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Screening of Von Willebrand Disease Among Children with Severe or Recurrent Attacks of Epistaxis

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Abstract
Mild mucosal bleeding is the hallmark of von Willebrand disease (VWD), a congenital bleeding illness caused by a malfunction or deficit of von Willebrand factor (VWF). Von Willebrand disease is a prevalent but underappreciated bleeding ailment; our study's objective was to assess infants with severe or recurring epistaxis for the likelihood of this disorder. Methods and Patients: A total of seventy children who presented to the emergency room or outpatient clinic with epistaxis were included in this cross-sectional research. Complete blood counts, PTs, APTTs, VWF Ag, and VWF activities were among the blood assays performed on all patients in addition to clinical examinations and history gathering. One patient was found to have VWD out of seventy who presented with severe or recurring epistaxis over the course of the research. In conclusion, children experiencing severe or recurring epistaxis should be evaluated for VWD.
Topics: Epistaxis in Children with Von Willebrand Disease.

Keywords:VWD,PTs,APTTs,VWF.

Introduction:

Among hereditary bleeding disorders, von Willebrand disease (VWD) is by far the most prevalent. A mucocutaneous bleeding phenotype is present, which may greatly affect one's quality of life [1]. The diagnosis and subclassification of VWD still provide substantial clinical hurdles, despite the disease's prevalence and the morbidity it is linked with. This is due, in part, to the fact that VWF serves a variety of physiological roles in living organisms and, secondarily, to the fact that typical population plasma VWF levels span a large range. In clinical practice, a diagnosis of VWD is made when there is bleeding as well as abnormal VWF tests in the laboratory. Family medical records may provide credence to a VWD diagnosis in some instances [2,3].

Patients with various forms of VWD show varied inheritance patterns and may need different therapy, hence it is directly relevant to the therapeutic setting that VWD be correctly classified. Several expert consensus recommendations have addressed VWD categorization [4]. There should be three main groups for patients with VWD, according to the recommendations put forth by the International Society for Thrombosis and Haemostasis (ISTH). Type 1 VWD, which makes up over 75% of all cases, is characterized by a partial quantitative deficit in plasma VWF. All patients with qualitative abnormalities that hinder one or more parts of VWF function (~25% instances) are included in Type 2 VWD. Based on the nature of the underlying VWF qualitative defect, Type 2 VWD is further categorized into four subtypes: 2A, 2B, 2M, and 2N, respectively (Table I). Lastly, a quantitative VWF deficit and the almost total lack of plasma VWF describe the uncommon Type 3 VWD, which affects one person per one million [5].

Laboratory testing confirms a diagnosis of VWD based on clinical characteristics, which include a personal and family history of bleeding or bruising. Because VWD is caused by problems with the plasma protein VWF, a battery of tests must be run in the lab to determine the amount and activity of VWF. An assay panel's comprehensiveness determines how likely it is to correctly diagnose or rule out VWD; a less comprehensive panel increases the likelihood of a mistake [6].

Patients and Methods:

Patients seen at Benha University Hospitals' ENT outpatient clinic and pediatric emergency department between 2019 and 2020 were the subjects of this cross-sectional research. Seventy kids who reported severe or frequent episodes of epistaxis were enrolled. The individuals and/or their caregivers were required to provide informed

permission before they could participate. Following the guidelines laid forth in the Declaration of Helsinki, this research received approval from the local Research Ethics Committee (Benha Faculty of Medicine Research Ethics Committee. All patients were asked to provide their informed permission before the trial began.

Those who met the inclusion criteria had severe or recurring epistaxis and were between the ages of 2 and 18.

Thrombocytopenia, aberrant PT findings, systemic reasons, local variables (such as allergic rhinitis), injuries, infections, and atypical anatomy are all things that cannot be considered.

Blood investigations (whole blood count, PT, APTT, VWF Ag, and cofactor activity) were administered to all patients in addition to the following: a clinical examination, history collection, and a local ear, nose, and throat (ENT) exam.

Sampling: Blood samples were taken from various parts of the body.For the coagulation assays (PT, APTT) and the tests for VWF Ag and VWF activity, one sample was citrated.

VWF display:

ELISA was used to determine the amount of the von Willebrand factor antigen (VWF: Ag).

VW The ELISA method was used to measure the cofactor activity, which is the von Willebrand factor.

Statistical analysis

Statistical Package for the Social Sciences (SPSS) for Windows (Standard version 26) was used for data analysis. For continuous data, the standard deviation and mean were used as representations. In order to describe the qualitative data, percentages and counts were used. For the purpose of analyzing correlations between categories, the Chi-square test was used. Continuous data was correlated using both parametric (Pearson) and non-parametric (Spearman) techniques of correlation. The ROC curve was used to examine the specificity and sensitivity at various cutoff points. A significant result was defined as a two-tailed P value less than 0.05.

Results:

Table (1): Participants' ages and sexes in the research.

Socio -demographic data	The studied children (n=70)
Age in years	
Mean ± SD	9.64±3.18
Min-Max	5.0-17.0
Gender	
Male	30 (42.3%)
Female	40 (57.7%)

The data in this table reveals that the average age of the participants was 9.64±3.18, ranging from 5 to 17 years, and that 42.3% of the participants were male and 57.7% were female. One table and one figure

Table (2): Concordance, family history of bleeding, and symptoms of bleeding in the research population.

	The studied children (n=70)	
Bleeding symptoms	**No.**	**%**
Epistaxis	57	81.4
Epistaxis & Bleeding gums	3	4.3
Epistaxis & Menorrhagia	2	2.9
Epistaxis & Ecchymosis	8	11.4
Family History	**No.**	**%**
Positive	9	12.9
Negative	61	87.1
Consanguinity	**No.**	**%**
Positive	11	15.7
Negative	59	84.3

Among the individuals surveyed, 81.4% had epistaxis alone, 11.4% had it with ecchymosis, 2.9% had it with menorrhagia, and 4.3% had it with bleeding gums, as shown in Table (2). Of the people that were part of the study, 15.7% had positive consanguinity. Figure 3 shows that 12.9% of the participants in the study had a positive bleeding family history.

Table (3): Levels of VWF Ag and VWF activity in the investigational group.

Variables	The studied children (n=70)	
	Mean ± SD	Min-Max
VWF Ag (%)	147.36±49.44	40-190

VWF activity (%)	175.35±68.05	44-243

The average value of VWF Ag was 147.36 ± 49.44, and the average value of VWF activity was 175.35± 68.05, as shown in Table (3).

Table (4): Coagulation profile among the examined group.

Coagulation profile	The studied children (n=70)	
	Mean ± SD	Min-Max
PLT count (10^3/ul); mean±SD	281.81±91.51	187-480
Bleeding time (min)	5.54±0.84	4-6
PT (sec)	12.51±0.51	11.5-13.5
APTT (sec)	34.86±3.86	28.50-38.00

The basic coagulation profile, as shown in Table (4), reveals normal results for the following: PLT count, bleeding time, PT, and APTT. The mean values for these parameters are 281.81±91.51, 5.54±0.84, 12.51±0.41, and 34.86±3.86, respectively.

Benha University Hospitals' outpatient clinic and emergency room saw 70 patients throughout the research period who complained of epistaxis. With a mean age of 9.64±3.18 years, all of the recruited patients were either older than 2 or less than 18 years old; 40 of the patients were female and 30 were male.

We found that 9 patients had a positive family history of hemorrhage, and 11 cases showed positive consanguinity. Only 57 individuals exhibited with epistaxis; the remaining 8 patients had ecchymosis, 2 had menorrhagia, and 3 had bleeding gums as concurrent bleeding symptoms. Two tables

Discussion

A frequent emergency in otolaryngology, epistaxis affects many children [7]. The vast majority of epistaxis episodes are harmless, short-lived, and very seldom fatal [8].

Both parents and medical professionals find severe and recurring epistaxis to be a significant source of stress. Determining whether the bleeding is local or caused by hereditary systemic coagulopathy is critical in severe and recurring episodes. Finding the root of the problem is crucial because it shows that the otolaryngologist or pediatric hematologist is strictly adhering to the treatment plan [9].

The majority of people in the community suffer from von Willebrand disease (VWD), a bleeding ailment. A lack of or malfunction in the Von Willebrand factor (VWF) is the underlying cause of vascular thrombosis (VWD). VWF facilitates platelet adhesion at vascular injury sites, binds to factor VIII, stabilizes the blood clot, and prolongs its half-life in the blood [1]. Von Willebrand disease is an underdiagnosed but prevalent bleeding ailment; our study's goal was to test infants who presented with severe or recurring epistaxis for this condition. Results from the screening tests showed that 1.4% of the participants in the present research had VWD, indicating a prevalence of the condition within the examined population. In a study of 63 children, the prevalence of VWD was found to be 3.3%.

Additionally, 6.6% of patients in an Egyptian trial that spanned 16 years were found to have VWD. This can be because of the huge sample size or the lengthy duration of the research.

Our investigation found a maximum frequency of less than 9 years. The most prevalent age range for this to occur is between three and eight years old, according to eleven reports. Our study's gender breakdown revealed that women made up 57.7% of the patients and men 42.3%. A total of 178 children suffering from recurrent epistaxis were included in the research [12]. There were 103 boys (57.8%) and 75 girls (42.2%), and the median age was 7 years. Our results are at odds with those of [13] who studied the same population in Bangladesh and found that men made up the vast majority of his patients (68% vs. 2:1). The greater prevalence of trauma among the patients accounted for the larger proportion of males because boys were more active when they were younger, they were more likely to have hemorrhage symptoms [14].

There was a history of bleeding in the patient's family for 12.9% (9 patients) of the individuals included in our research. Having a history of bleeding disorders in a family member might help narrow down the list of people who need further evaluation [15]. Patients having a positive family history of the same illness accounted for 44.4% of the total in the sample of 9.

Among the participants in this research, 15.7% had positive consanguinity. Also, according to their analysis of 298 pediatric cases, the researchers found no evidence that consanguinity is a predictor of VWD in children [16]. Additional bleeding symptoms in our research included epistaxis with bleeding gums in 4.3%, menorrhagia in 2.9%, ecchymosis in 11.4%, and epistaxis alone in the remaining cases. While 33% of the VWD group

has bleeding via the mucosal membranes, 53% have menorrhagia, according to the research [17].

Conclusion

When dealing with severe or recurring epistaxis in children, VWD should be seriously evaluated.

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