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Congenital von Willebrand factor deficiency in single Iraqi teaching hospital: A descriptive study

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Abstract:

BACKGROUND: Von Willebrand disease (vWD) is a common, inherited hemorrhagic disorder caused by a deficiency or dysfunction of the protein von Willebrand factor (vWF).

OBJECTIVES: The aim of this study is to assess the diagnosis and treatment of vWD in a single Iraqi teaching hospital.

PATIENTS AND METHODS: This descriptive study was conducted on 778 patients with bleeding tendency, 107 patients were diagnosed to have vWD, and from the first of October 2013 to the first of August 2015. The diagnosis of the disease was made by a wide spectrum of characteristics including family history, clinical manifestations, and laboratory tests.

RESULTS: The common manifestations of the disease at the time of the diagnosis were epistaxis (39.2%), gum bleeding (24.2%), and menorrhagia (23.4%) in female patients. The age of patients at time of presentation was between 1 and 10 years. Family history was positive in most patients. Hepatitis C was rare in the patients after cryoprecipitate administration.

CONCLUSIONS: It is a common inherited hemorrhagic disease in Iraq, mostly presented as minor bleeding involving mainly mucocutaneous regions which appears at an early childhood with positive family history in most cases.

Key words:

Cryoprecipitate transfusion, desmopressin, menorrhagia, von Willebrand disease

Von Willebrand disease (vWD) is a common, inherited hemorrhagic disorder caused by a deficiency or dysfunction of the protein termed von Willebrand factor (vWF). Consequently, defective vWF interaction between platelets and the vessel wall impairs primary hemostasis. Males and females are affected equally by vWD. However, it may be more pronounced in females because of menorrhagia. Bleeding-related symptoms may occur at a young age. vWD is divided into three major categories: (1) Partial quantitative deficiency (Type I), (2) qualitative deficiency (Type II) divided into four variants (IIA, IIB, IIN, and IIM), based on characteristics of dysfunctional vWF, and (3) total deficiency (Type III).[1]

The abnormal bleeding associated with vWD may presented as recurrent and prolonged nosebleeds, bleeding from the gums, excessive bleeding from a cut or following a tooth extraction or other dental procedure, blood in the stool or urine, bleeding from shaving with a razor, or other similarly minor injury. Heavy menstrual bleeding is often the main sign of vWD in women.[2]

Diagnosis of the disease based on these tests: The complete blood count might be normal but could also show thrombocytopenia, specifically in Type IIB vWD. The activated partial thromboplastin time (aPTT) is often normal but may be prolonged when the factor VIII level is reduced as can be seen in severe Type I vWD, Type IIN vWD, or Type III vWD. The prothrombin time (PT) is normal.[3] Factor VIII: C which measures the amount of factor VIII-clotting activity, vWF: Antigen (Ag) which measures the amount of vWF, ristocetin cofactor activity which measures how well the vWF works, and vWF multimers which examine the structure of the vWF.[4]

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Diagnosing vWD is difficult. There are factors that cause the level of vWF to rise in the blood and appear to be normal such as being pregnant, breastfeeding, normal hormonal changes during a woman's monthly menstrual cycle, being on oral contraceptive pills, having an infection, having recently undergone surgery, or having recently had a blood transfusion. The vWF tends to increase with age. In addition, people with blood Group O have naturally lower levels of vWF.[5,6]

Treatment may vary depending on the type and severity of the disorder. Desmopressin (DDAVP) is administered by injection into a vein or through a nasal spray called Stimate®. It stimulates the body to release more vWF already stored in the lining of the blood vessels. It is usually effective in people with Type I and some subtypes of Type II diseases.[7]

Infusions of concentrated vWF and factor VIII can be useful in all disease types. Contraceptives can be useful for controlling heavy bleeding during the menstrual periods. Antifibrinolytic such as aminocaproic acid can slow down the breakdown of clotting factors.[6]

Patients and Methods

This is an observational descriptive study. The study participants included all patients who were admitted and discharged from the Hemophilia Center in Children Welfare Teaching Hospital in Baghdad/Medical City with the diagnosis of vWD, from October 2013 to August 2015.

Platelet count and PT were found normal. Patients were diagnosed on the basis of prolonged bleeding time in Type II, abnormal aPTT, reduced level of vWF: Ag, factor VIII, vWF: Ristocetin cofactor (RiCoF), and ratio of vWF: RiCoF/vWF Ag. Patients were identified using coded discharge records with the diagnosis of coagulation/factor deficiency which are available in Iraq for the last years and was done in all patients, for diagnosis of vWD; those found positive were labeled as vWD.

Data collected include

Data collected include gender, age at presentation, presenting complaint, family history, and type of treatment (desmopressin and cryoprecipitate), hepatitis B, C in patients, and its relation to cryoprecipitate. All our patients have a normal lifestyle with repeated admissions to our ward for cryoprecipitate transfusions or desmopressin administration when they presented with bleeding during a period of observation from 2013 to 2015.

Results

A total of 778 patients were evaluated for bleeding tendency, 107 patients were diagnosed to have vWD. Out of these 107 patients, 60 were males (56%) and 47 were females (43.9%). The age of the patients at time of presentation was mostly between 1 and 10 years, and the range was from <1–40 year with mean = 3.8 and standard deviation = 2.7 as shown in Figure 1. Epistaxis and gum bleeding were the major presenting complaints in 68 patients (63.4%), followed by menorrhagia (23.4%) in female patients, bleeding after circumcision (11.6%) of males, and vaccine in seven patients (8.5%) as shown in Table 1.

Family history was positive in 67 patients (62%) and negative in 40 patients (37%) as shown in Figure 2. The treatment used in patients when presented with bleeding is cryoprecipitate. Testing for transmission of viral infections was also done in all patients where 17 patients were found to have hepatitis C positive after repeated transfusions of cryoprecipitate as shown in Figure 3.

Discussion

The incidence of vWD may vary according to country and ethnic origin. In Iraq, it appears to be a common bleeding disorder that to date, 107 patients have been identified in our Hemophilia Center in Children Welfare Teaching Hospital, similar to that in Jordan were it is the second most commonly seen inherited bleeding disorder after hemophilia A.[8] Studies conducted from countries such as India and Iran showed low prevalence of vWD.[9,10] In these patients, the prevalence of different subtypes of vWD is not known because the diagnosis was done on the basis of factor VIII level, vWF: Ag assay, RiCoF activity, and ratio of RiCoF to VWF: Ag without performing vWF multimeric analysis till the last few years. In Pakistan, Type III was found to be the most common type then Type II and only one case of Type I.[11]

In this study, it presents commonly at the age of 1–10 years (48%), similar to Pakistani an study which presents with bleeding tendency commonly at age 1–12 years (37%).[11] Epistaxis is the most common cause of bleeding in our patients at time of

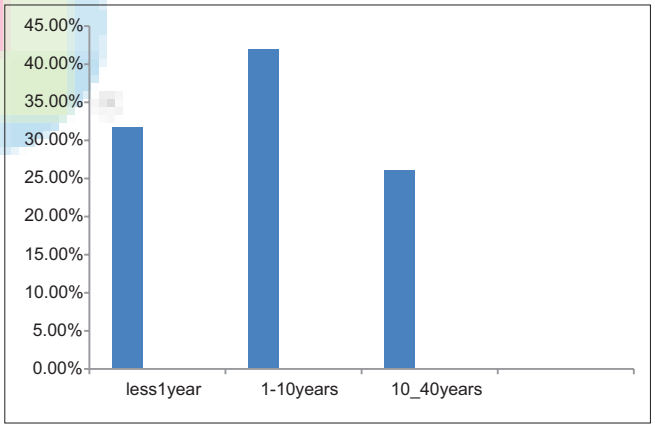

Figure 1: The age of the patients at time of presentation of 107 patients

Table 1: The presenting complaints at the time of diagnosis in 107 patients

Bleeding type	Frequency	Percentage
Epistaxis	42	39.2
Gum bleeding	26	24.2
Menorrhagia	11	23.4 of females
After circumcision	7	11.6 of males
After vaccine	7	8.5
Hemarthrosis	5	4.6
Ecchymosis	4	3.7
Hematuria	3	2.8
Umbilical cord bleeding	2	1.8
Total	107	

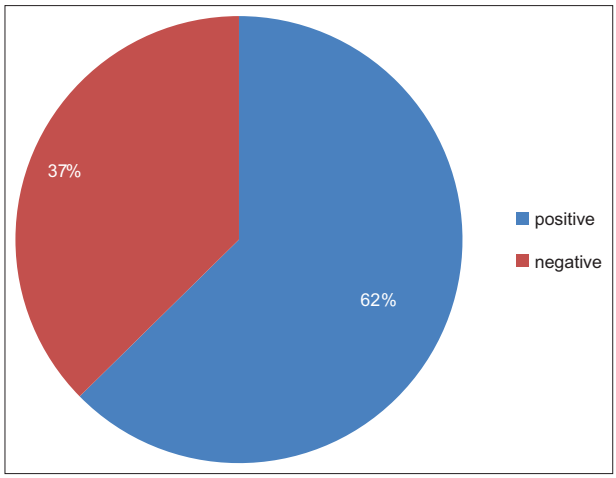

Figure 2: The family history in 107 patients

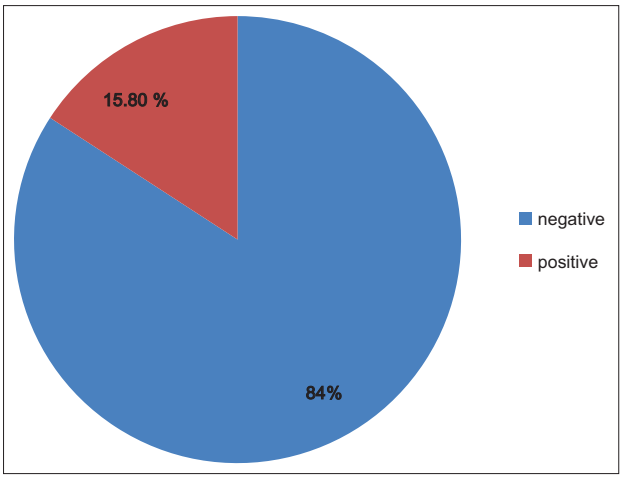

Figure 3: The results of hepatitis C screening in 107 patients

diagnosis, and it is typically more severe in children than in adults. It occurred in 30.2% of our patients. Gum bleeding is the next most common manifestation in our study occurring in 24.2% of the patients, followed by menorrhagia (23.4%) of female patients; in contrast to the Pakistanis, easy bruising was the most commonly observed clinical presentation in 21 (41.18%) patients, followed by epistaxis in 7 (13.73%), gum bleed in 4 (7.84%), menorrhagia in 5 (9.80%), hemarthrosis in 2 (3.92%), and bleeding after circumcision in 2 (3.92%).[11] This may be attributed to the fact that ecchymosis had passed unnoticed in our patients. Menorrhagia was found in 23.4% of our female patients. Similar that in Pakistan study occurring in 22% of their female patients.[12,13] It has also been reported by others to be one of the most common and most serious bleeding tendencies necessitating repeated blood transfusions. No intracranial hematomas or gastrointestinal bleeding was observed in our patients. In this study showed that most of patients treated with cryoprecipitate and only 3% treated with desmopressin while vWF is not available till now, FVII is used if no response. While in Pakistan, 8% were treated with desmopressin and recombinant vWF is available if no response.[14] This may be due to our patients came to the hospital complaining mainly from severe bleeding.

Conclusion

Congenital vWD is a common hemorrhagic disease in Iraq, mostly presented as minor bleeding involving mainly mucocutaneous regions which appears at an early childhood with positive family history in most of the patients. All our patients respond to cryoprecipitate transfusion only.

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Conflicts of interest
There are no conflicts of interest.

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