The prevalence of Von-Willebrand disease in menorrhagia and post partum hemorrhage

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Abstract :

Objective: To estimate the prevalence of Von-Willebrand disease in women with menorrhagia and post partum hemorrhage.

Patients & method: It is a cross sectional study done in the department of obstetrics and gynecology in Al Yarmouk teaching hospital from 1st of October 2004 to 30th of October 2005.Ninety nine women participated in this study. Thirty nine women with menorrhagia,30 women with post partum hemorrhage and 30 women as control. Blood sample from each case was drawn for von Willebrand factor antigen (vWf-Ag), factor 8(fvIIIc), prothrombin time (P.T.), activated partial thromboplastine time (APTT),bleeding time, C.B.P, renal function test and liver function test. Laboratory results for menorrhagia and post partum hemorrhage patients were compared with those of control group to estimate the prevalence of von Willebrand disease.

Results: Von-Willebrand disease was found in five(12.8%), four (13.3%)and zero(0.0%)from women with menorrhagia, post partum hemorrhage and control groups respectively.

Conclusion: The measurement of the laboratory investigations for Von- Willebrand factor should be incorporated into the diagnostic evaluation of patients referred to gynecological clinic with menorrhagia or post partum hemorrhage of certain criteria, otherwise; it may lead to hemorrhagic complications associated with surgical intervention in patients with Von- Willebrand disease.

Key wards: Von-Willebrand disease, menorrhagia, post partum hemorrhage.

Introduction:

Von-Willebrand disease (VWD) is the most common inherited mucocutaneous bleeding disorder[1]. VWD is genetically and clinically heterogeneous hemorrhagic disorder caused by deficiency or dysfunction of protein termed Von-Willebrand factor (vwf)[2] . Primary hemostasis is impaired because of defective interaction between platelets and vessel wall[2]. Vwf is released from storage granules in platelets and endothelial cells[2]. Haemostatic plug formation plays an important role in uterine haemostasis and menstrual loss is increased with primary haemostatic disorders as Von-Willebrand diseases[3]. Menorrhagia is the commonest initial bleeding symptom in Von-Willebrand disease[3].

Aim of the study :

To estimate the prevalence of Von-Willebrand disease in women with menorrhagia and women with post partum hemorrhage .

Patients & methods :

This study was carried out in the department of obstetrics and gynecology in Al Yarmouk Teaching Hospital from 1st of October 2004 to 30th of October 2005.Three groups of women were included in the study, 39women with menorrhagia, 30 women with post partum haemorrhage and 30 women as control .Exclusion criteria included previous thromboembolic disease or known bleeding disorders, patients with underlying uterine pathology such as uterine fibroids, carcinoma of endometrium or carcinoma of cervix .Regarding post partum haemorrhage 10 cases were primary and 20 cases were secondary post partum haemorrhage, we excluded from them atonic uterus, retained placental tissue, traumatic delivery, sepsis, placenta acereta and uterine inversion. All women in the control group were of normal menstrual blood loss. A thorough history was obtained from each patient, this included reproductive history, menstrual history, assessment of menstrual blood loss, any bleeding disorder like epistaxis, skin bruises, family history of bleeding disorders, medical and surgical history and drugs intake including hormones and anti coagulant therapy. All women we did for them complete physical examination, abdominal and pelvic examination. 10 ml of venous blood sample was drawn from each patient and send for coagulation testing as follows:

1-Activated partial thromboplastine time (APTT):
2-Prothrombine time (PT).
3-Bleeding time.
4-Factor V111:
5-Von-Willebrand antigen assay (Vwf Ag assay)

This test was performed by immunoturbidimetric assay of vwf .

Also every patient was sent for complete blood picture, renal function test, liver function test, blood group and Rh.

Statistical analysis was performed using Chi – square, Fisher exact probability, F test and regression analysis were used to assess the

significant and independent association of Von-Willebrand disease and Von-Willebrand factors and others with menorrhagia and post partum haemorrhage. P value less than 0.05 was considered as statically significant .

Results:

Out of the total groups, five (12.8%), four(13.3%) and zero (0.0%) were diagnosed as Von-Willebrand disease from women with menorrhagia, post partum haemorrhage and control group respectively.

Table (1) shows that mean age± SD of women with menorrhagia, post partum haemorrhage and control group were 35.6± 5.6 years ,32.1 ± 6.1 years and 32.6 ± 7.3 years respectively .There was no significant difference in the age of the studied groups(p> 0.05).Statistical significant differences were noticed in Von-Willebrand factor (p= 0.05), factor V111(p=0.036), APTT (P=0.001) between the studied groups .No statistical significant difference was noticed in blood groups between the studied groups .

Table (2) shows no significant statistical difference in age between women with Von-Willebrad disease and those without the disease among women with menorrhagia (p>0.05). Significant lower level of factor V111 and Vwf (0.56± 0.22, 0.34± 0.22) were demonstrated in women with Von-Willebrand disease (1.1± 0.2, 0.96± 0.31, respectively) than those without Von-Willebrand disease (p=0.001). APTT was significantly higher among those with Von-Willebrand disease (39.6± 8.8) than women without Von-Willebrand disease (36.2±3.8) (p=0.001) .No significant statistical differences in blood group between those with VWD and those and without VWD (p=0,14).However 40% of women with VWD were of blood group O and the rest of the other blood groups.

Table (1) :- Distribution of variables among the studied groups

	Menorrhagia	**Post partum haemorrhage**	**controls**
NO.	39	30	30
	Mean ± SD	Mean±SD	Mean±SD
Age(years)[1]	35.6± 5.6	32.1± 6.1	32.6± 7.3
Von-Willebrand factors[2]	0.87± 0.36	0.95± o.37	1.1± 0.21
Factor V111[3]	1.1± 0.3	1.4± 2.02	1.25± 0.22
Bleeding time[4]	4.2± 2.2	4.1± 1.9	3.2± 0.3
APTT[5]	36.7± 4.8	37± 5.1	13.3± 0.5
Blood groups[6]	**NO. (%)**	**NO. (%)**	**NO (%)**
A	9 23.1	7 23.3	11 34.4
B	3 7.7	4 13.3	3 9.4
AB	5 12.8	7 23.3	3 9.4
O	22 56.4	12 40.0	13 40.6

1f = 3.06, d.f.=2.96 , p=0.05
2f = 3.06, d.f.=2,96 , p=0.05
3f = 3.46,d.f.=2,89 , p=0.036
4f = 0.4,d.f.=2,87 , p=0.38
5f = 256,d.f.=2,80 , p=0.001
6X^2 = 5.03,d.f.=6 , p=0.05

Table(2):- Distribution of variables among women with menorrhagia according to the diagnosis of Von-Willebrand disease

variable	Menorrhagia with VWD		Menorrhagia without VWD	
NO.	5(12.8)		34	
	Mean±SD		Mean±SD	
Age[1]	36.2±3.9		35.46±5.8	
VWF[2]	0.34±0.22		0.96±0.31	
Factor V111[3]	0.56±0.32		1.1±0.2	
Bleeding time[4]	8.3±0.57		3.5±1.5	
APTT[5]	39.6±8.8		36.2±3.8	
Blood group[6]	**NO.**	**(%)**	**NO.**	**(%)**
A	1	20	8	23.5
B	1	20	2	5.9
AB	1	20	4	11.8
O	2	40	20	58.8

1 t = 0.26, d.f.=37, p=0.79
2 t = 4.4,d.f.= 35 , p=0.001
3t = 5.6 ,d.f.= 35 , p=0.001
4t = 6.7,d.f.= 33 , p=0,001
5t = 1.4,d.f.= 32 , p=0,14
6 fisher exact probability test = o.46

Table(3) shows that the age was not significantly differing between those with Von-Willebrand disease and those without Von-Willebrand disease among patients with post partum haemorrhage (p>0.05) .VWF and factor V111 were significantly lower among women with Von-Willebrand disease (0.33±0.3, 0.6±0.28, respectively) than among those without Von-Willebrand disease (1.1± 0.3,1.6± 2.2, respectively) among patients with post partum haemorrhage (p=0.001, p=0.037 ,respectively).APTT was significantly higher (42.5±2.8)among women had Von-Willebrand disease than those without it (35.9±4.7) (p=0.014).

Only one (20.0%) and one (25%)of women with Von-Willebrand disease had positive family history among those with menorrhagia and post partum haemorrhage, respectively. No statistical significant variation was noticed in family history (positive or negative) among those had Von-Willebrand disease in patients with menorrhagia and post partum haemorrhage (p=0.2).These findings are shown in tables (4,5&6).

Table(3):- Distribution of variables among women had post partum haemorrhage according to the diagnosis of Von-Willebrand disease

Variable	Postpartum haemorrhage with Von-Willebrand disease		Postpartum haemorrhage without Von-Willebrand disease	
NO.	4 (13.3)		26	
	Mean± SD		Mean± SD	
Age[1]	28.7± 4.8		32.6 ± 6.2	
Von-Willebrand factor[2]	0.33 ± 0.3		1.1 ± 0.3	
Factor V111[3]	0.6 ± 0.28		1.6 ± 2.2	
Bleeding time [4]	7.7± O.28		3.4 ± 1.04	
APTT[5]	42.5± 2.8		35.9 ± 4.7	
Blood group[6]	**NO.**	**(%)**	**NO.**	**(%)**
A	0	0	7	26.9
B	1	25	3	11.5
AB	0	0	7	26.9
O	3	75	9	34.6

1t = 1.2 , d.f.= 28 , p=0.24
2t = 5.2 , d.f.= 23 , p =0.001
3t = 2.01 ,d.f.=23, p=0.37
4t = 8.1 , d.f.=22, p=0.001
5t = 2.6 , d.f.=22, p=0.014
6 fisher s exact probability test =0.25

Table(4):- family history among women with Von-Willebrand disease presented with menorrhagia.

Family history	Menorrhagia with Von-Willebrand disease		Menorrhagia with out VW D	
	NO.	**(%)**	**NO.**	**(%)**
Positive	**1**	**20**	**4**	**11.7**
negative	**4**	**80**	**30**	**88.2**

Fisher' s exact probability test = 0.253

Table (5):- family history among women with and without Von-Willebrand (VWD)disease in patients postpartum haemorrhage(PPH)

Family history	PPH with VWD		PPH with out PPH	
	NO.	(%)	NO.	(%)
Positive	1	25	1	3.8
Negative	3	75	25	96.2

Fisher's exact probability test =0.217

Table (6):- family history with Von-Willebrand disease & non Von-Willebrand disease

Family history	VWD		Non VWD	
	NO.	(%)	NO.	(%)
Positive	2	22.2	5	8.3
negative	7	77.8	55	91.7

Fisher's exact probability test =0.2

Table (7) show that other bleeding symptoms like bruising, epistaxis, post operative bleeding and bleeding after dental extraction are significantly higher among women with Von-Willebrand disease than those without the disease .

Table (7):- other bleeding symptoms in women with and without Von-Willebrand disease.

Bleeding symptoms	Von-Willebrand disease n=9		Non Von-Willebrand disease n=90		P value
Bruising	5	55.5%	20	22.2%	< 0.05
Epistaxis	3	33.3%	10	11.1%	< 0.05
Postoperative bleeding	3	33.3%	5	5.5%	< 0.05
Bleeding after dental extraction	2	22.2%	5	5.5%	< 0.05
Gum bleeding	0	0%	1	1.1%	> 0.05

Discussion

Von-Willebrand disease is most frequent inherited bleeding disease. An estimated prevalence ranging from 4- 10 per 100000 inhabitants[4]. This study revealed that 12.8% of women with menorrhagia had Von- Willebrand disease this high figure is consistent with that of recent studies by Edlunt et al 1996[5] ,Kadir et al 1998[6] and Woo et al 2002[7]. In these studies the prevalence of Von-Willebrand disease was 10.9% range 7-20% among patients with menorrhagia compared to1.3% in general population. These studies were similar to our study including patients presented with menorrhagia. They excluded patients with uterine pathology. All these raised the importance of screening for Von- Willebrand disease as a part of routine investigation in menorrhagia in the absence of uterine pathology[7,8].

Our study revealed that 13.3% of women with post partum haemorrhage had Von-Willebrand disease, a finding that is consistent with that of Trasi et al 2005[9], Indian studies. Workers reported that post partum bleeding is rare in patients with Von-Willebrand disease because of normalization of factorV111 and Von-Willebrand factor at the end of pregnancy[10] . Other workers stated that women with Von-Willebrand disease appear to be at high risk in developing delayed or secondary post partum haemorrhage[10,11]. In this study other bleeding symptoms like bruising, epistaxis, bleeding after surgery and dental extraction were statically significant, this goes with other studies[5,6] . The finding that the level of Von-Willebrand factor was positively associated with age is similar to that of other workers[9]. They showed that Von-Willebrand factors level significantly increases with age .The study showed that the level of Von-Willebrand factor is related to the blood group and the lowest level was in blood group O, it is similar to study done by Kobrinsky in 1997[12].

Family history of bleeding was not significantly associated with prevalence of Von-Willebrand factor, in women with menorrhagia or post partum haemorrhage. This may be attributed to the fact that inheritance pattern of Von-Willebrand factor is a recessive one[9].

Conclusion :

This study has demonstrated a high prevalence of Von-Willebrand disease in patients who had menorrhagia in the absence of uterine pathology indicates that the investigation of patients with menorrhagia should include haemostatic assessment. Our study also has demonstrated a high prevalence of Von-Willebrand disease in patients with post partum hemorrhage of certain inclusion criteria, this may have important implication in their management. Blood group was not related in the diagnosis of Von-Willebrand disease, however blood group O had the lowest Von-Willebrand factor level .

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