DOI: https://doi.org/10.53350/pjmhs2216587

ORIGINAL ARTICLE

Frequency of Factor V Deficiency (F5d) Among Patients with Bleeding Complaints

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ABSTRACT

Background: Commonest genetic defect includes mutation of F5 gene on the long arm of chromosome1q23 thus both parents carry defective gene.
Aim: To evaluate the frequency of inherited Factor V deficiency among patients presenting with bleeding at T.C hospital.
Study design: Cross sectional study.
Methodology: A total of 300 patient presented with complain of bleeding were included in this study. Detailed history was noted. PCR was performed. After preparation of PCR reaction mixture, incubate tubes into thermal cycler having specific cycling condition. Primer was use for both PCR amplifications and sequencing reactions was designed. Applied bio-system was used for mutation detection. The collected data was analyzed by using SPSS version 25.
Results: The average age of the patients was 36.87±9.40 years. There were 213(71%) male and 87(29%) female. Frequency of inherited factor V deficiency in patients presented with complains of bleeding was 3.33% (10/300). **Conclusion**: It was concluded that frequency of inherited factor V deficiency in present study was low.
Conclusion: frequency of inherited factor V deficiency in present study was low (3.33%).
Keywords: Mutation, Factor V deficiency, bleeding, PCR reaction.

INTRODUCTION

There are some bleeding disorders that are rare but have serious complications if remain untreated and undiagnosed. Isolated factor V deficiency is one of them with approximately 8.3% of all rare bleeding disorders[1,2]. This disorder has an incidence of around 1 in 1,000,000 as per documented by literature review[3-5]. Commonest genetic defect includes mutation of F5 gene on the long arm of chromosome1q23 thus both parents carry defective gene[6,7]. Homozygous deficiency of factor v is usually manifests early in the life[2]. If only one parent is a carrier than child usually remains asymptomatic. Both sexes are equally affected[3] It's a rare disease but more cases were reported among inter-cousin marriages.[8,9] This health issue usually presents from mild to severe life threatening blood loss from gums or mucosa of the body[10,11].

Human factor v is a crucial 330KDa that is synthesized in the liver and then released into the blood circulation. High molecular weight single chain glycoprotein plays a vital role in the blood co-agulation cascade by having both pro-coagulant and anticoagulant functions[10]. Normally, Factor v circulates in the blood plasma in an inactive form and almost 25% is found into the platelets α-granules. Activated form of factor v serves to form fibrin clot formation as documented previously[11-13].

Mutations like mis-sense, frame shift, non-sense and splice site mutations etc cause factor V deficiency as shown by literature review[2,3]. Deficiencies of factor V arise due to acquired inhibitors to factor V and defects that affect its storage and processing. In the light of above description, it's a health issue that remained untouched in our society but it's a common health issue that needs investigations. Hence, we planned current project to see its prevalence in our society.

The objective of the study was to evaluate the frequency of inherited Factor V deficiency among patients presenting with bleeding at T.C hospital.

METHODOLOGY

Patients (n=300) having both genders with age ranging from 18 to 65 years who presented with bleeding regardless of their marital status were enrolled. After IRB permission detailed history was noted. PCR was performed. Genomic DNA was extracted from the blood. After preparation of PCR reaction mixture, incubate tubes into thermal cycler having specific cycling condition. Primer was use for both PCR amplifications and sequencing reactions was designed. Applied bio-system was used for mutation detection. All women who were pregnant, having anti-platelet or oral contraceptive pills, recent history of blood transfusion or factor concentrate with wash out period of 2 weeks were excluded.
Statistical analysis: Data was analyzed by using SPSS v.25. Variables like age, hemoglobin level, Factor V Assay and APTT were presented by mean±SD. Post stratification chi square test was applied by taking p ≤0.05 as significant.

Received on 24-10-2021
Accepted on 13-04-2022

RESULTS

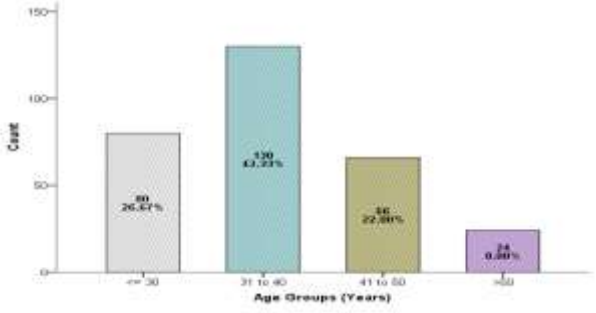
Average age was 36.87±9.40 years of enrolled subjects. Average hemoglobin, factors V assay and APTT (Table 1).

Table-1: General parameter of enrolled subjects (n=300)

Variables	Groups	Frequency	%age
Gender	Males	213	71
	Females	87	29
Complaint of bleeding or bruising	Yes	70	23.3
	No	230	76.7
AGE (Yrs)	Mean + SD	36.87±9.40	
Hemoglobin (mg/dl)		11.61±1.23	
Factor V Assay		36.82±12.27	
APTT (sec)		40.75±10.75	

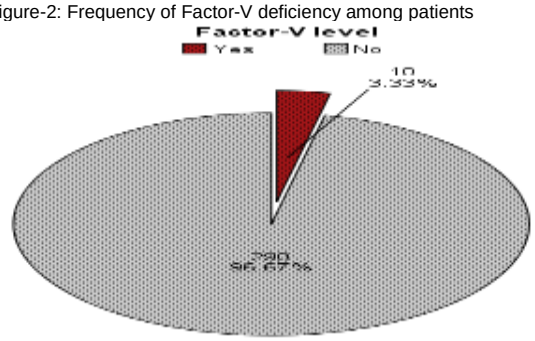
Majority of patients (43.3%) with bleeding complaints presented at young age group (31-40 yrs), 24(8%) patients were presented at age older than 50 years as shown in figure-1.

Figure-1: Age Distribution among Patients



Frequency of inherited factor V deficiency in patients presented with complains of bleeding was 3.33% (10/300) as presented in figure-2.

Figure-2: Frequency of Factor-V deficiency among patients



Rate of factor V deficiency was observed according to age groups but insignificant difference was observed (p=0.704) as shown in table-2.

Table-2: Frequency of inherited factor-v deficiency by age groups (n=300)

Age Groups (Years)	Factor-V Level		Total
	Yes	No	
≤30	2(2.5%)	78(97.5%)	80
34-40	5(3.8%)	125(96.2%)	130
40-50	3(4.5%)	63(95.5%)	66
>50	0(0%)	24(100%)	24

P value 0.704

DISCUSSION

As inherited factor V deficiency has a diverse clinical manifestation from asymptomatic to life-threatening hemorrhagic episodes. This makes it a mystery as well as a challenge for its correct diagnosis. Thus it is a need of current situation to identify and diagnose it with perfection before this disease develops complications like heavy bleeding from critical sites. Literature review revealed that acquired factor V deficiency occurs rarely due to many reasons that include development of inhibitors against factor V following antibiotic therapy, infection or malignancy. However, among elderly patients, this disease has a prevalence of about 39% as per literature review.[14] Due to lack of research data on spontaneous disappearance of these inhibitors, this bleeding disorder remained unrevealed. However, it has been documented by one researcher that factor V inhibitors departed within 10 weeks of initial recognition[15].

Laboratory investigations like prothrombin time (PT) and activated partial thromboplastin time (aPTT) show prolongation (increased time) with normal thrombin time (TT). As these investigations play an important and defining role in its initial screening. However, bleeding profile can be corrected by mixing patient plasma with a normal plasma pool in inherited form whereas correction is partial in other form.

In present study, majority were males (71%) while females were (29%). Average age was 36.87±9.40 years of enrolled subjects. Our findings were in line with another study that enrolled males (77%) as their majority participants while females were just 23%.[16] However, average age in their study was 8.44 ± 6.63 years (range 2-22 years) that was paradoxical to current study.

Presenting complaint of bleeding or bruising was observed as 23.33% in present study. Our findings were in line with another study that showed bleeding gums, epistaxis and bruising after minor trauma as their major complaint. However, only 3% and 1.5% cases had soft tissue bleeding and haemarthrosis respectively. Our results were in line with the results of other studies that showed high rates of this disease due to consanguineous marriages[16-18].

Risk of bleeding does not correlate with factor V inhibitor levels, prolongation of PT or aPTT, factor V activity thus making a difficult task to predict bleedings[18]. However, better response was seen with inhibitor eradication therapy in acquired deficiency case[19].

Limitations: This study lacked genetic workup among patients in-order to find the genetic cause with limited resources and financial constrains.

CONCLUSION

It was concluded that frequency of inherited factor V deficiency in present study was low (3.33%). Awareness about the disorder is the need of time in order to prevent life threatening bleeding. Comprehensive assessment of patients, followed by careful laboratory testing is necessary to diagnose factor-V deficiency.

Author's contribution: NUAA&QUAQ: Conceptualized the study, analyzed the data, and formulated the initial draft, **SK&M:** Contributed to the proof reading, **NA&IDU:** Collected data,

Conflict of interest: None

Funding: None

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