DOI: https://doi.org/10.53350/pjmhs2023171729

ORIGINAL ARTICLE

To Determine the Effect of Prothrombin Time (PT), Activated Partial Thrombopalstin Time (APTT), and International Normalized Ratio (INR) Levels on Gender and Age

AYSHA SULTANA[1], FIDA HUSSAIN[2], RAZIA ASIF[3], AMANULLAH BHUTTO[4], SHABNAM[5], AZHAR ALI[6], KIRAN AAMIR[7], AAMIR RAMZAN[8]

[1,2]Lecturer in Pathology Department, Bilawal Medical college, Liaquat university of medical and health sciences Jamshoro.
[3]Assistant professor in pathology Department Bilawal Medical College, Liaquat university of Medical and Health Sciences Jamshoro.
[4]Assistant Professor, Pathology Department, Ghulam Mohammad Mahar Medical College Sukkur.
[5]Lecturer in Pathology Department, Liaquat university of medical and health sciences Jamshoro.
[6]Medical Officer Rural health Center Jhall Magsi
[7]Associate Professor in Pathology Department, Liaquat university of Medical and Health Sciences Jamshoro
[8]Lecturer in Pathology Department, Liaquat university of medical and health sciences Jamshoro
Corresponding author: Aysha Sultana, Email: draysha.imran@hotmail.com, Cell: 03173017421

ABSTRACT

Background: Hepatic function, coagulation disorders, and the risk of postoperative bleeding can all be detected with PT assay. When it comes to measuring "extrinsic route" coagulation factors, the PT is the most commonly used test. It is possible to check for a lack of intrinsic or common route factors by measuring the duration to trigger partial thromboplastin (aPTT). A solution to the problem of inconsistent PT measurements among laboratories was the creation of the International Normalized Ratio (INR). Laboratory-specific reference intervals can have a significant impact on the quality of patient treatment by influencing clinical decision-making.

Objective: The purpose of this study is to determine if gender and age affect PT, International normalised ratio (INR), and aPTT levels in people without known liver disease or anticoagulant therapy.

Method: Between July and December of 2021, patients without a past history of bleeding were admitted to the LUMHS Hyderabad civil hospital for minor surgical procedures (inguinal/umbilical hernia repair, caesarean section, rectal polyp excision, and diagnostic cystoscopy). There were 2274 patients in all, with 766 males and 1508 females. According to their chronological age, patients were separated into three groups. The study sampled 268 men and 22 women aged 0-14, 222 men and 1335 women aged 15-50, and 151 women and 276 men in the third age range (over the age of 50 year). Systemex CA-500 auto analyzer was used to conduct the analyses.

Results: Males and females have considerably different PT and INR values. Men and women between the ages of 15 and 50 were more likely to have increased PT, INR, and aPTT readings than those between the ages of 0 and 14. Males and females between the ages of zero and fourteen had the lowest aPTT levels. Between the ages of 15 and 50, women and men had higher PT, INR, and aPTT values than women and men over 50. PT, INR, and aPTT reference values based on a 95% confidence interval for men and women, as well as sexes and ages.

Conclusion: In this arena, a dearth of study has established that gender and age have little effect on PT, INR, and aPTT levels. Gender and age disparities in clinically used reference ranges for PT, INR, and aPTT must be taken into account.

Keywords: Prothrombin Time, INR, APTT, Outcomes

INTRODUCTION

The prothrombin time (PT) assay can be used to identify extrinsic coagulation [1]. Quick et al. pioneered anticoagulant treatment monitoring in 1935, and our laboratories continue to use it today. Citrated plasma is combined with calcium and tissue thromboplastin in this method to initiate the clotting process. Preoperative PT is important to rule out clotting difficulties, assess liver function, and calculate the possibility of significant blood loss following the operation. This approach can be used to monitor deep vein thrombosis, heart valve replacements, pulmonary embolisms, and other thromboembolic illnesses (OAT). Coagulation tests that identify parameters of the "extrinsic route" are the most often used in clinical laboratories. Due to the wide range of PT measurements between laboratories, the International Normalized Ratio (INR) was developed. The INR values for coagulation factors I, II, V, VII, and X can be used to determine the extrinsic pathway of the coagulation cascade. The International Normalized Ratio (INR) is a commonly used standard reporting technique for anticoagulant medicine use in a number of nations. Oral anticoagulant drug laboratory tests based on INR have received general acceptability in Canada, Europe, and the United States in recent years [2,4]. This test can be used to determine whether Factors II, V, VIII, IX, and XI and XII have intrinsic or common-route inadequacies. [1,2,3]

The International Sensitivity Index (ISSI) can be used to measure the consistency and quality of various thromboplastins (ISI). To obtain an accurate PT reading, more sensitive thromboplastin reagents with a lower ISI value are required. A lower ISI value indicates that the reagents are more sensitive. Laboratory-specific reference ranges, which are required for proper interpretation of test results, can have a substantial impact on clinical decision-making and the quality of patient treatment. Each clinical laboratory establishes reference intervals for test results. The findings of tests may be influenced by dietary intake, the population of a city, and the analytical technologies used. Rather than developing their own reference range, laboratories frequently rely on the manufacturers.

Manufacturer-recommended coagulation test reference ranges usually exclude reference ranges for children and adolescents, leaving adult age groups significantly underrepresented. The coagulation and fibrinolysis physiology of young children is statistically distinct from that of older children and adults. Context. The hemostasis system of a baby is still developing, and these functional discrepancies are tolerated. In infants, there are less signs of bleeding and thrombosis than in adults [4, 5].

Laboratory findings must be interpreted in light of the child's age, analyzer, and suitable reagent reference ranges in order to provide the right treatment for hemostatic diseases in children. It is likely that faulty test findings will result in extra diagnostic investigations and consultation requests, as well as wrong therapies and surgical operations that must be cancelled, leaving the patient's family and doctor in a financial bind. The number of studies investigating coagulation test reference ranges has been limited thus far due to factors such as the need for additional staff to collect and analyse samples from paediatric age groups, the time and difficulty involved in sampling, the higher pre-analytical variance associated with coagulation tests, the high cost of the

studies, and concerns about time constraints and ethical issues. In this study, we aim to determine whether PT, INR, and aPTT levels differ by gender and age in individuals who do not have liver disease or take anticoagulants.

METHODOLOGY

Between July and December 2021, records of patients undergoing minor surgical procedures (inguinal hernia repair, umbilical hernia repair, rectal polyp excision, and diagnostic cystoscopy) at Civil hospital LUMHS were analyzed for plasma PT (INR), INR, and aPTT. Blood samples were collected using tubes containing 3.2 percent sodium citrate. Separating plasma from cells in whole blood samples required 5 minutes of centrifugation at 3000 g. There were 2274 patients in all, with 766 males and 1508 females. According to their chronological age, patients were separated into three groups. The study sampled 268 men and 22 women aged 0-14, 222 men and 1335 women aged 15-50, and 151 women and 276 men in the third age range (over the age of 50 year).

Plasma PT and aPTT levels were determined using Siemens commercial test kits in a SYSMEX CA1500 auto analyzer. The INR was estimated for the PT by timing it in seconds. The calibration and control samples were analysed using this procedure. Monthly external quality control inspections and daily comparisons to normal and atypical controls were utilised to assure the correctness of these tests (KBUD, Turkey).

Analyze Statistical Data: SPSS 25.0 statistical software was used to conduct the analyses. In this instance, the Shapiro-Wilk test was applied to determine normality. The PT, INR, and aPTT values all have a non-parametric distribution. To evaluate if there was a difference, we used the Kruskal-Wallis test for total age groups and the Mann-Whitney U test for differences between two groups. The researchers considered a p value of <0.05 to be significant.

RESULTS

The PT and INR levels in women were much greater than in men (Table 1). Males and females between the ages of 15 and 50 had significantly higher PT, INR, and aPTT values than those between the ages of 0 and 14. This age group (A) exhibited the lowest levels of both male and female aPTT. Males and females between the ages of 15 and 50 demonstrated greater PT, INR, and aPTT values than females and males above the age of 50; however, the difference was also statistically significant. Both males and females In age grtoup 0-14years were found to have much lower levels of PT, INR, and aPTT than those over the age of 50. PT and INR levels were also lower in men over 50 than in any other age group. Table 2 and 3 indicates there were notable differences in PT, INR, and aPTT levels between the young (0-14 year olds) and older (15-50 year olds) and elder (over 50 year olds) groups (Table 2)

Table 1: Information of included patients with respect to gender

	No. of Males (766)	No. of Females (1508)	P Value
PT (Mean±SD)	11.90 ±4.52	13.50 ±4.24	0.001
INR (Mean±SD)	0.88 1.24	1.34 ±1.53	0.001
aPTT (Mean±SD)	26.40 ±9.09	26.50 ±9.80	0.875

Table 2: Outcomes with respect to age groups

				P Value (Independent t test)		
Age	Group A (0-14 years)	Group B (15-50 years)	Group C (>50 years)	Group A and B	Group B and C	Group A and C
PT	11.02 ±4.32	12.90 ±4.98	11.30 ±4.34	0.001	0.001	0.732
INR	0.82 ±1.53	1.87 ±1.76	0.98 ±1.54	0.001	0.001	0.546
aPTT	24.32 ±3.13	27.99 ±3.23	25.89 ±3.21	0.001	0.001	0.653

Table 3: Indications of differences in PT,INR and aPTT

	No. of Males	No. of Females
0-14 years	N=268	N=22
PT	10.92 ±4.32	11.12 ±4.32
INR	0.82 ±1.53	0.82 ±1.53
aPTT	24.12 ±3.13	24.42 ±3.13
15-50 years	N=222	N=1335
PT	12.90 ±4.98	12.90 ±4.98
INR	1.85 ±1.76	1.89 ±1.76
aPTT	27.99 ±3.23	27.99 ±3.23
>50 years	N=151	N=276
PT	11.20 ±4.34	11.40 ±4.34
INR	0.97 ±1.54	0.99 ±1.54
aPTT	25.87 ±3.21	26.79 ±3.21

DISCUSSION

Andrew et al. established the first formal concept of developing hemostasis in 1987. (11). A vast amount of research corroborates the study's claims [5, 10, 13, 14]. According to this study, adults and children should have unique reference ranges. If a misdiagnosis occurs, it may have negative consequences for the healthcare system, patients, their families, and healthcare workers.

According to Flanders et al.[10], the PT (Diagnostica Stago) values were substantially greater (14.0 s) in the 7-17 age group than in the adult group (13.2 s). On the other hand, no significant variation in aPTT (Diagnostica Stago) results was seen. This study discovered a difference of one second in the same age range (7 - 17 years). All four systems examined, including our device, revealed age-related physiological changes, including increasing PT and aPTT values [5,13].

Due to the critical use of reference ranges in the analysis of laboratory findings, physicians routinely utilise them to distinguish healthy individuals from those who are ill. This entails developing a suitable reference range based on a representative sample of patients. Reference ranges should be appropriately adjusted to account for the differences between adult and paediatric hemostases [8]. This is the first study of its sort in Konya, and it will include people of all ages. Participants in the study were compared to one another. This is the first time men and women have been compared across generations. Aral and colleagues [9] discovered that neither gender nor age had an effect on the levels of the three aPTT-related proteins (PT) or the INR. Thus, if the direct technique does not confirm the results of this study, they will be limited, particularly when it comes to aPTT in adults aged 40 and older, as well as physical testing variations between males and females (PT). Physical activities are undertaken by men and women of all ages and genders (PT). Men and women have significantly varied aPTT levels between the ages of 15 and 50.

According to Greenway and Monagle P et al. [8], many youngsters may be misdiagnosed with Von Willebrand disease because their aPTT values are longer than those of adults. We identified considerable disparities between adults and children ages 0-14 during our analysis. The aPTT values in this study were significantly different from ours. The mismatch may be explained by the fact that the population and analyzer utilise different reference intervals. Adults and children have comparable aPTTs, albeit children's aPTTs are slightly longer by about one second. Children aged zero to fourteen take an average of 0.04 seconds longer than adults, according to our poll. Numerous research on the physiological differences between children and adults have been undertaken [11]. When generating therapeutically effective reference ranges for the PT, INR, and aPTT, gender and age differences should be considered.

REFERENCES

1 Rizzo F, Papasouliotis K, Crawford E, Dodkin S, Cue S. Measurement of prothrombin time (PT) and activated partial thromboplastin time (APTT) on canine citrated plasma samples following diff erent storage conditions. Research in Veterinary Science 85, 166–170, 2008.

2 Rankin JA, Then KL. The international Normalized Ratio (INR): a review for orthopaedic nurses. Journal of Orthopaedic Nursing 5, 89–92, 2001.

3 Boroumand M, Goodarzynejad H. Monitoring of Anticoagulant Therapy in Heart Disease:Considerations for the Current Assays. J Teh Univ Heart Ctr 2, 57-68, 2010.

4 Zhang H, Gao C, Fang L, Yao SK. Increased international normalized ratio level in hepatocellular carcinoma patients with diabetes mellitus. World J Gastroenterol April 21;19(15), 2395-2403, 2013.

5 Jung B, Adeli K. Clinical laboratory reference intervals in pediatrics: The CALIPER initiative. Clinical Biochemistry 42,1589–1595, 2009.

6 Solberg HE. Using a Hospitalized Population to Establish Reference Intervals: Pros and Cons. Clin Chem 40/12, 2205-2206, 1994.

7 Djemli A, Vliet GV, Belgoudi J, Lambert M, Delvin EE. Reference intervals for free thyroxine, total triiodothyronine, thyrotropin and thyroglobulin for Quebec newborns, children and teenagers. Clinical Biochemistry 37, 328– 330, 2004.

8 Greenway A, Monagle P. Abnormal haematology results in children. Aust Prescr 27,64–66, 2004.

9 Aral H, Usta M, Cilingirturk AM, Inal BB, Bilgi PT, Guvenen G. Verifying reference intervals for coagulation tests by using stored data. Scandinavian Journal of Clinical & Laboratory Investigation 71, 647–652, 2011.

10 Flanders MM, Crist RA, Roberts WL, Rodgers GM. Pediatric Reference Intervals for Seven Common Coagulation Assays. Clinical Chemistry 51(9), 1738-1742, 2005.

11 Andrew M, Vegh P, Johnston M, Bowker J, Ofosu F, Mitchell L. Maturation of the hemostatic

12 Horn PS, Pesce AJ. Reference intervals: a user's guide. Washington: American Association for Clinical Chemistry; 2005. [Google Scholar]

13 Appel IM, Grimminck B, Geerts J, Stigter R, Cnossen MH, Beishuizen A. Age dependency of coagulation parameters during childhood and puberty. J Thromb Haemost. 2012;10(11):2254–63. doi: 10.1111/j.1538-7836.2012.04905.x. [PubMed] [CrossRef] [Google Scholar]

14 Ignjatovic V, Kenet G, Monagle P, Perinatal. Paediatric Haemostasis Subcommittee of the S, Standardization Committee of the International Society on T, et al. Developmental hemostasis: recommendations for laboratories reporting pediatric samples. J Thromb Haemost. 2012;10(2):298–300.