

Adolescent Menorrhagia: Study of the Coagulation Profile in a Tertiary Centre in South India

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ABSTRACT

Background: Abnormal uterine bleeding accounts for approximately 50% of the visits of adolescent girls to gynaecologists. These complaints encompass disorders which range from minimal spotting to profuse bleeding. These affect the quality of life in a majority of women who are affected. The prevalence of menorrhagia in the adolescent population with bleeding disorders varies between 14 to 48%. The common conditions which are associated with adolescent menorrhagia include the von Willebrand disease (vWD), platelet functional disorders, and coagulation factor deficiencies. This prospective study was conducted to identify the frequency of the bleeding disorders in women who presented with menorrhagia from the Indian subcontinent.

Materials and Methods: 688 adolescent girls were evaluated, amongst which 40 cases were included in our study. Each case was analyzed for the demographic profile, the duration

of menorrhagia, the severity of the symptoms, the degree of anaemia, and laboratory investigations.

Results: Amongst the 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. A majority of the girls had anaemia (97.5%). 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.

Conclusion: Menorrhagia may be an important clinical manifestation in an inherited bleeding disorder and it has been suggested that these patients need to be investigated for these disorders, especially for vWD. Early diagnosis and treatment with individualization of each case is the keystone in the management of adolescent menorrhagia.

Key Words: Menorrhagia, vWD, Bleeding disorder, Adolescent

INTRODUCTION

Abnormal uterine bleeding accounts for approximately 50% of the visits of adolescent girls to gynaecologists. These complaints encompass disorders which range from minimal spotting to profuse bleeding. Adolescent menorrhagia is defined as excessive bleeding which occurs between menarche and 19 years of age. In 80% of the cases, puberty menorrhagia is caused by anovulatory cycles. There is an immaturity of the hypothalamus and an inadequate positive feedback results in sustained high levels of oestrogen. An organic disease or malignancy in particular, is very rare [1-5].

Heavy, irregular menstrual bleeding is a frequent complaint in adolescent girls. The prevalence of menorrhagia in adolescent populations with bleeding disorders varies between 14 to 48%. It is likely to be caused by mechanisms which are different from those which occur in women in the fourth or fifth decades of their life, where anatomic causes of bleeding are common. The common conditions which are associated with adolescent menorrhagia include the von Willebrand disease (vWD), platelet function disorders, and coagulation factor deficiencies. The other conditions that lead to increased blood loss in this age group include hypothyroidism, genital tuberculosis, and polycystic ovarian disease [1-5].

Coagulation disorders are prevalent in 1% of the general population and their incidence may be as high as 5% in the gynaecological population [4,5,6]. Yet, gynaecologists underestimate the coagulation disorders in the aetiology of abnormal uterine bleeding [2,4]. A majority of the studies which have been conducted in the west

have reported vWD is the most common inherited bleeding disorder which leads to menorrhagia, whereas studies from south-east Asia have found platelet functional disorder as the leading cause [5,6]. Limited information exists on the inherited causes which underlie the women bleeders, especially in the Indian subcontinent. This research was conducted to study the frequency of bleeding disorders in women who presented with menorrhagia from the Indian subcontinent.

MATERIALS AND METHODS

This was a prospective study which evaluated 688 cases of adolescent girls with menorrhagia at a multidisciplinary tertiary care institute over a period of 2 yrs (Sept 2004 to Sept 2006). The data was collected from medical records in each of these cases.

Each case was evaluated for age of the patient, age at menarche, clinical features, family history, drug history, menstrual history, quantity of bleeding, and associated dysmenorrhoea or other symptoms. The laboratory investigations included the evaluation of haemoglobin, packed cell volume, blood grouping, platelet count, bleeding time (BT), clot retraction, clotting time (CT), peripheral smear, prothrombin time (PT), activated partial thromboplastin time (APTT) and inhibitor screening, correction studies and bone marrow examination.

The inclusion criteria included all the adolescent females who were referred to the Haematology Unit from the Gynaecology Department of a tertiary hospital in Davanagere, with the history of

heavy, irregular periods i.e. when the interval between the start of the successive cycle was > 21 days or the duration of the menstrual blood flow was >7 days.

Patients with gynaecological causes of menorrhagia, patients who were diagnosed with endocrine disorders and those who received treatment with anticoagulants, antifibrinolytics and non-steroidal anti-inflammatory drugs were excluded from the study.

RESULTS

The present study was conducted over a period of two years. During this period, 40 patients with puberty menorrhagia were studied. All the 40 cases were evaluated for coagulation disorders. Amongst the 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 various cases are as shown in [Table/Fig-1] and these cases formed the crux of the study.

Clinical Features

The age range of the patients was between 12 to 19 years, with a median age of 16 years. Bleeding immediately after menarche was a presenting feature in 5/40 (12.5%) cases. The remaining cases presented at variable periods after the attainment of menarche.

The assessment of blood loss during menstruation was done by checking the detailed history of pad/tampon changing. In 16/40 (40%) cases, heavy blood loss, amounting to approximately more than 100 ml/cycle was seen, whereas in the remaining 24/40 cases (60%), there was moderate loss of blood. In patients with haemostatic disorder, the amount of blood loss was severe in 7/14 (50%) cases. Dysmenorrhoea was an associated complaint in 16/40 (40%) cases. However, it was not a consistent symptom in patients with haemostatic disorders [3/14 (21%) cases].

It is found that 5/40 cases were associated with a positive family history and all of them were found to have haemostatic disorder. Other types of bleeding which were noted in our study included epistaxis, posttraumatic, gum bleeding and petechial bleeding.

Diagnosis	Number of cases	Percentage
Thrombocytopenia	6	42.85
vWD	4	28.58
Glanzmann thrombasthenia	3	21.43
Factor V deficiency	1	7.14

[Table/Fig-1]: Spectrum of haemostatic disorders in the present study

Diagnosis	Platelet count	BT	CT	Clot retraction	PT	APTT	Inhibitors	Adsorbed plasma Correction	Aged plasma correction	Von willebrand antigen
Thrombocytopenia	↓	↑	N	poor	N	N	N	-	-	-
vWD	N	↑	N	N	N	↑	N	Corrected	Not corrected	↓
Glanzmann thrombasthenia	N	↑	N	poor	N	N	N	-	-	-
Factor V deficiency	N	N	↑	N	↑	↑	N	Corrected	Not corrected	-

[Table/Fig-2]: Complete coagulation profile of various cases in the study
N= normal, ↑= increased, ↓=decreased

Laboratory Investigations

A majority of the cases were anaemic (97.5%) and they were found to have Hb between 8.1–10 gm/dl (70%) cases. The average Hb level was 8.52gm/dl. The packed cell volume varied between 9–40%, the average value being 26.24%. The commonest blood group was O, followed by the A group.

The haematological profiles of the cases are as shown in [Table/Fig-2]. The platelet count was done in all the cases and six cases were found to have thrombocytopenia which ranged from 30,000 to 90,000 cells/cumm.

The BT values ranged from 2 to 20 minutes, with a mean of 7 min and 83 seconds. In haemostatic disorders, the values ranged from 3 min 30 seconds to 20 minutes, the mean being 13 min 15 seconds. In a majority of the haemostatic disorders, the BT was prolonged i.e., in 13/14 (92%) cases.

Clot retraction was noted and it was found to be within normal limits in 31/40 (77.5%) cases. The retraction was poor in 9 cases, which were subsequently diagnosed as quantitative or qualitative platelet disorders. The CT values ranged from 6 to 14 min 30 seconds, with an average of 8 min 85 seconds.

A detailed morphological study was done on Leishman stained peripheral smears, which showed dimorphic anaemia in 19/40 (47.5%) cases, followed by normocytic hypochromic anaemia in 9/40 (22.5%) cases. The peripheral smears showed thrombocytopenia in 6/40 (15%) cases. The discrete distribution of platelets was noted among the three patients of Glanzmann thrombasthenia.

The PT was found to be normal in all the cases, except in one case. The APTT was found to be abnormal in 5 (12.5%) patients. Later, they were diagnosed to have coagulation disorders. In haemostatic disorders, the average APTT was 36.2 seconds and the values in the clotting factor deficiency disorders had an average of 48.04 seconds. In all the cases of prolonged clotting tests, the inhibitor screening was done and none of the cases were found to be positive for the same.

The cases with the prolonged clotting tests were evaluated further by using correction studies. In one case, both the PT and the APTT were prolonged, and it was corrected by using normal control plasma and adsorbed plasma but not by aged plasma, which strongly suggested the deficiency of Factor V. In this case, the thrombin time was found to be within normal limits. The Factor V assay could not be done due to a lack of facilities for it.

In four cases where the APTT was prolonged and where the PT was normal, the correction studies with normal plasma and adsorbed plasma showed correction. No correction with aged plasma suggested a low level of Factor VIII activity. These cases

Age(yrs)	Associated bleeding manifestations	BT (min)	APTT(sec) Control/test	PT(sec) Control/test	Blood group
12	Epistaxis, gum bleeding, skin bleeding, post traumatic	15	16 / 27	12 / 13	O +ve
19	Epistaxis, gum bleeding	13	23 / 37	12 / 12	O – ve
14	Epistaxis, gum bleeding	16	28 / 58	14 / 15	O – ve
12	Epistaxis, post traumatic	15	31 / 55	12 / 14	O + ve

[Table/Fig-3]: Lab parameters in vWD patients in the present study

had a prolonged BT and they clinically presented with mucosal bleeding, thus strongly suggesting the diagnosis of vWD. A serum von Willebrand antigen assay was done, which showed low levels in all these cases. The various laboratory parameters in vWD are as shown in [Table/Fig-3]. However, the further expensive investigations like ristocetin induced platelet aggregation (RIPA) could not be done in our study.

A bone marrow examination was done only in cases of thrombocytopenia as a part of the evaluation. In all these cases, we found megaloblastic changes.

DISCUSSION

Gynaecological problems of adolescents occupy a special place in the spectrum of gynaecological disorder of all age groups. This is because of the physical nature of the problems which are so unique, special and specific for the age group and also because of the associated psychological factors which are very important in the growth and psychological remodeling of someone who is in the transition between childhood and womanhood [1,2,3,5,6]. Yet, adolescent gynaecology is a subspecialized area of gynaecology which has still not been explored optimally, especially in developing countries like India [3,4,7].

During the study period, 688 adolescents with menorrhagia were consulted in the Department of Gynaecology. After a thorough clinical evaluation, by applying our inclusion and exclusion criteria, we found 40 cases with possible haemostatic disorders, which accounted for 5.9% of the adolescents who were evaluated during the study period. Roy Chowdhury et al, found an incidence of 9.2%, which was almost comparable to our findings [5]. Amongst these, 14 cases were classified under haemostatic disorders. The higher incidence of haemostatic disorders in our study in comparison with the above studies, may be explained, based on the selection criteria which we followed, which included only the adolescent age group and the small sample size. The distribution in various studies is as shown in [Table/Fig-4] [1,8,9,10].

The commonest primary haemostatic disorder which was found in our study was menorrhagia due to quantitative platelet disorder, which was seen in 6/40 (15%) cases, followed by qualitative disorder, which was seen in 3/40 (7.5%) cases. In a study which was conducted by Bevan A et al, 9 / 71 (13%) girls had quantitative platelet disorder and 6/71 (9%) cases had qualitative platelet disorder, which correlated well with the findings of our study [1]. A study by Roy Chowdhury et al, found thrombocytopenia (9.2 %) as the leading haematological cause, which was similar to that which was seen in our study [5].

All the patients with quantitative platelet disorder were evaluated further and they were found to have megaloblastic anaemia. Our findings were unlike those of other studies, in which most of the thrombocytopenias were caused due to idiopathic thrombocytopenic purpura [1,2]. In teenagers where there is an increased nutritional demand and compounded with a decreased intake of

Vitamin B [12] and folate, it is not unusual for them to have megaloblastic anaemia. It is well known that megaloblastic haematopoiesis can cause dyshaematopoiesis, which causes thrombocytopenia. The literature states that patients with megaloblastic anaemia may present with bleeding manifestations [11].

We found that 3 / 40 cases had functional platelet disorder, which accounted for 7.5% cases. These three patients with bleeding manifestations were diagnosed as Glanzmann thrombasthaenia, based on the marked prolongation of BT, normal CT, poor clot retraction with a normal platelet count and the discrete arrangement of platelets in the peripheral blood smear. Saxena R et al study showed inherited platelet dysfunction as the predominant cause in 83.9% of the cases, of which Glanzmann thrombasthaenia accounted for 10.6% cases, which correlated well with the findings of our study [8]. Hossain et al reported three cases of puberty menorrhagia due to platelet function disorders like Glanzmann thrombasthaenia and the Bernard Soulier syndrome [6].

The diagnosis of vWD was made in four cases and one case had factor V deficiency. vWD accounted for 10% of the cases and factor V constituted for 2.5% cases. The prevalence as compared with other studies is shown in [Table/Fig-5] [9,10]. All four cases of vWD were of the O blood group. Our study correlated well with findings which were elicited by Dilley et al and Shankar M et al [10,12]. The common association of blood group O with vWD is well documented [10,12-14]. The O blood group tends to have low levels of the von Willebrand antigen as compared to other blood groups [Table/Fig-6].

Study	Primary(%)	Secondary(%)
Rao S et al (1)	5.7	-
Saxena R et al (8)	83.9	16
Kadir A et al(9)	-	17
Roychowdhury et al(5)	80	20
Present study (2006)	64	36

[Table/Fig-4]: Distribution of Haemostatic disorders in various studies

Study	No. of women	No. with vWD	Prevalence %
Kadir et al (9)	150	20	13
Dilley et al (10)	121	8	6.6
Present study	40	4	10

[Table/Fig-5]: Prevalence of vWD in various studies

Blood group	N	vWF : Ag mean, %	Range
O	456	74.6	35.6 – 157
A	340	105.9	48.0 – 233.9
B	196	116.9	56.8 – 241.0
AB	109	123.3	63.8 – 238.2

[Table/Fig-6]:vWD and Blood group association (10,12-14)

The rare coagulation factor deficiency which we found in our study was factor V, which accounted for 2.5% of the cases. This case of factor V deficiency presented with menorrhagia and abdominal pain and after evaluation, was found to have acute appendicitis. The patient developed life threatening post-operative bleeding and on further evaluation, was found to have factor V deficiency. This observation reiterates the importance of pre-operative PT and APTT. On review of literature, the rare coagulation factor deficiencies which were seen were found to be factor XIII, factor X, factor VII, factor XII and combined deficiencies, whereas, none of the studies showed the factor V deficiency which was seen in our study [12-18].

Menorrhagia, at all stages of life, severely affects the quality of life. The common treatment modalities which are available for this age group include anti-fibrinolytic agents, desmopressin, replacement therapy with factor VIII concentrates (in diagnosed cases of vWD), hormonal therapy, blood and blood products and the use of rFVIIa to control acute episodes of blood loss [5,6,12-18]. The use of progestins to control acute episodes of bleeding, followed by maintenance with combined oral contraceptive pills in a cyclical manner, have been found to be effective.

CONCLUSION

In the present study, an effort was made to evaluate the causes of menorrhagia among adolescent girls who consulted the tertiary center in Davangere. Menorrhagia may be an important clinical manifestation in a bleeding disorder and it has been suggested that these patients need to be investigated for these disorders, especially for vWD. For the evaluation of puberty menorrhagia, more emphasis should be given to rule out primary haemostatic disorders i.e., quantitative as well as qualitative. The lack of awareness of this common inherited bleeding disorder and a paucity of good diagnostic facilities add to the problem.

Future suggestions

- The haematology laboratory facilities should be improved by adding the coagulation profile including RIPA and the vWF Ag assay to the investigations.
- A general public awareness regarding the proper evaluation of menorrhagia should be created for those who are affected to get appropriate treatment.
- The pre-operative evaluation of haemostatic disorders by a battery of screening tests like PT and APTT should be made mandatory.

- More and more studies need to be undertaken, as there is inadequate data in the literature on this topic from the Indian subcontinent.

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