



Frequency of Various Bleeding Disorders Among Gynecological and Obstetric Patients Presenting with Bleeding

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ABSTRACT

Introduction: Bleeding issues specific to women and adolescent females are common across the world. These issues can present either due to gynecological causes or obstetric one; however these can result in significant morbidity and work up needs to be done to rule out any underlying bleeding diathesis. **Aims & Objectives:** To determine frequency of various bleeding disorders among gynecological and obstetric patients presenting with bleeding. **Place and duration of study:** It is a cross sectional study which was conducted in the Hematology Department, Services Institute of Medical Sciences, Lahore. The duration of study was 6 months i.e from 21st Oct, 2018 to 30th April, 2019. **Material & Methods:** Females with age range of 15 to 50 years irrespective of pregnancy presenting as menorrhagia, metrorrhagia or obstetrical bleeding were included. **Results:** In the present study there were total 140 cases with mean age of 30.14±9.59 years. There were 98 (70%) cases that were pregnant. There were 35 (25%) cases presented with PPH (Post Partum Hemorrhage), 42 (30%) with IPH (Intra Partum Hemorrhage), 49 (35%) with menorrhagia and 14 (10%) with metrorrhagia. HELLP (Hemolysis, Elevated Liver enzymes and Low Platelet count) syndrome was seen in 13 (9.29%) cases, DIC (Disseminated Intravascular Coagulation) in 2 (1.43%), gestational thrombocytopenia in 7 (5%), while factor deficiency in 34 (24.29%) cases; and 84 (60%) of cases revealed none of the bleeding disorder. Out of total 34 cases of factor deficiencies, vWD was the most common, seen in 20 (58.82%) cases. There was none of the cases seen having deficiency of factor II, VII, VIII, XI, XII. HELLP syndrome was seen in 11 (84.62%) of the cases with age group 15 to 32 years and similarly both cases of DIC were seen in same age group; but the difference in both the age groups regarding these bleeding disorders was not statistically significant with $p=0.38$. There was no significant difference in terms of pregnancy; however, both cases of DIC were seen in pregnancy with insignificant p value of 0.51. HELLP syndrome was more seen in IPH affecting 5 (38.40%), factor deficiency in menorrhagia affecting 13 (38.2%) with p value of 0.61. vWD and factor V Leiden presented in 44.4% cases each with PPH, and vWD affected 87.5% of cases in IPH without any significant difference with $p=0.42$. **Conclusion:** Bleeding disorders are not uncommon in gynecological and obstetric conditions. Factor deficiency were the most common causes and amongst these vWD was the most deficient factor. There was no significant association with any confounding variable; however, DIC was only seen in obstetrical conditions.

Key words: Bleeding, menorrhagia, HELLP, DIC, IPH, PPH

INTRODUCTION

Bleeding issues specific to women and adolescent females are common across the world. These issues relate particular to menses, pregnancy and childbirth. Women with bleeding disorders can have symptoms that result in significant morbidity and impact their quality of life.¹⁻² Menorrhagia and metrorrhagia are important issues reflecting excessive bleeding at the time of menstruation and

irregular in between respectively and often reflect the underlying bleeding disorders in females. According to a study it affects as many as 10-50% of women.³ Others gynecological complications of bleeding disorders are hemorrhagic ovarian cyst, endometrial hyperplasia and endometriosis. While in pregnancies intra and post-partum hemorrhage are important presentations and pose a lot of stress in the acute emergency conditions. Other important obstetrical conditions leading to bleeding disorders are DIC, HELLP syndrome and gestational

thrombocytopenia.⁴⁻⁵ Bleeding disorders can be inherited and acquired. Inherited bleeding disorders are not so infrequent and can increase frequency and severity of bleeding complications during and after pregnancy.⁴ Studies have shown that Von willebrand disease is the commonest inherited bleeding disorder in gynecological patients with menorrhagia, consistently reported to be 10% to 20%.⁴ According to another study by Janbabai G et al deficiencies of different factors were seen as factor II, V, VII, VIII, IX, X, XI, XII, XIII in 0.73, 1.0, 1.80, 1.50, 0.37, 0.37, 1.80, 2.20 and 0% respectively.⁶ A study by Ashraf M et al revealed HELLP syndrome in 28%, gestational thrombocytopenia in 22%, von Willibrand disease in 16.66% and factor V deficiency in 6% of cases.⁷ The data regarding the causes and frequencies of different bleeding disorders is variable⁶⁻⁷ and factor deficiencies is an under reported cause of bleeding specially in pregnant females. Therefore this study was planned, to determine the frequency of bleeding disorders in such patients and help to develop some practical recommendations for routine practice guidelines. This would enable early diagnosis and management and reduce the morbidity and mortality rate.

MATERIAL AND METHODS

It is a cross sectional study which was performed in the Department of Hematology, Services Institute of Medical Sciences, Lahore. Duration of study was 6 months from 21st Oct, 2018 to 30th April, 2019. The sample size was calculated as 140 by non-probable and consecutive method, keeping in view the confidence level equal to 95% and the margin of error equal to 4% and p (the prevalence of factor deficiency) as 6%..

Inclusion criteria:

1. Female patients with age between 15-50 years.
2. All obstetric/gynae patients with bleeding manifestations like intra and postpartum haemorrhage, menorrhagia and metrorrhagia as per operational definition.

Exclusion criteria:

1. All patients taking warfarin, aspirin, clopidogril or on heparin within last 2 weeks.
2. Women using oral contraceptive pills on their previous menstrual cycles
3. Patients having IUD (Intrauterine device).

Data Collection Procedure: After permission from the Ethical Review Committee, total number of 140 patients fulfilling the inclusion and exclusion criteria were selected. After taking informed written consent, relevant history was taken from patients regarding pregnancy and bleeding. Every patient

underwent complete blood count (by Sysmex KX21), Prothrombin time and activated Prothrombin time (performed manually using water bath and reagent) and ALT. Amongst the cases that did not have pregnancy and had platelet count less than 100,000 μ l were noted as thrombocytopenia and the cases that had normal platelet but raised level of PT or APTT were checked directly for clotting factor assay as per operational definition by STAGO kit and the result were noted. Those cases that had pregnancy and had platelet count less than 100,000 μ l; were again assessed for ALT, fibrinogen level and FDP level. They were then labeled as gestational thrombocytopenia, DIC, or HELLP syndrome as per operational definitions. Those cases with all these normal studies underwent factor assay and were labelled for any factor deficiency as per operational definition and Von Wilibrand disease was labelled when Vwf; RCO was < 30 iu /dl and Vwf; ag <30-50 iu/dl. The results were noted on a specially designed proforma.

Statistical analysis:

Statistical analysis was performed using SPSS version 20. Results were presented as mean and standard deviation for quantitative variables i.e. age, frequency and percentage were calculated for qualitative variable like pregnant or not, thrombocytopenia, HELLP syndrome, DIC, gestational thrombocytopenia, factor deficiency and type of factor deficiency. Effect modifiers were controlled through stratification of age, pregnancy, type of bleeding. Post stratification Chi Square test was applied and p value ≤ 0.05 was considered as significant.

RESULTS

In the present study there were total 140 cases with mean age of 30.14 \pm 9.59 years with minimum age of 15 years and maximum 49 years as shown in table 01. There were 98 (70%) cases that were pregnant as in fig-1. There were 35 (25%) cases presented with PPH, 42 (30%) with IPH, 49 (35%) with menorrhagia and 14 (10%) with metrorrhagia (Fig-2). Thrombocytopenia was detected in 20 (14.29%) of cases out of which 13 were cases of HELLP and 7 in gestational thrombocytopenia (Fig-3). HELLP syndrome was seen in 13 (9.29%) cases, DIC in 2 (1.43%), gestational thrombocytopenia in 7 (5%), while factor deficiency in 34 (24.29%) cases; and 84 (60%) of cases revealed none of the bleeding disorder (Fig-4). Out of total 34 cases of factor deficiencies, vWD (Vwf; RCO< 30 iu/dl and Vwf; ag <30-50 iu/dl) was the most common seen in 20

(58.82%) of cases followed by Factor V Leiden seen in 11 (32.35%) of cases as in fig-5. There was none of the cases seen having deficiency of factor II, VII, VIII, XI, XII. HELLP syndrome was seen in 11 (84.62%) of the cases with age group 15 to 32 years and similarly both cases of DIC were seen in same age group; but the difference in both the age groups regarding these bleeding disorders was not statistically significant with $p= 0.38$ as shown in Table-2. There was no significant difference in terms of pregnancy; however, both cases of DIC were seen in pregnancy as well with insignificant p value of 0.51 as in Table-3. HELLP syndrome was more seen in IPH affecting 5 (38.40%), factor deficiency in menorrhagia affecting 13 (38.2%) with p value of 0.61 (table 04). vWD and factor V Leiden presented in 44.4% cases each with PPH, and vWD affected 87.5% of cases in IPH without any significant difference with $p= 0.42$ (Table-5)

		Age
Mean		30.14
95% Confidence Interval for Mean	Lower Bound	28.54
	Upper Bound	31.75
Median		26.50
Std. Deviation		9.59
Minimum		15
Maximum		49

Table-1: Study Variables (Age) n=140

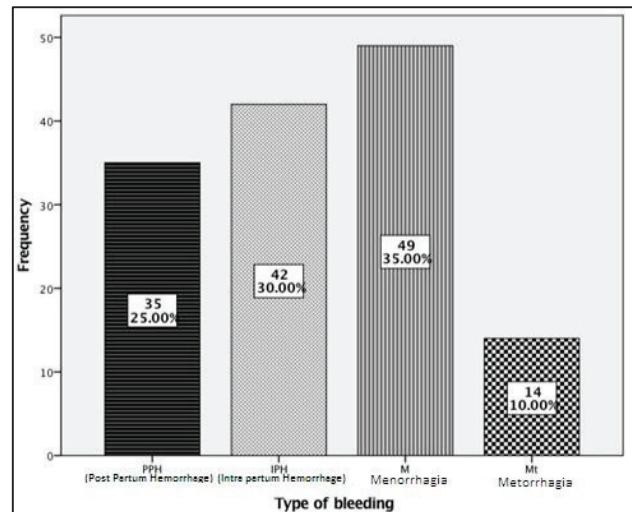


Fig-2: Type of bleeding n= 140

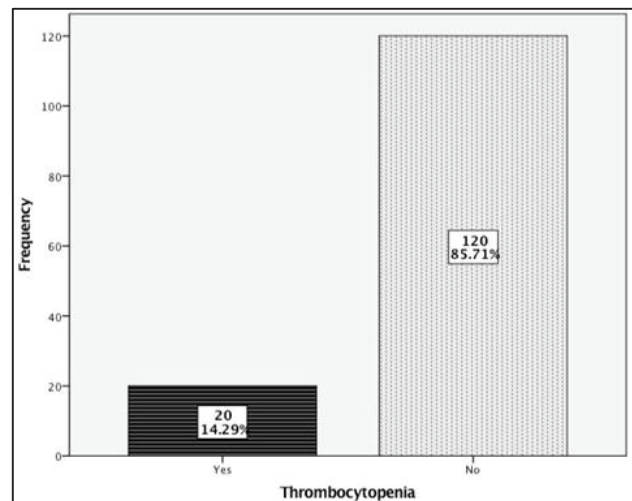


Fig-3: Thrombocytopenia detected n= 140

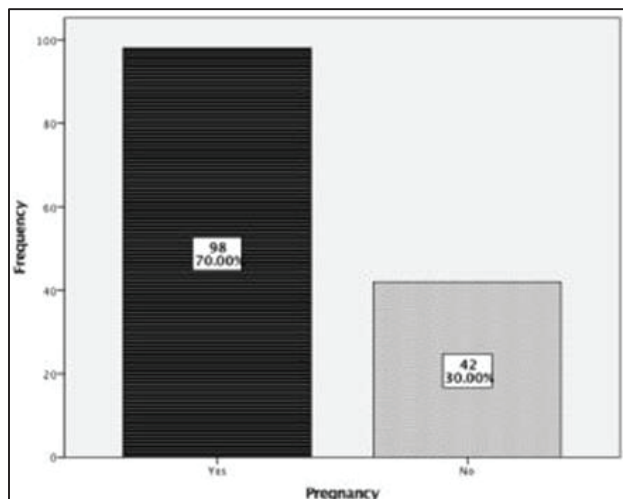


Fig-1: Pregnancy in study subjects n= 140

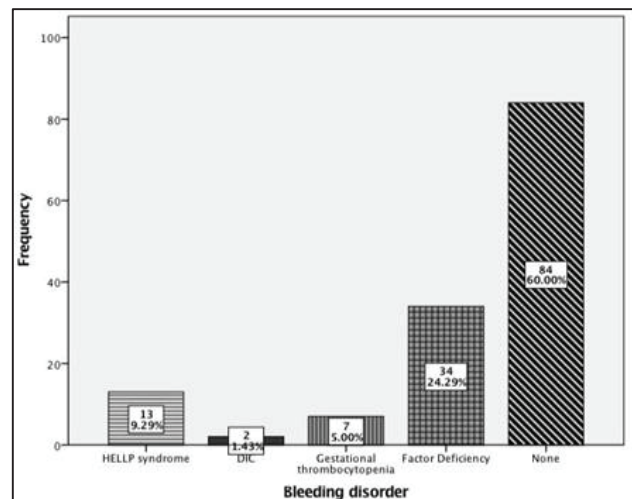


Fig-4: Type of bleeding disorder detected n= 140

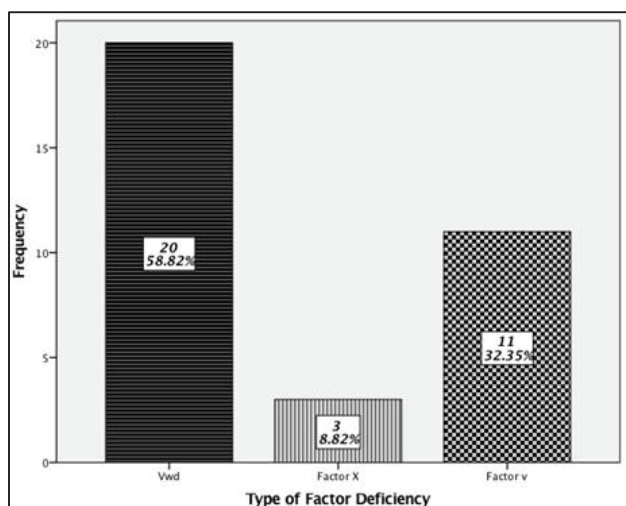


Fig-5: Type of factor deficiency n= 140

Bleeding Disorder	Type of Bleeding				Total
	PPH	IPH	M	Mt	
HELLP syndrome	2 (15.3%)	5 (38.46%)	4 (30.7%)	2 (15.3%)	13 (100%)
DIC	2 (100%)	0 (0%)	0 (0%)	0 (0%)	2 (100%)
Gestational thrombocytopenia	0 (0%)	1 (14.3%)	4 (57.1%)	2 (28.6%)	7 (100%)
Factor deficiency	9 (26.5%)	8 (23.5%)	13 (38.2%)	4 (11.8%)	34 (100%)
None	22 (26.2%)	28 (33.3%)	28 (33.3%)	6 (7.14%)	84 (100%)
Total	35 (25%)	42 (30%)	49 (35%)	14 (10%)	140 (100%)

n= 140, p= 0.61

Table-4: Bleeding disorder with respect to type of bleeding

Bleeding Disorder	Age Groups		Total
	15-32	33-50	
HELLP syndrome	11 (84.62%)	02 (15.38%)	13 (100%)
DIC	02 (100%)	00 (00%)	02 (100%)
Gestational thrombocytopenia	05 (71.43%)	02 (28.57%)	07 (100%)
Factor deficiency	21 (61.76%)	13 (38.24%)	34 (100%)
None	51 (60.71%)	33 (39.29%)	84 (100%)
Total	90 (64.28%)	50 (35.72%)	140 (100%)

n= 140, p= 0.38

Table-2: Bleeding disorder with respect to age groups

Types of Bleeding	Type of Factor Deficiency			Total
	vWD	Fact X	Factor V	
PPH	4 (44.4%)	1 (11.2%)	4 (44.4%)	9 (100%)
IPH	7 (87.5%)	0 (0%)	1 (12.5%)	8 (100%)
M	8 (61.5%)	1 (7.6%)	4 (30.8%)	13 (100%)
Mt	1 (25%)	1 (25%)	2 (50%)	4 (100%)
Total	20 (11.8%)	3 (8.82%)	11 (32.4%)	34 (100%)

n= 34, p= 0.42

Table-5: Type of bleeding with respect to type of factor deficiency

Bleeding Disorder	Pregnancy		Total
	Yes	No	
HELLP syndrome	8 (61.53%)	5 (38.47%)	13 (100%)
DIC	02 (100%)	00 (00%)	02 (100%)
Gestational thrombocytopenia	7 (100%)	0 (0%)	07 (100%)
Factor deficiency	26 (76.47%)	8 (23.53%)	34 (100%)
None	55 (66.67%)	29 (33.33%)	84 (100%)
Total	98 (70%)	42 (30%)	140 (100%)

n= 140, p= 0.51

Table-3: Bleeding disorder with respect to pregnancy

DISCUSSION

Bleeding disorders can be inherited and acquired. Inherited disorders improve during pregnancy while acquired disorders tend to worsen and bleeding problems unique to pregnancy may occur. Similarly, incidence of bleeding disorders is higher in patients with menorrhagia than in general population.⁸ In developing countries like ours majority of bleeding disorders remain undiagnosed until the patient presents with massive haemorrhage or undergoes some surgery. The purpose of this study was to evaluate the frequency and type of bleeding disorders in gynaecological and obstetrical practice in Pakistan and also to determine the common presenting symptoms.

There were 35 (25%) cases presented with PPH, 42 (30%) with IPH, 49 (35%) with menorrhagia and 14 (10%) with metrorrhagia in the present study. This finding was similar to the studies done in previous settings. According to a study done by Trasi SA et al, they also found that menorrhagia was the most

commonly observed bleeding subtype that presented for the workup of bleeding disorders and it was seen in 25-30% of the cases.⁸ According to this study, it was observed that this was the major factor and due to excessive bleeding, risk of anemia and fear of any complications were the major concerns that led to the workup of any bleeding disorders as compared to the other entities. These findings of menorrhagia in highest number leading to diagnostic workup was also seen by James et al in their study in 2010.⁹

In the present study HELLP syndrome was seen in 13 (9.29%) cases, DIC in 2 (1.43%), gestational thrombocytopenia in 7 (5%), while factor deficiency in 34 (24.29%) cases; and 84 (60%) of cases revealed none of the bleeding disorder. Out of total 34 cases of factor deficiencies, factor VIII was the most common seen in 16 (47.06%) of cases followed by Factor V Leiden seen in 11 (32.35%) of cases. These findings were close to the studied done in the past. According to a study done by Ashraf M et al on 3523 cases, the bleeding disorders were seen in eighteen patients (0.5%) cases.¹⁰ The types of bleeding disorders in decreasing order of frequency were HELLP syndrome (27.7%, n=5), gestational thrombocytopenia (22%, n=4), Von Willebrand disease (16.66%, n=3), Glanzmann's thrombocytopenia (11.11%, n=2), autoimmune haemolytic anaemia (11.11%, n=2), post-transfusion purpura (6%, n=1) and factor V deficiency (6%, n=1).

Gestational thrombocytopenia was the second most common bleeding disorder in this study and was seen in 24% (24.29%) of cases. This finding was also similar to the studies done in Pakistan where it was seen in 22% of the cases¹⁰. However, in the data from the other survey, the reported incidence of this condition is 8% of all pregnancies¹¹. This difference in the frequency of this disorder can be due to the difference in the operational definitions. Because the results were similar from study of Ashraf et al where they also used the same cut off value where they only evaluated those patients who had thrombocytopenia less than 100,000/ul.

vWD was the most common factor deficiency was seen and was noted in 20 (58.82%) of the cases, followed by Factor V Leiden seen in 11 (32.35%) and factor X deficiency seen in 3 (8.82%) out of 34 cases with factor deficiencies in this study. Similar result was seen in other studies, where Von Willbrand disease was the most common bleeding disorder in terms of factor deficiency with a frequency of 0.2%. In another study this was reported to have incidence of 0.8 - 1.3%¹². In terms of frequency vWD disease was seen in 14.28% of the cases which was slightly high as compared to

the previous studies. In a study by Shankar et al vWD was seen in 5.9% of the cases¹³.

According to a study done in Iran they found factor V Leiden as the most among eh factor deficits and it was seen in 8% of the cases while vWD was seen in 5.9% of the cases¹⁴. In another study by Anne Dilley they also found vWD as the most common causes and they found in in 6.6% of the cases¹⁵. Interestingly they found factor deficiencies in the least number of cases where the overall incidence was seen in only 1.6% of the cases. Whereas conflicting results were observed in the present study and since it was the most common cause, seen in 34 (24.29%) of the cases. This marked difference of incidence of high number of cases diagnosed with bleeding disorders presenting with heavy bleeding can be explained by the fact that people usually don't seek medical attentions at earlier stages as compared to the developed countries and only those cases were reported which are highly morbid and suffer such illness again and again

This was also supported by the study of Saxena et al, where they only studied the cases presented with menorrhagia and it was seen that bleeding disorder was seen in as high as 15.3% of the cases.¹⁶ This also supports our study as we conducted the four parameters and amongst them the incidence rate to find such illness was high. The above mentioned statement can be further strengthened by this Indian study as they also have same health care system as in Pakistan with similar poverty rates as well. The study from Trasi et al also revealed the incidence of bleeding disorder in 19.16% of the cases.⁸

Gestational thrombocytopenia was seen in 7 (5%) cases in the present study. The results were similar to the studies done by Philipp et al.¹⁷ There was no significant difference in terms of age groups for the involvement of the any particular bleeding disorder. According to a study done by Janbabai G et al, they also did not find any significant difference in different age group; however, they used slight different groups than our study and used the cut off value of less than 20 and 20 to 40 years of age.¹⁴

The data was lacking in terms of confounding factor of pregnancy and which affected the both cases of disseminated intravascular coagulation and none of the gynaecological case suffered this. This explains the complex pathophysiological changes that can lead to development of DIC. And both of these cases presented with post partumhaemorrhage.

There were few limitations of these studies as this study did not compare this workup with a control group. Secondly this study also did not collect the data regarding the duration of illness for which these cases were suffering this disorder.

However, there were many strengthening points as well as this study comprehensively discussed a wide range of not only inclusion criteria; but also the variety of the bleeding disorders; also studied such cases irrespective of pregnancy.

CONCLUSION

Bleeding disorders are not uncommon in gynecological and obstetric conditions. Factor deficiency was the most common causes and amongst these vWD was the most deficient factor. There was no significant association with any confounding variable; however, DIC was only seen in obstetrical conditions.

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