and managing various conditions, including hemophilia, thrombophilia, and complex coagulopathies [8]. These tests, often referred to as routine coagulation tests or screening tests, find application in clinical settings before surgery, as follow-up investigations for patients under scrutiny for bleeding tendencies, or to monitor anticoagulant therapy. In many cases, a mixing study serves as the initial reflexive test, offering valuable insights to guide further assessments [9]. The objective of this study is to document the prevalence of coagulation disorders among patients at King Khaled Hospital, reflecting the extent of coagulation issues within the Al Kharj population.

2. Materials and Methods

This retrospective study was conducted within the medical laboratory department of King Khaled Hospital in Al Kahrj City, encompassing a dataset comprising 1884 random patient samples. These patients were specifically referred for coagulation profile tests, encompassing Prothrombin Time (PT) and Activated Partial Thromboplastin Time (APTT) measurements. The study's subjects were drawn from various clinics within the hospital, with data collection spanning the first quarter of 2023. The primary research objectives were to document PT and APTT results (first objective) and to examine the distribution of these outcomes with respect to both gender and age

(second objective). All necessary materials for this investigation were generously provided by King Khaled Hospital in Al Kahrj City.

Coagulation tests in this study were conducted using plasma samples, as serum preparations could remove clotting factors. Venous blood samples were obtained from 1884 patients through standard percutaneous phlebotomy using a 21-gauge needle, typically collected from the antecubital vein. Adhering to the institutional guidance of the Ethics Committee of the Medical University of Prince Sattam Bin AbdulAziz, phlebotomists used plastic tubes with a light blue top containing 3.2% sodium citrate for blood sampling. This sodium citrate acted by chelating the calcium in the blood, preventing the activation of the coagulation cascade and maintaining the sample in stasis until testing. The tubes were filled to approximately 90 percent of their full collection volume, with a blood to sodium citrate ratio of 9 to 1. Gently inverting the tube a few times ensured proper mixing of the sodium citrate solution with the blood, avoiding any shaking that could lead to hemolysis and inaccurate results. When the blood sample was ready for testing, calcium chloride was added to restore the necessary calcium for coagulation activation, with clot formation being optically detected based on the instrumentation employed.

2.1 Study Procedure

The Stagogroupe STA R Max® machine (Figure 1), operating on a photo-optical principle, played a central role in this study. The PT test, a fundamental component of the coagulation discipline and accounting for over 50% of tests conducted globally, was a key focus. Additionally, Figure 2 illustrates the STA-NeoPTimal reagent, which was utilized in the study. The principle of the test consists of the use of calcium thromboplastin to measure the clotting time of the patient plasma sample and to compare it with that of a normal standard. The test measures, as a whole, the activity of the coagulation factor II (prothrombin, factor V proaccelerin), factor VII (proconvertin), factor X (Stuart factor) and factor I (fibrinogen)

PT	STA-NeoPTimal 5	STA-NeoPTimal 10	STA-NeoPTimal 20
Cat Nr./Packaging	01163 - 6 x 5 mL	01164 - 12 x 10 mL	01165 - 12 x 20 mL
Thromboplastin origin	Rabbit brain Extraction		
ISI	0.9 - 1.1		
Heparin sensitivity	UFH : 1.0 UI/mL / LMWH : 1.5 UI anti-Xa/mL		
HIL interferences	Insensitive		
On-board stability	48 h / 4 days*		48 hours
Stability at 2-8°C	8 days	-	-

*On STA Satellite®

QC	STA-Routine QC 2 mL	STA-Coag Control N+P	STA-System Control N+P	STA-Coag Control N+ABN Plus*
Cat Nr./Packaging	00554 -12 x 2 x 2 mL	00679 - 12 x 2 x 1 mL	00678 - 12 x 2 x 1 mL	00677 - 12 x 2 x 2 mL
Levels	STA®-Routine QC 2 mL N STA®-Routine QC 2 mL P	STA®-Coag Control N STA®-Coag Control P	STA®-System Control N STA®-System Control P	STA®-Coag Control N Plus STA®-Coag Control ABN Plus
On-board stability	24 h	8 h	8 h	24 h

*For United Kingdom only

Figure 1: STA-NeoPTimal reagent versions

2.2 STA®-Routine QC quality control plasmas

Figure 2: STA®-Routine control plasmas

In accordance with regulatory requirements, laboratories are mandated to conduct routine internal quality control (IQC) assessments on their testing systems, covering at least two concentration levels, normal and abnormal. This quality control procedure is essential for verifying and validating the performance of their testing systems. For this study, the laboratory employed STA®-Routine QC 2 ml Ref. 00554 (Figure 2), encompassing both normal and abnormal levels, to assess various parameters, including Prothrombin Time (PT) in seconds, PT percentage, International Normalized Ratio (INR), APTT, fibrinogen, thrombin time, and antithrombin activity. Additionally, for ultra-abnormal level assessments, STA®-Routine QC P Plus Ref. 00714 was utilized, covering PT in seconds and percentage, APTT, fibrinogen, thrombin time, and antithrombin activity. These quality control measures ensure the reliability and accuracy of the laboratory's testing procedures and results.

2.3 STA®-PTT

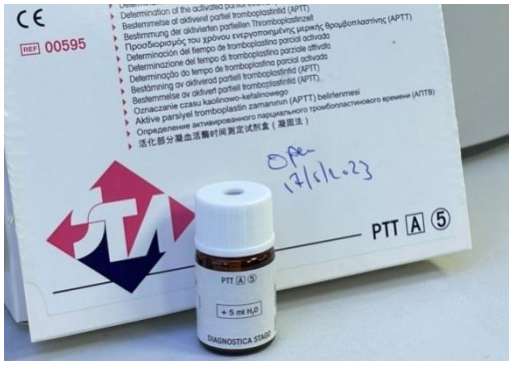

Figure 3: STA®-PTT reagent

The kit under consideration in this study is designed to provide the necessary reagents for the determination of the APTT. Each kit consists of 12 vials, each containing 5 ml of the required reagent, ensuring an adequate supply for conducting multiple APTT tests (Figure 3).

2.4 Test principle:

The APTT testing process involves the re-calcification of plasma while utilizing a standardized amount of cephalin (a platelet substitute) and a particulate activator, specifically silica. This assay serves as a comprehensive screening test for evaluating the functionality of several coagulation factors, including XII, XI, IX, VIII, X, V, II, as well as fibrinogen levels. In terms of sample management, primary centrifuged tubes with or without barcodes, characterized by diameters of 11 mm for 3 mL tubes and 11.6 to 13.4 mm for 5 mL tubes, along with lengths ranging from 65 to 100 mm, are employed. Additionally, BD Vacutainer® pediatric tubes with a 10 mm diameter and heights of 47 mm or 64 mm are utilized. Microcontainer sampling necessitates a minimum volume of 200 µL. For capped tubes, a list of recommended options can be found in document 0932182x, titled "Cappiecing option: list of tubes." The sample processing includes racks of 5 tubes, trays containing 15 racks, and an analyzer with a capacity for 43 racks, with 28 available for immediate pipetting and 15 for storage. Furthermore, the process incorporates positive identification and barcode reading, as well as automated dilution capabilities to ensure efficient and accurate APTT testing procedures.

3. Results

Refer to the analysis of collected data of coagulation profile tests (PT & APTT) which represents the results of both tests among first 3 months of 2023 the result showed that : the total tested plasma sample were 1884 for both gender, patients with abnormal results were 628 representing 33% of the total collected data 1884; where 284 were females (45.2%) and 344 males(54.8%) from total patients with coagulation disorder(628). Regarding to age and sex, at age from 20-30 years the total patients were 106 (16.8%), females were 48 (7.6%) and 58 males (9.2%) have coagulation disorders. Within age group 30-40 years the total patients with coagulation disorders were 92 (14.7%) of genders, 33 (5.3%) females and 59 (9.4%) males. Age group 40-50 years the total was 88 (14%), 48

females (7.6%) and 40 males (6.4%). At age of 50-60 years the total patient with coagulation disturbances were 74 (11.8%) whereas 30 females (4.8%) and 44 males (7%). Finally, ages over 60 years the total patients with coagulation abnormalities were 268 (42.7%), 125 female (19.9%) and 143 males (22.8%). (Table 1 and figure 4)

Table 1: Results of coagulation disturbances according to age and gender

AGE	Total abnormal results		Female		Male	
	No.	%	No.	%	No.	%
20-30	106	16.8%	48	7.6 %	58	9.2%
30-40	92	14.7%	33	5.3%	59	9.4%
40-50	88	14%	48	7.6%	40	6.4%
50-60	74	11.8%	30	4.8%	44	7%
Over 60	268	42.7%	125	19.9%	143	22.8%
Total	628		284	45.2%	344	54.8%

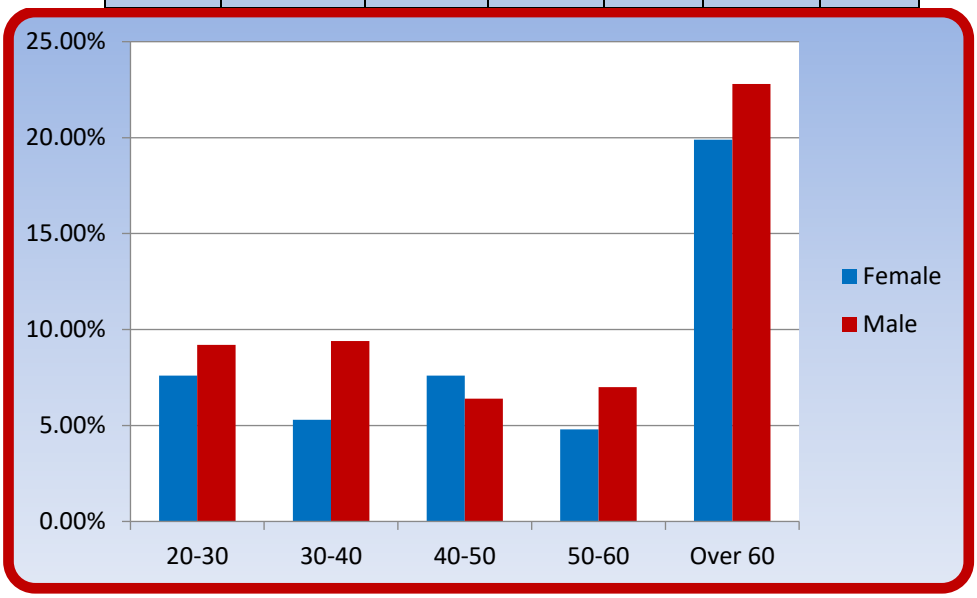

Figure 4: Results of coagulation disturbances according to age and gender

The collected data for evaluation of patients with high PT during the first quarter of 2023 with the regard to the age and gender, showed that the total results of high PT of both gender were 20 representing 3.18 % of the total abnormal results (628). At age of 20-30 years there were no patients with high PT, while at ages of 30-40 years the total were 4 (20%), 1 female (5%) and 3 males (15%), at age 40-50 there were 7 patients (35%) of total cases 4 females (20%) and 3 males(15%), at age 50-60 the total cases were1femal only (5%) and finally at age over 60, there were 8 patients (40%) with high PT 4for each gender (20%).(Table 2 and figure 5)

Table 2: Results of prolonged APTT according to age and gender

AGE	Total no of both gender		Female		Male	
	No.	%	No.	%	No.	%

20-30	0	0	0	0	0	0
30-40	4	20%	1	5%	3	15%
40-50	7	35%	4	20%	3	15%
50-60	1	5%	1	5%	0	0
Over 60	8	40%	4	20%	4	20%
Total	20		10		10	

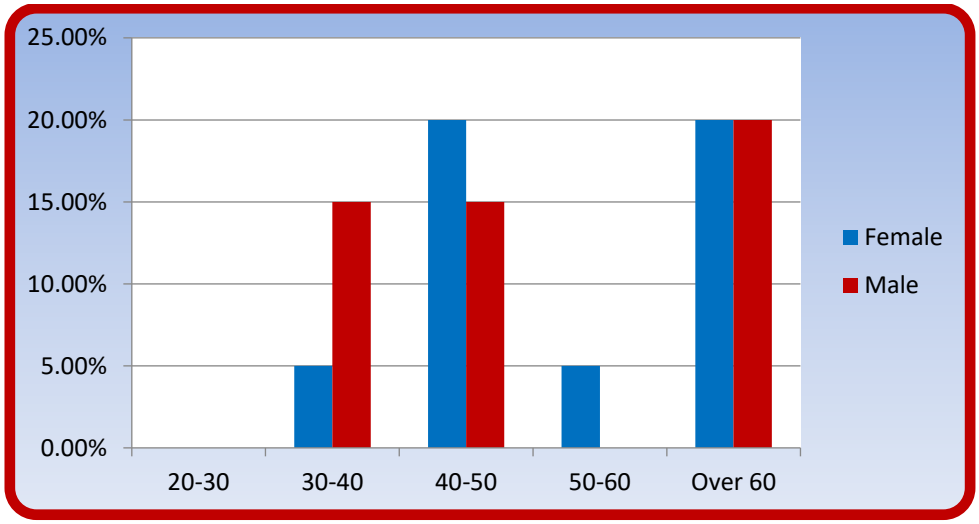

Figure 5: Results of prolonged APTT according to age and gender

Results of patients with shorten APTT according to age and gender. The collected data showed that the total patients with shorten APTT were 120 (19.1%) of the total abnormal results (628). At age of 20-30 years there were 16 patients with low PT(13.3%),8 of both genders (6.7%), while at ages of 30-40 years there were 21 (17.5%) of the total cases; 13 female (10.8%) and 8 male (6.7%), at age 40-50 there were 20 patients (16.7%) of total cases for both genders recording shorten PT 14 females (11.7%) and 6 males (5%).At age 50-60, the total cases were 21 (17.5%);13 female (10.8%) and 8 males (6.7%). Finally at age up to 60, there were 42 patients (35%) with low APTT 15 female (12.5%) and 27 male (22.5%). (Table 3 and figure 6)

Table 3: Results of shortened APTT according to age and gender

AGE	Total no of both gender		Female		Male	
	No.	%	No.	%	No.	%
20-30	16	13.3%	8	6.7%	8	6.7%
30-40	21	17.5%	13	10.8%	8	6.7%
40-50	20	16.7%	14	11.7%	6	5%
50-60	21	17.5%	13	10.8%	8	6.7%
Over 60	42	35%	15	12.5%	27	22.5%
Total	120		63		57	

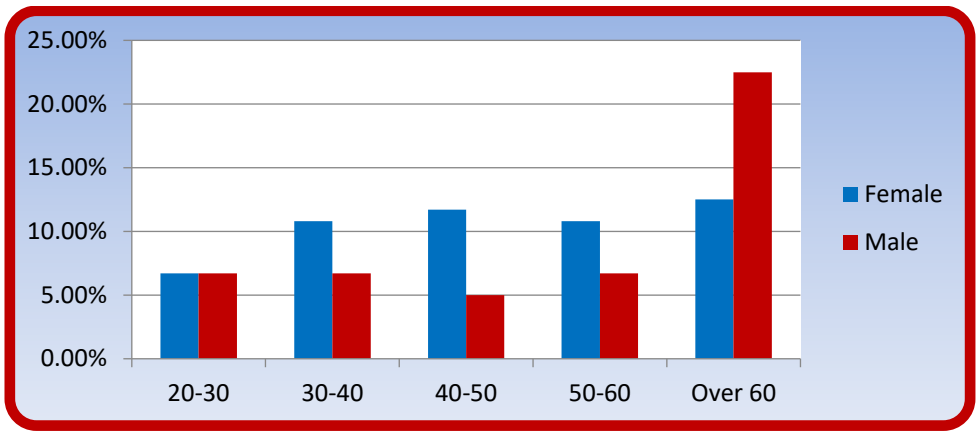

Figure 6: Results of shortened APTT according to age and gender

The results of patients with prolonged APTT according to age and gender showed that the total patients were 357 (56.4%) out of total abnormal patients (628). At age of 20-30 years the total patients with prolonged APTT time were 74(20.7%), 32 females (9%) and 42 males (11.7%).At age of 30-40 years the total were 40 (11.2%), 10 females (2.8%) and 30 males (8.4%). At age of 40-50 years the total were 39 (11%), 20 females (5.6%) and 19 males (5.3%), at age 50-60 years the total were 31 (8.6%);6 females (1.7%) and 25 males (7%) and finally at age over 60 there were 173 (48%) patients 84 females (23.5%) and 89 males (25%). (Table 4 and figure 7)

Table 4: Results of prolonged PT according to age and gender

AGE	Total no of both gender		Female		Male	
	No.	%	No.	%	No.	%
20-30	74	20.7%	32	9%	42	11.7%
30-40	40	11.2%	10	2.8%	30	8.4%
40-50	39	11%	20	5.6%	19	5.3%
50-60	31	8.6%	6	1.7%	25	7%
Over 60	173	48%	84	23.5%	89	25%
Total	357		152		205	

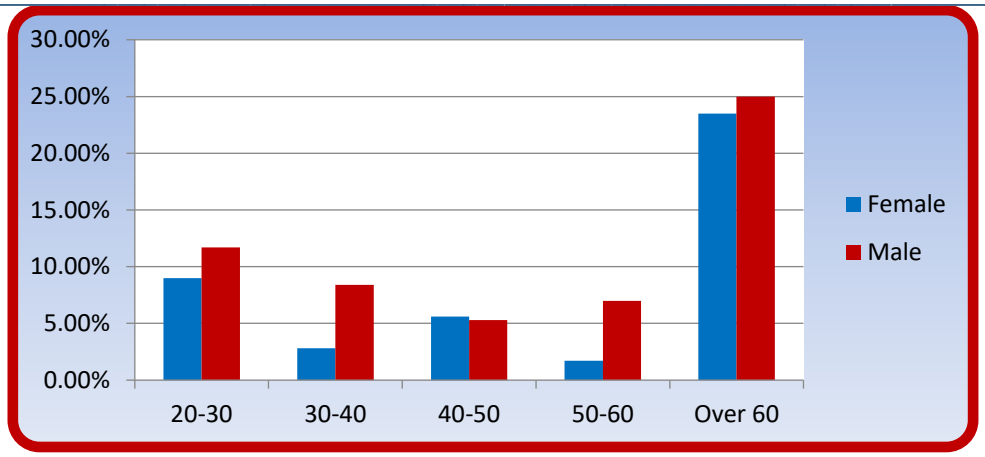

Figure 7: Results of prolonged PT according to age and gender

Results of the patients with short PT time showed that the total number were 35 out of 628 representing (5.6%). At age 20-30years the patients with Short PT time were 2 out of 35 for both females and male, while at age of 30-40 years they were 13 (37%); 5 females (14.3%) and 8 males (22.9%). At age of 40-50 years were 10 (28.6 %); 3 females (8.6%) and 7 males (20%). In addition, at age 50-60 years patients with short PT were 7 (20%); 6 female (17.1 %) and 1 male (2.8%). Finally at age over 60 years there were 3 (8.5%) patients, 1 female (2.8%) and 2 males (5.7%). (Table 5 and figure 8)

Table 5: Results of shortened PT according to age and gender

AGE	Total no of both gender		Female		Male	
	No.	%	No.	%	No.	%
20-30	2	5.7%	0	0	2	5.7%
30-40	13	37%	5	14.2%	8	22.8%
40-50	10	28.6%	3	8.6%	7	20%
50-60	7	20%	6	17.1%	1	2.8%
Over 60	3	8.5%	1	2.8%	2	5.7%
Total	35		15		20	

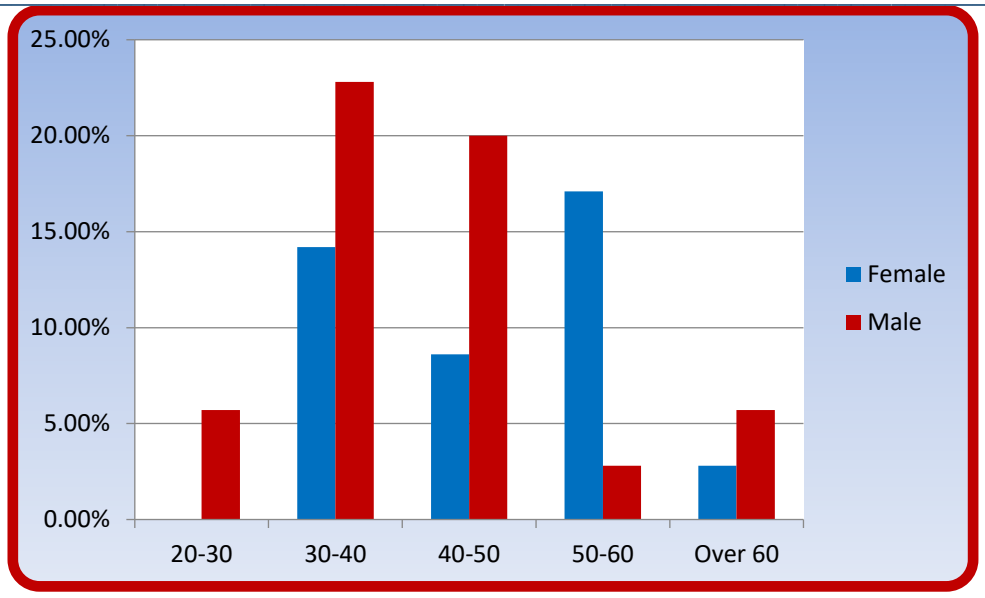

Figure 8: Results of shortened PT according to age and gender

Regarding to the prolongation of both PT and APTT the collected data showed the total results were 84(13.4%). At age of 20-30 years the total cases were 12(14.3%), 7 of them were females (8.3%) while 5 were males (5.95%). At age 30-40 years the total cases were 9(10.7%),4 of them were females (4.76%) and 5 were males (5.95%), while at age 40-50 years the total number of cases was 11 (13%),7 of them were females (8.3%) and 4 were males (4.76%).At age 50-60 years the total cases were 11(13%), 3 were females (3.57%) and 8 were males (9.52%).At age over 60 the total cases where 41(48.8%); 20 of them females (23.8%) while 21 males (25%).(Table 6 and figure 9)

Table 6: Results of prolonged both PTT and APTT according to age and gender

AGE	Total no of both gender		Female		Male	
	No.	%	No.	%	No.	%
20-30	12	14.3%	7	8.3%	5	5.95%
30-40	9	10.7%	4	4.76%	5	5.95%
40-50	11	13%	7	8.3%	4	4.76%
50-60	11	13%	3	3.57%	8	9.52%
Over 60	41	48.8%	20	23.8%	21	25%
Total	84		41		43	

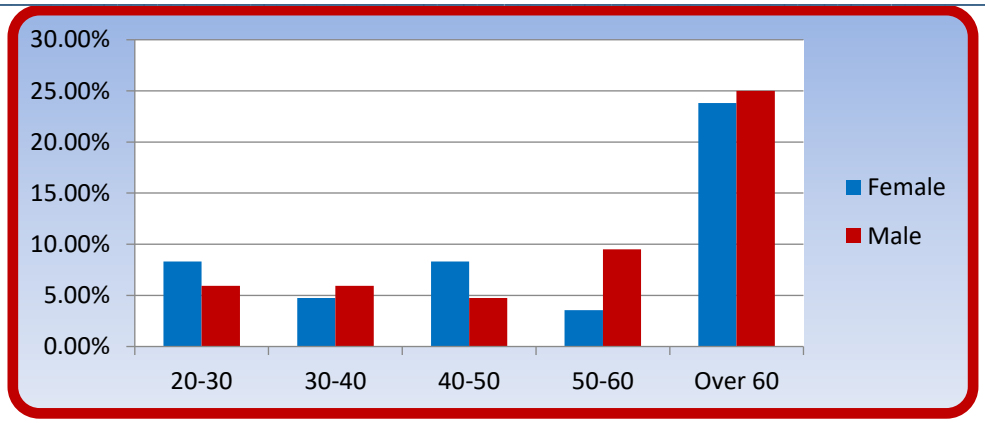

Figure 9: Results of prolonged both PTT and APTT according to age and gender

Regarding to the results of shorten PT and APTT, the collected data showed that the total results among the three month were 12(1.9%) out of 628 abnormal results .At age of 20-30 years the total cases were 2(16.7%); 1 of them were female (8.33%) and 1 male (8.33%). At age 30-40 years the total cases were 5 (41.6%) all of them were males only, while at age of 40-50 years the total number of cases was 1male (8.33%) only. In addition, at age 50-60 years the total cases were 3(25%); 1 female (8.33%) and 2 males (16.2%). At age over 60 the total cases where 1female (8.33) only. (Table 7 and figure 10)

Table 7: Results of shortened both PTT and APTT according to age and gender

AGE	Total no of both gender		Female		Male	
	No.	%	No.	%	No.	%
20-30	2	16.7%	1	8.33%	1	8.33%
30-40	5	41.6%	0	0	5	41.6%
40-50	1	8.33%	0	0	1	8.33%
50-60	3	25%	1	8.33%	2	16.2%
Over 60	1	8.33%	1	8.33%	0	0
Total	12		3		9	

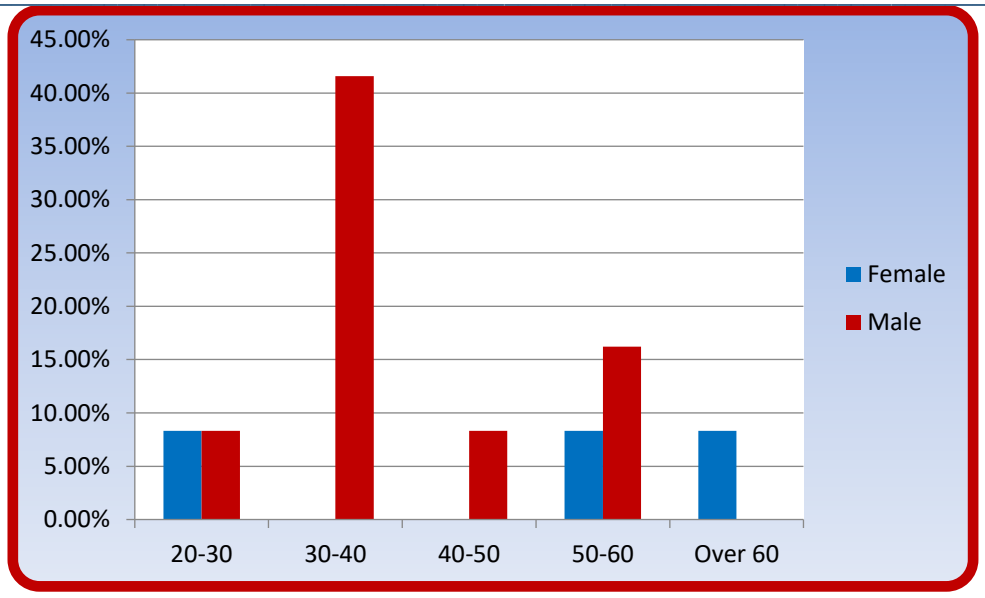

Figure 10: Results of shortened both PT and APTT according to age and gender

Discussion

Hemostasis involves a series of enzymatic reactions that lead to the formation of a blood clot at a wound site. This process utilizes blood platelets and fibrin to effectively manage and halt further bleeding. As the wound heals, the clot undergoes remodeling and eventually dissolves, allowing the injured area to return to its original state. The hemostatic cascade plays a crucial role in governing the body's defense against excessive bleeding. In situations of hypercoagulability, where there is no active bleeding but blood is present within the vessel, this hemostatic process can unintentionally activate, leading to the development of a pathological condition known as thrombosis [2]. Conversely, in cases of hypocoagulation, one or more components of the hemostatic cascade may be compromised, resulting in inadequate hemostasis and the inability to control hemorrhage. This can lead to significant blood loss, hemorrhage, and adverse effects on blood flow to vital organs [1].

Regarding our research findings, we conducted Prothrombin Time (PT) and Activated Partial Thromboplastin Time (APTT) tests, which are commonly employed to evaluate abnormalities in the coagulation process. The results of these tests are as follows:

The age group most affected by coagulation disorders is individuals aged over 60. Prothrombin time (PT), a test that assesses deficiencies in factors I, II, V, VII, and X, along with low fibrinogen levels, is used to evaluate both extrinsic and common coagulation pathways [10]. Prolonged PT can be observed in individuals of different ages and genders, and it may be attributed to various factors such as liver disease or liver malfunction, which hinder the production of coagulation factors. This could be a contributing factor to prolonged PT in both males and females, often accompanied by noticeable symptoms like petechiae and easily bruised skin [11]. Furthermore, a deficiency in vitamin K, which is essential for the development of factors II, VII, IX, and X, can lead to prolonged PT [12]. Inherited disorders affecting factors II, VII, IX, and X can also impact PT results. Conditions like disseminated intravascular coagulation (DIC) trigger widespread activation of the coagulation system, reducing the availability of coagulation components, and resulting in extended PT values. Typically, prothrombin levels decrease due to an increase in the conversion of prothrombin to thrombin in vivo, leading to elevated PT values. In some cases, the presence of antiphospholipid antibodies is associated with repeated thromboembolic episodes and/or pregnancy loss, further influencing PT results.

In terms of age and gender, individuals over 60 years old, both males and females, were found to be the most susceptible to prolonged Prothrombin Time (PT), with a prevalence of 25% in males and 23.5% in females. This extended PT in the elderly population may be attributed to factors such as significantly low levels of fibrinogen and elevated levels of heparin and circulating inhibitors [13]. Conversely, storing blood samples at low temperatures (4 degrees Celsius or lower) can lead to increased activation of factor VII, resulting in shorter PT values in both males and females across different age groups [14].

Patients with high lipid profiles, characterized by elevated cholesterol and triglyceride levels, tend to exhibit shorter PT measurements due to higher levels of fibrinogen and factor VII [15]. Additionally, increased intake of vitamin K through supplements or vitamin K-rich diets, as well as fasting, can diminish factors II, VII, and X, ultimately leading to lower PT values [16]. Notably, the male population showed a high percentage of shortened PT in the age groups of 30-40 years (22.8%) and 40-50 years (20%). This observation may be associated with very low levels of fibrinogen and high levels of heparin and circulating inhibitors in these individuals.

To assess intrinsic and common coagulation pathways, the Activated Partial Thromboplastin Time (APTT) test is employed. With the exception of factor VII (tissue factor) and factor XIII (fibrin stabilizing factor), this test measures all clotting factors [17]. The disturbances, characterized by prolongation of APTT, were evenly distributed across both sexes. Such APTT prolongation can be attributed to conditions such as lupus anticoagulants, anticoagulant therapy (mainly unfractionated heparin or argatroban), and coagulation factor deficiencies in certain patients.

Additionally, acquired clotting factor inhibitors are commonly directed against factor VIII and can manifest as either auto-antibodies, as seen in acquired hemophilia A, or allo-antibodies in individuals with severe hemophilia A following exposure to exogenous factor VIII. Furthermore, prolonged Activated Partial Thromboplastin Time (APTT) was observed in a range of other medical conditions, including liver disease, excessive bleeding, or disseminated vascular disease. Most cases with APTT prolongation were found in individuals up to the age of 60, accounting for 20% of total patients. At ages 40-50, both females and males exhibited APTT prolongation, with rates of 20% and 15%, respectively. This could be attributed to a higher prevalence of complications related to liver diseases and positive lupus anticoagulant and anti-cardiolipin antibodies coagulation [18]. Conversely, disturbances in APTT resulting in shorter times, especially in males aged over 60 years (22.5%), may be linked to factors like heavy cigarette smoking, exposure to insecticides [19], acute-phase inflammation responses leading to elevated levels of factor VIII, and challenges in the collection of blood samples, which can activate coagulation within the collection tube [20].

Numerous factors can contribute to both prolonged Prothrombin Time (PT) and APTT, including anticoagulant therapy, vitamin K deficiency, and various diseases. Our results indicated a higher prevalence of PT and APTT prolongation in both females and males, especially in those aged over 60 years (23.8% and 25%) [21]. These findings may be linked to decreased activity of one or more factors, such as deficiencies in factor VIII, IX, or XI, as well as bleeding [22]. Additionally, the use of anticoagulant medications like heparin (which prolongs both APTT and TT), warfarin (which decreases factors II, VII, IX, and X), direct thrombin inhibitors (which prolong APTT and TT), direct factor X inhibitors, and abnormal anti-factor X activity can impact coagulation profiles (23). Vitamin K deficiency (which decreases factors II, VII, IX, and X activity) and liver failure (which results in decreased activity of all coagulation factors except factor VIII, which is not produced by hepatocytes) are also contributing factors (24, 25).

Males exhibited a higher susceptibility to shortening of both PT and APTT (75%) compared to females (25%), potentially due to factors such as disseminated intravascular coagulation (DIC), advanced cancer (except when the liver is involved), and acute-phase reactions that temporarily elevate factor VIII levels (26).

Conclusion

According to the findings of this study, the results of prolongation and shortening of PT and/or APTT are age and risk factor related. These results increase the incidence of bleeding and thrombosis so laboratory testing should be pursued especially without an obvious explanation for the disturbances of the PT or APTT. The most susceptible age groups were over 50 years due to their greater exposure to coagulopathies and other risk factors.\

Acknowledgment

This study is supported via funding from Prince Sattam bin Abdulaziz University project number (PSAU/2023/R/1445)

Funding and Acknowledgement

This publication was supported by the deanship of scientific research at Prince Sattam bin Abdulaziz University

References

1. LaPelusa, A. and H.D. Dave, *Physiology, Hemostasis.[Updated 2021 May 9].* StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing, 2021.
2. Smith, S.A., R.J. Travers, and J.H. Morrissey, *How it all starts: Initiation of the clotting cascade.* Critical reviews in biochemistry and molecular biology, 2015. **50**(4): p. 326-336.
3. Zaidi, A. and L. Green, *Physiology of haemostasis.* Anaesthesia & Intensive Care Medicine, 2019. **20**(3): p. 152-158.
4. Bennett, J.D. and E.M. Ferneini, *Coagulopathy, An Issue of Oral and Maxillofacial Surgery Clinics of North America*. Vol. 28. 2016: Elsevier Health Sciences.
5. Méndez Rojano, R., et al., *Kinetics of the coagulation cascade including the contact activation system: sensitivity analysis and model reduction.* Biomechanics and modeling in mechanobiology, 2019. **18**: p. 1139-1153.
6. Hayward, C.P.M., *How I investigate for bleeding disorders.* International journal of laboratory hematology, 2018. **40**: p. 6-14.
7. Caspers, M., et al., *Global Coagulation Testing in Acute Care Medicine: Back to Bedside?* Hämostaseologie, 2022. **42**(06): p. 400-408.
8. Senst, B., P. Tadi, and A. Goyal, *Hypercoagulability.[Updated 2021 Sep 29].* StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing, 2022.
9. Kershaw, G., *Performance and interpretation of mixing tests in coagulation.* Hemostasis and Thrombosis: Methods and Protocols, 2017: p. 85-90.
10. Levy, J.H., et al., *Clinical use of the activated partial thromboplastin time and prothrombin time for screening: a review of the literature and current guidelines for testing.* Clinics in Laboratory Medicine, 2014. **34**(3): p. 453-477.
11. Barcellona, D., L. Fenu, and F. Marongiu, *Point-of-care testing INR: an overview.* Clinical Chemistry and Laboratory Medicine (CCLM), 2017. **55**(6): p. 800-805.
12. Satti, H.H., et al., *Subacute administration of Astaxanthin inhibits vitamin K-dependent clotting factors in rats.* Journal of Food Biochemistry, 2020. **44**(10): p. e13407.
13. Kremers, R.M.W., et al., *Prothrombin conversion is accelerated in the antiphospholipid syndrome and insensitive to thrombomodulin.* Blood advances, 2018. **2**(11): p. 1315-1324.
14. Tyler, P.D., et al., *New uses for thromboelastography and other forms of viscoelastic monitoring in the emergency department: a narrative review.* Annals of Emergency Medicine, 2021. **77**(3): p. 357-366.
15. Kim, J.-A., et al., *Influence of blood lipids on global coagulation test results.* Annals of laboratory medicine, 2015. **35**(1): p. 15.
16. Bolliger, D. and K.A. Tanaka. *Point-of-care coagulation testing in cardiac surgery*. Thieme Medical Publishers.
17. Poli, G., et al., *Troubleshooting an isolate prolongation of activated partial thromboplastin time in a patient with acute myocardial infarction—a paradigmatic case report.* Annals of Translational Medicine, 2016. **4**(21).
18. Tripodi, A. and P.M. Mannucci, *The coagulopathy of chronic liver disease.* New England Journal of Medicine, 2011. **365**(2): p. 147-156.
19. Elkhalifa, A.M., *Effects of cigarette smoking on coagulation screening tests and platelet counts in a Sudanese male adults population.* Saudi Medical Journal, 2018. **39**(9): p. 897.
20. Bronić, A., et al., *Reporting of activated partial thromboplastin time (aPTT): Could we achieve better comparability of the results?* Biochemia Medica, 2021. **31**(2): p. 302-308.
21. Kamal, A.H., A. Tefferi, and R.K. Pruthi. *How to interpret and pursue an abnormal prothrombin time, activated partial thromboplastin time, and bleeding time in adults*. Elsevier.

22. Winter, W.E., S.D. Flax, and N.S. Harris, *Coagulation testing in the core laboratory.* Laboratory medicine, 2017. **48**(4): p. 295-313.

23. Seasor T, Moser KA. Abnormal PT and PTT - causes. PathologyOutlines.com website. https://www.pathologyoutlines.com/topic/coagulationabnormalPTPTT.html. Accessed June 2nd, 2023
24. Crookston K, Rosenbaum LS, Gober-Wilcox J. Vitamin K deficiency / Warfarin use. PathologyOutlines.com website. https://www.pathologyoutlines.com/topic/coagulationtopicvitk.html. Accessed June 2nd, 2023
25. Chan A. Hepatic failure. PathologyOutlines.com website. https://www.pathologyoutlines.com/topic/liverhepaticfailure.html. Accessed June 2nd, 2023
26. Moake, J. (Reviewed 2013 December). Coagulation Disorders Caused by Circulating Anticoagulants. The Merck Manual. Available online through https://www.merckmanuals.com. Accessed May 2014