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RESEARCH ARTICLE

PREVALENCE OF COAGULATION DEFECTS IN PATIENTS OF ABNORMAL UTERINE BLEEDING AND INCIDENCE OF VON WILLEBRAND DISEASE IN SUSPECTED CASES

Chauhan Rooplekha *, Sahni Sonal, Nigam Vibha*****

***Professor and Head of Department , Obstetrics and Gynaecology, N.S.C.B. Medical College, Jabalpur (Madhya Pradesh).**
****Assistant Professor , Department of Obstetrics and Gynaecology, Netaji Subash Chandra Bose Medical College Jabalpur (Madhya Pradesh)**
*****Post graduate resident 3rd year in Department of Obstetrics and Gynaecology, Netaji Subash Chandra Bose Medical College Jabalpur (Madhya Pradesh)**

Department of Obstetrics and Gynaecology, N.S.C.B. Medical College, Jabalpur

Corresponding Author: Dr Prof Rooplekha Chauhan;Resi:"Vibhor",99-b Nayagaon Hills,Jabalpur (M.P.)

ABSTRACT:
Abnormal uterine bleeding is one of the gynaecological complaints seen in women of reproductive age.To date there is no consensus on application of coagulation testing specifically Vwf testing as a part of routine investigation in menorrhagia.Von willebrand disease (VWD) prevalence is estimated from 5-20% in women with menorrhagia,lower prevalence in Asian-African (1%).The aim of our prospective study was to find prevalence of coagulation defects in women presenting with menorrhagia and incidence of VWD in those patients.Seventy four patients with unexplained menorrhagia were included in this study .Hemostatic profile such as hemoglobin, platelet count,prothrombin time, activated partial thromboplastin time(APTT),bleeding time were measured in all patients and those who had abnormal values further went for factor VIII activity and Von Willebrand factor antigen testing, in our study among various causes of coagulation defects Thrombocytopenia in 7(9.4%),factor VIII deficiency in 1 (1.3%),Chronic ITP in 1 (1.3%) and Von willebrand factor value lower range in 1 patient (1.3%).From present study it appears that AUB may mask underlying coagulation defects including VWD.So awareness program including diagnostic facilities for VWD is required for management of these patients.
KEYWORDS-AUB-Abnormal uterine bleeding,VWD-Von Willebrand disease,APTT-Activated partial thromboplastin time,ITP-immune thrombocytopenic purpura,VWF-von willebrand factor.

INTRODUCTION

Abnormal uterine bleeding is one of the most common gynaecological complaints seen in women of reproductive age.Approximately 10-15% women complain of heavy menses.Around 20% gynecological visits are for AUB and 1/4TH of gynaecological surgeries are for AUB .Recently there has been growing recognition that menorrhagia is a common manifestation for Von Willebrand disease .its prevalence was estimated from 5 to 20% (1,2).Various coagulation defects are also found to be prevalent in adolescent,reproductive and perimenopausal women. Abnormal uterine bleeding defined in terms of disturbances of regularity,frequency,amount and duration . Von Willebrand disease and other inherited and acquired disorders of coagulation and hemostasis should be considered in the differential

diagnosis of all patients being evaluated for heavy menstrual bleeding, regardless of age. It is an autosomally inherited congenital bleeding disorder, von Willebrand disease involves a qualitative or quantitative deficiency of Von Willebrand factor (vWF), a protein critical for proper platelet adhesion and protection against coagulant factor degradation. Dominant and recessive patterns of inheritance exist. There are three main types of Von Willebrand disease. Type 1 (deficiency of vWF), the most common, is usually mild; type 2 (abnormal vWF) has several subtypes and is less common; and type 3 (absence of vWF), which is rare, is the most severe form(3). There are many factors contributing to the fluctuations of Von Willebrand antigen and activity as well as factor VIII (FVIII) levels such as age (levels increased with age), race and ABO blood group (for O-group vWF levels generally lower than non-O blood group levels). Plasma Von Willebrand factor (vWF) levels also fluctuate in individuals according to individual variation (different results are possible on sequential-day samples), diurnal variation (levels appear higher later in the day) and hormonal influenced (e.g., fluctuations within menstrual cycles, and higher levels in pregnancy) (4). Young girls with blood coagulopathies are at a high risk of abnormal bleeding with the onset of menarche, bleeding is usually heavy causing anemia and may require blood transfusion. Claessen et al found (5) 20% of cases of menorrhagia to be due to primary coagulation disorders. Platelet function defects are an important cause of menorrhagia. Saxena (6) et al found platelet function disorder in 83% of women with menorrhagia due to coagulation defects. Phillip et al2 reported an incidence of abnormal platelet aggregation in 45% of women with bleeding disorder. 3 patients (8.6%) had idiopathic thrombocytopenic purpura. Abnormal uterine bleeding is a commonly reported symptom among women with a diagnosis of Von Willebrand disease, with 74–92% experiencing heavy menstrual bleeding (7). Additional symptoms or signs that may be present include epistaxis (38–63%), gingival bleeding (26–35%), bleeding after dental extraction (29–52%), bleeding from minor cuts or abrasions (36%), postoperative bleeding (20–28%), gastrointestinal bleeding (14%), and joint bleeding (6–8%) (8, 9). Awareness of Von Willebrand disease as a cause for menorrhagia is important for the following reasons-

- Health implications like future surgery and childbirth.
- Effective medical treatment of menorrhagia with desmopressin in nasal spray in addition to Oral contraceptive pills and antifibrinolytic agents
- Avoidance of major surgical intervention.
- Furthermore this disease has mostly autosomal dominant inheritance and identification of case would lead to screening and early diagnosis of vWD in relatives of index case.
- Genetic counseling

AIMS AND OBJECTIVES

The aim of our study is to find out the prevalence of coagulation defects in patients of Abnormal uterine bleeding and Incidence of Von Willebrand Disease in suspected cases .

MATERIALS AND METHODS

A prospective cross sectional study was conducted in Department of Obstetrics and Gynaecology ,NSCB Medical college and hospital Jabalpur from 1st October 2014 to 1st October 2015 .Study included 74 women of age group 12-55 years.Approval from

institutional ethical committee was taken before conducting the study .An informed written consent was taken from all patients.

A preformed proforma was used to collect thorough history and information regarding bleeding diathesis. Examination was done including per speculum and bimanual examination (if indicated) .Investigations like Hemoglobin,platelet count,ABO blood group,T3 T4 TSH and detailed hemostatic profile BT,PT,APTT was done.In patients with abnormal hemostatic profile vWF Ag and factor VIII activity was done by automated enzyme immunoassay on citrated plasma. The normal reference range for vWF Antigen- O blood group;35-150 % and Non O blood group:50-241%..

INCLUSION CRITERIA

- Patients with menorrhagia since puberty.
- Patients presenting with unexplained menorrhagia with no organic disease.
- Patients with family history of bleeding disorders.
- Bleeding tendencies from other sites.

EXCLUSION CRITERIA

- Women who had other known causes of menorrhagia
- IUCD in situ
- Patient on anticoagulants,NSAIDs like aspirin and other platelet impairing agents ,OCP use, anticancer drugs
- Submucous uterine myoma, uterine polyp
- Gynaecological malignancy
- Patients of aplastic anemia, leukemia etc.

RESULTS

• In our study, it was found that out of 74 cases, most of the patients belonged to age group of 12-20 years (45.94%) and had menorrhagia since puberty (22.9%).

• 13 cases (17.56%) had history of heavy menstrual bleeding in mother,17 cases (22.9%) had menorrhagia since puberty.

• In our study, after eliciting history; 3 cases (4.05%) had history of PPH and epistaxis each, 12 (16.21%) cases with history of blood transfusion,1 case (1.3%) had Surgical site bleeding and h/o bleeding disorder ,5 cases (6.7%) had h/o OCP intake.

• In patients who presented with menorrhagia, the degree of anemia in cases-very severe anemia account for 6 cases (8.1%), and severe anemia found in 16 cases (21.62%), moderate anemia in 44 cases (59.45%).

Hypothyroidism was found to be associated with acquired von willebrand disease and it was found in 7 cases (9.4 %) but no patient had associated vWF antigen deficiency. One case who was hypothyroid, had low Factor VIII value. That shows it might be acquired VWD.

• Patients with blood group O had low value of vWF antigen as compared to other blood group according to studies; In our study patients with blood group O had values towards lower limit of normal comparatively.37.83% cases belonged to O group those presented with menorrhagia.

• In our study, among various causes of menorrhagia, physiological pubertal menorrhagia found in 17 cases (22.9%), thrombocytopenia in 7 cases (9.4%), factor VIII deficiency in 1 case (1.3 %), and one case of chronic immune thrombocytopenic purpura (1.3%) were found.

- vWF values came out to be normal in 17 cases and towards lower limit in 1 case (1.3%) which was 50.6 with blood group AB+.One case had increased values which may be due to acute illness.
- One case with hypothyroidism had low level of factor VIII ,which might be because of acquired Von Willebrand disease.This need further evaluation .
- In our study vWF is found to be positively associated with values of aPTT.

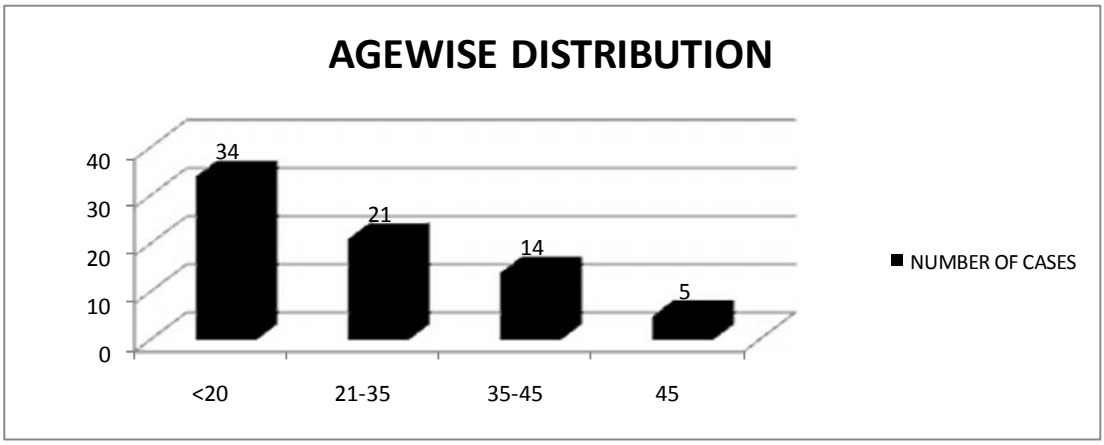

DIAGRAM 1:BAR CHART SHOWING AGEWISE DISTRIBUTION OF CASES

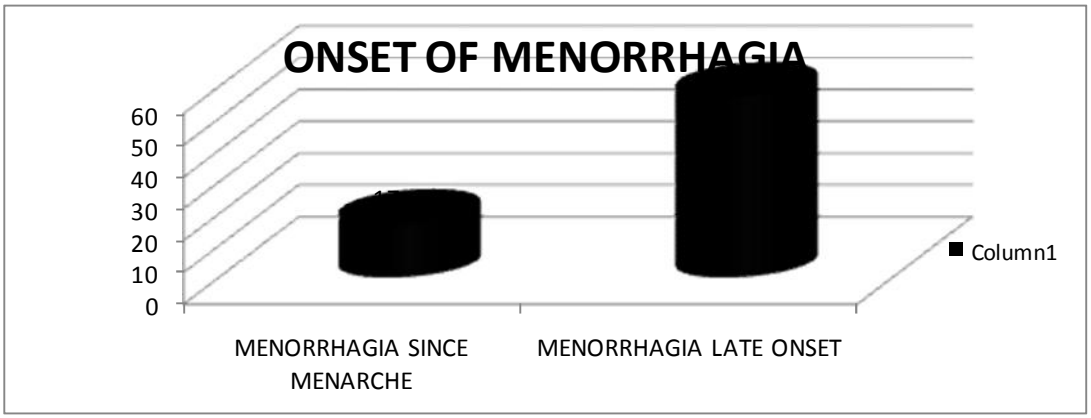

DIAGRAM 2:ON BASIS OF ONSET OF MENORRHAGIA

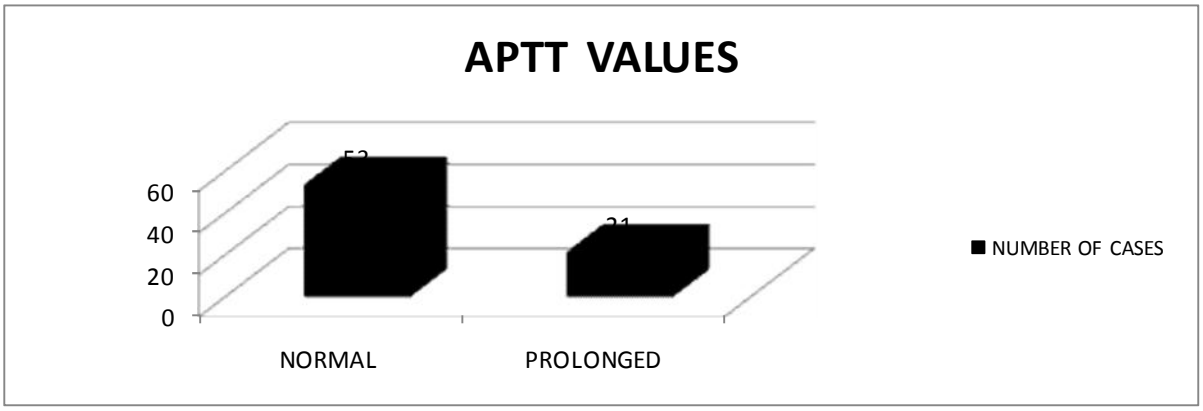

DIAGRAM 3: SHOWING DISTRIBUTION OF CASES ON THE BASIS OF APTT

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TABLE 1:VARIOUS CAUSES OF MENORRHAGIA

CAUSES OF AUB (COAGULATION DISORDERS)	NO. OF CASES
IDIOPATHIC	0
PUBERTY MENORRHAGIA (PHYSIOLOGICAL)	17
THROMBOCYTOPENIA [Plt <1 lac]	7
ITP	1
FACTOR VIII DEFICIENCY	1

TABLE 2: ON BASIS OF FACTOR VIII ACTIVITY

FACTOR VIII ACTIVITY	NO OF CASES
NORMAL	13
DECREASED	1

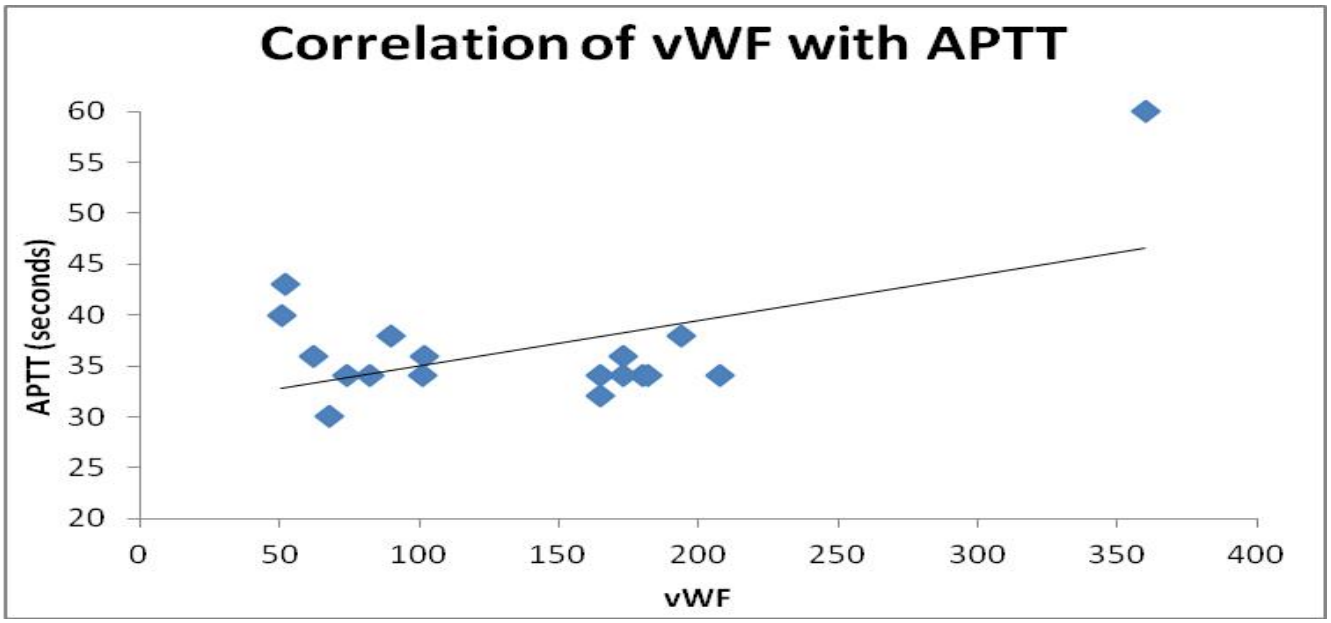
TABLE 3: VWF ANTIGEN TEST VALUES

VON WILLEBRAND FACTOR ANTIGEN TEST	NO. OF CASES(19)
NORMAL [50-200]	17
INCREASED	1
DECREASED	1

TABLE 4 : CORRELATION OF VWF WITH PT, PLATELET, BT AND APTT

	Platelet	BT	PT	APTT
Pearson Correlation	-0.325	0.12	-0.15	0.525
Sig. (2-tailed)	0.174	0.623	0.539	0.021
N	19	19	19	19

GRAPH1



DISCUSSION:

The present study was undertaken to find the prevalence of coagulation defects in patients with menorrhagia i.e. 74 women ,age group 12-55 years with mean age 25.46 +-10.95 years.And incidence of von willebrand disease in those patients. In our study most of the patients belonged to age group of 12-20 years (45.94%) and had menorrhagia since menarche (22.9%).

According to study by Kishan Prasad H.L. et al., evaluated 688 cases of adolescent girls with menorrhagia over a period of 2 yrs (2004-2006) , amongst which 40 cases were included in study, out of 40 cases, 14 (35%) cases were found to be suffering from haemostatic disorders.The haemostatic disorders were divided into platelet related abnormality i.e., primary (9 cases) and clotting factor abnormality i.e., secondary disorders (5 cases). The leading cause of menorrhagia was found to be vWD and quantitative platelet disorders.

In our study 4.05% had history of pph and epistaxis,16.21% with history of blood transfusion,1.3% had history of surgical site bleeding and bleeding disorder. In a study by saxena R et al total of 337 of the 2200 menorrhagic women investigated were characterized to have an inherited bleeding disorder, 221 of these 337 women presented with menorrhagia alone while 116 also had other associated bleeding manifestations as prolonged bleeding from injury site, ecchymotic patches in the skin, epistaxis, haematomas, haemarthroses and major bleeds like intracerebral bleeding. Amongst these, von Willebrand disease (vWD) was the most frequent being seen in40 (11.9%) of the cases. Factor XIII deficiency was seen in one (0.3%).

The present study found that ,degree of anemia directly related to onset of menorrhagia very severe anemia in 8.1% patients ,severe anemia found in 21.62% patients,59.45% was moderately anemic ;In a study by Jennifer A Bevan et al Excessive menstrual bleeding commonly results in anemia. One half of the total group had anemia (haemoglobin <12.0 g/dL). Seven girls (10%) had potentially life-threatening anemia (haemoglobin <5.0 g/dL).

In the study done by Kishan prasad H L et al,the commonest blood group which was found in the girls was O, followed by the A group, with all the cases of vWD having the O group. In our study maximum patients who came with menorrhagia belonged to o blood group (37.83%), but none of them had low level of VWF.

In our study among platelet disorders, thrombocytopenia found in 10.8% patients,while severe thrombocytopenia in 1.3% patients,one case of chronic ITP found;among coagulation defects 1.3% with factor VIII deficiency,1.3 % in lower limit of normal of vWF antigen.In a study by Jennifer A Bevan et al 9 of the 71 girls (13%) had thrombocytopenia (platelet count <150,000/µL; range, 5000-106,000/µL). The most common causes for thrombocytopenia were immune thrombocytopenic purpura (n = 5). Of 14 girls who underwent a more detailed hemostatic evaluation, 8 were given a diagnosis of a hereditary coagulation disorder: 6 had platelet function defects and 2 had type 1 Von Willebrand disease.

The majority of studies in the west report Von Willebrand disease as the most common inherited bleeding disorder leading to menorrhagia whereas studies in South East Asia have found platelet function disorders as the leading inherited bleeding disorder in women with menorrhagia(10).

In our study vWF antigen statistically related to aPTT (p=0.021);aPTT found to be raised in 28.37% patients ; and in those patients VWF antigen testing done ,but only one case had VWF value towards lower limit of normal (i.e. 50.6) and one suspected case of acquired von Willebrand disease found.

In our study 9.4% patient were found to be hypothyroid but none associated with vWF deficiency,this is similar with the study by N.E. Blesing et al(11) on acquired von willebrand disease and menorrhagia. In our study one case of menorrhagia with severe hypothyroidism had low factor VIII level,which might be the case of acquired VWD.

CONCLUSION

Prevalence of coagulation defects(including all hemostatic defects) found to be 12.16 % in patients presented with menorrhagia (74 cases) in our study.
Incidence of vWD was 1.3% in our study.
These results demonstrate that underlying bleeding disorders are frequently found in adolescent, post adolescent reproductive age, and perimenopausal-age women presenting with menorrhagia and suggest that women with menorrhagia should be considered for further hemostatic evaluation.
We felt that vWD with infrequent and mild bleeding episodes remain undiagnosed either because of unawareness of the disease in society or due to paucity of diagnostic facilities available in our country. The conclusion is that the Von Willebrand disease is uncommon in the study population cannot be generalized because of constraints in sample size in our study.

REFERENCES

[1]. Phillip CS, Dilley A, Miller CH, Evatt B, Baranwal A, Schwartz R, Bachmann G, Saidi Pl. Platelet function defects in women with unexplained menorrhagia. J Thromb Heamost. 2003;1(3):477–484. doi: 10.1046/j.1538-7836.2003.00061.x.
[2]. Woo YL, White B, Corbally R. vWD: an important cause of DUB. Blood Coagul Fibrinolysis. 2002;13(2):89–93. doi: 10.1097/00001721-200203000-00003.
[3].James AH. Von Willebrand disease. Obstet Gynecol Surv 2006;61:136–45.
[4]. Rezan A, Kadir MB. Women and vWD: controversies in diagnosis and management. Semin Thromb Hemost. 2006;32:605–615. doi: 10.1055/s-2006-949665.
[5].Claessens CA, Cowell CA Acute adolescent menorrhagia American journal obstet Gynaecol 1981; 139(3); 277-80.
[6].James A, et al. Testing for von Willebrand disease in women with menorrhagia: a systematic review. *Obstet Gynecol*. August 2004;104:381–8. [7]. James AH, Kouides PA, Abdul-Kadir R, Dietrich JE, Edlund M, Federici AB, et al. Evaluation and management of acute menorrhagia in women with and without underlying bleeding disorders:consensus from an international expert panel.Eur J Obstet Gynecol Reprod Biol 2011;158:124–34
[8].Valente MJ, Abramson N. Easy bruisability. South Med J 2006;99:366–70.
[9]. National Heart, Lung, and Blood Institute. The diagnosis, evaluation, and management of vWD NIH Publication No. 08-5832.
Bethesda (MD):NHLBI;2007.Availableat: http://www.nhlbi.nih.gov/guidelines/vWD/vWD.pdf. Retrieved August 9, 2013.
[10]. Saxena R, Gupta M, Gupta K, Kashyap R, Choudry VP Inherited bleeding disorder in Indian Women with menorrhagia Haemophilia 2003; 9: 193-96.
[11]. N.E. Blesing, H. Hambley and G.A. McDonald et al. Acquired von Willebrand's disease and hypothyroidism: report of a case presenting with menorrhagia; Postgrad Med J (1990) 66, 474 – 476 doi: 10.1136/pgmj.66.776.474.