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ORIGINAL ARTICLE

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Systemic causes of menorrhagia

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OBJECTIVE(S) : To find the incidence of different nonpelvic causes of menorrhagia with special emphasis on careful history taking, clinical examination and inclusion of simple blood tests to diagnose hemostatic disorders.

METHOD(S) : Fifty women of 15-45 years age, having menorrhagia without any pelvic cause and treated from 1st June, 2004 to 31st May, 2005 were selected for this retrospective study. After a detailed history and general examination all patients were subjected to blood tests for complete blood count, bleeding time, prothrombin time, activated partial thromboplastin time (aPTT) and serum T_3, T_4, TSH levels. Special tests were reserved, wherever applicable, to diagnose the cause of menorrhagia. Results were analyzed statistically by 2 x 2 chi square test with Yate's correction.

RESULTS : Hypothyroidism (20%) and inherited coagulopathy (18%) were the two most common nonpelvic causes of menorrhagia. Menorrhagia from menarche (P<0.001), bleeding from other sites (P=0.007), history of previous operative bleeding (P<0.001), and history of postpartum bleeding (P<0.001) were statistically significant in patients with underlying hemostatic disorders.

CONCLUSION(S) : A detailed history, clinical examination and simple blood tests can detect various nonpelvic causes of menorrhagia.

Key words: menorrhagia, nonpelvic causes of menorrhagia, coagulopathy, hypothyroidism

Introduction

Menorrhagia, defined as regular cyclical bleeding, excessive in amount (>80mL) and/or duration (>5 days) is essentially a symptom and not in itself a disease. Although menorrhagia is a common gynecological symptom, a specific cause is identified in less than 50% of affected women[1]. In majority of cases the cause lies in the pelvis and can be easily identified. However, less commonly the bleeding may be due to undiagnosed underlying coagulation defect [2], endocrine disorder or systemic disease.

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Menorrhagia may be the only clinical manifestation of an inherited bleeding disorder [1]. Recent studies have shown that inherited bleeding disorder, especially in mild form, is the underlying cause in a large number of women with menorrhagia and the incidence may be as high as 20% [3]. Menorrhagia is a considerable burden on resources and may ultimately lead to surgery [4]. Therefore it is very important that patient having menorrhagia without obvious pelvic pathology should be routinely studied to diagnose underlying endocrine and hemostatic disorders.

The present study was undertaken to know the incidence of different nonpelvic causes of menorrhagia and to highlight the importance of history, clinical examination and inclusion of some simple routine blood tests in our day to day practice to diagnose underlying hemostatic disorders in patients with menorrhagia.

Methods

One hundred and twenty six patients between the ages of 15

and 45 years attended our outpatient department from 1st June, 2004 to 31st May, 2005 complaining of menorrhagia. After history taking, clinical examination, and investigations including sonography, endometical histology, laparoscopy and hysteroscopy those with a pelvic pathology like fibroids, adenomyosis, tuboovarian masses, cervical or endometrial malignancy, cervical polyp, tuberculous endometritis, and intrauterine contraceptive device, and those taking anticoagulants, oral contraceptive pills, hormones and non-steroidal antiinflammatory drugs were excluded from the study (n=76). The remaining 50 were included in this retrospective study. The power of the study as indicated by interrater reliability is kappa 0.382 and Forbes NM 10.146.

A detailed menstrual history and history of other bleeding symptoms like easy bruising, bleeding from other sites, and postoperative bleeding or postpartum hemorrhage (PPH) was taken. History suggestive of thyroid, renal or liver disease was also taken. Family history of bleeding disorder was recorded. A detailed general physical examination was done to look for pallor, bleeding spots, hepatosplenomegaly, and thyroid enlargement.

These patients were subjected to routine tests of complete blood count, platelet count, peripheral smear, bleeding time (BT), prothrombin time (PT), and activated partial thromboplastin time (aPTT) besides estimation of serum T_3 T_4 and TSH.

Wherever history, clinical examination, and the above routine tests indicated underlying medical disorders, patients were referred to the department of medicine for further evaluation and diagnosis by special tests like renal function tests, liver function tests, anti DS-DNA, and bone marrow study.

The results obtained in the study were statistically analyzed using the 2 x 2 chi square test with Yate's correction.

Results

Table 1 shows the incidence of different nonpelvic causes of menorrhagia. Hypothyroidism was seen in 10 (20%) cases whereas hyperthyroidism accounted for menorrhagia in only 1 (2%) case. Of the inherited bleeding disorders, coagulopathy was the most common cause in 9 (18%) cases. Idiopathic thrombocytopenic purpura (ITP), systemic lupus erythematosus (SLE), renal disease, aplastic anemia, and liver disease were other causes. However, in 22 (44%) cases history, clinical examination, and laboratory tests could not reveal any definite cause for menorrhagia.

Table 2 shows the age distribution of the 28 cases in whom the cause could be identified. Hypothyroidism was commoner in the older age group (36-45 years) whereas inherited coagulopathy was commoner in young menorrhagic patients (15-25 years).

Table 1. Nonpelvic causes of menorrhagia (n=50).

Cause	Number of patients	Percentage
Hypothyroidism	10	20
Hyperthyroidism	1	2
Idiopathic thrombocytopenic purpura	3	6
Inherited coagulopathy	9	18
Systemic lupus erythematosus	1	2
Liver disease	2	4
Renal disease	1	2
Aplastic anemia	1	2
No definite cause identified	22	44

Table 2. Age distribution of the patients in whom nonpelvic cause could be identified (n=28).

	Age (years)		
Cause	15-25	26-35	36-45
Hypothyroidism	1	4	5
Hyperthyroidism	0	1	0
Idiopathic thrombocytopenic purpura	1	2	0
Inherited coagulopathy	6	2	1
Systemic lupus erythematosus	0	1	0
Liver disease	0	2	0
Renal disease	0	0	1
Aplastic anemia	0	1	0

Table 3 shows the comparative study of menstrual history, family history, history of other bleeding symptoms, postoperative and postpartum bleeding, and hemoglobin level among those with hemostatic disorders (inherited coagulopathy + ITP) and those with no such underlying disorders. Menorrhagia since menarche was seen in 66.67% of those with such disorders but only in 10.53% of those without, which is highly significant (P<0.001). Menorrhagia of less than 24 months was significantly less (P=0.026) in patients with hemostatic disorders. Family history of bleeding disorder and history of other bleeding symptoms in the patient were present in those with the disorder in 25% but only in 7.89% of those without it (P=0.28). Bleeding from other sites was significantly higher (P=0.007) in those with hemostatic disorders. Four out of 12 patients with hemostatic disorder gave previous history of operation, out of whom two (50%) had an episode of excessive postoperative

bleeding, whereas similar episode was experienced by 11.76%(2/17) of women without hemostatic disorder (P<0.001). Five of 12 patients with hemostatic disorder had history of delivery of whom 3 (60%) had an episode of PPH. This was higher (P<0.001) than 16% (4/25) of those without hemostatic disorder. Severe anemia (Hb < 6 g/dL) was seen in 33.33% with hemostatic disorder in comparison to 15.79% in those without (P=0.362).

Table 4 shows the results of different laboratory tests which helped us to diagnose different nonpelvic causes of menorrhagia.

Table 3. Comparative study of those with hemostatic disorders (ITP+inherited coaguloathy) and those without.

Variable	Patients with underlying hemostatic disorder (n=12)	Patients without underlying hemostatic disorder (n=38)	P value
Duration of menorrhagia			
Since menarche	8(66.67%)	4 (10.53%)	<0.001
>24 months	3 (25%)	15 (39.47%)	0.572
<24 months	1 (8.33%)	19 (50%)	0.026
Family history of bleeding disorders	3 (25%)	3 (7.89%)	0.280
History of other bleeding symptoms [a]	5 (41.67%)	2 (5.3%)	0.007
Postoperative bleeding [b]	2/4 (50%)	2/17 (11.76%)	<0.001
Postpartum bleeding [b]	3/5 (60%)	4/25 (16%)	<0.001
Hemoglobin level			
< 6g/dL	4 (33.33%)	6 (15.79%)	0.362
6-10g/dL	3 (25%)	18 (47.37%)	0.171
>10g/dL	5 (41.67%)	14 (36.84%)	0.967

[a] Bruising and gum or nose bleeding [b] Expressed as a percentage of women who had the procedure or event

Table 4. Significance of different laboratory tests performed.

Laboratory values	Significance	No. of patients (n=28) [a]
T_3, T_4 - normal, TSH - High	Hypothyroidism	8
T_3, T_4 - low, TSH - High	Hypothyroidism	2
T_3, T_4 - high, TSH - Low	Hyperthyroidism	1
Prolonged BT, normal aPTT, thrombocytopenia	ITP	3
Prolonged BT, prolonged aPTT, normal platelet count	Inherited coagulopathy	9
Prolonged PT with altered LFT, thrombocytopenia	Liver disease	2
Thrombocytopenia, slightly prolonged BT, altered renal function test	Renal disease	1
Pancytopenia, prolonged bleeding time aplastic bone marrow	Aplastic anemia	1
Thrombocytopenia, lymphopenia, anti DS-DNA +ve	SLE	1

[a] Remaining 22 patients had all laboratory values within normal limits

Table 5. Effectiveness criteria of the four statistically significant (95% CI) parameters in the study.

Effectiveness criteria	Menorrhagia since menarche (P<0.001)	History of bleeding from other sites (P=0.007)	History of postoperative bleeding (P<0.001)	History of postpartum hemorrhage (P<0.001)
Sensitivity	0.667	0.714	0.810	0.789
Specificity	0.895	0.837	0.638	0.677
Positive predictive value	0.667	0.417	0.500	0.600
Negative predictive value	0.895	0.947	0.882	0.840
Positive likelihood ratio	6.333	4.388	2.238	2.447
Negative likelihood ratio	0.373	0.341	0.298	0.311
Diagnostic odds	17.000	12.857	7.503	7.875
Error odds	0.235	0.486	2.409	1.786

Discussion

Hypothyroidism (20%) and inherited coagulopathy (18%) were the two most important nonpelvic causes of menorrhagia in our study. Fifty percent of hypothyroid patients were in the age group of 36-45 years. According to Doifode and Fernandez [5] menorrhagia is the most common menstrual irregularity is hypothyroid women. T_3 T_4 TSH estimation should be made mandatory in cases of dysfunctional uterine bleeding to detect apparent and occult hypothyroidism [5].

In studies by Trasi et al[6] and Kadir et al[1] inherited coagulopathy accounted for 19.16% and 17% of cases of menorrhagia respectively. This is similar to our result of 18%.

Menorrhagia since menarche (66.67%) was significantly higher (P<0.001) in patients with hemostatic disorder. Similar results were noted by Ragni et al[7] (53.1%) and Kadir et al [1] (65%) in their studies of menorrhagic women with coagulation disorders.

The frequency of other bleeding symptoms like bruising and gum or nose bleeding was significantly higher (P=0.007) in those with hemostatic disorder, consistent with the findings of Kadir et al [1].

Similar to the findings of Kadir et al[1], our study also revealed that history of postoperative bleeding and of postpartum bleeding were significantly more (P<0.001 each of the two) in those with underlying hemostatic disorder. However, though family history and severe anemia were more common in women with hemostatic disorder it was not statistically significant.

Prolonged BT and aPTT with normal platelet count were stamped as cases of inherited coagulopathy. Though tests to diagnose von Willebrand's disease were suggested, this being the most common coagulopathy in menorrhagic patients [3]. No patient could afford them. Wherever history, clinical examination, and routine tests indicated medical disorder, patients were referred to department of medicine to carry out special tests which helped us to diagnose different causes as shown in Table 4 .

The four parameters that were statistically significant in our study, namely, menorrhagia since menarche, history of bleeding from other sites, postoperative bleeding, and postpartum haemorrhage fulfill the criteria required to be declared as effective diagnostic criteria, even in a comparatively small population of study. The values with 95% confidence limits are being given in Table 5.

However, no definite cause was found in 44% cases which may be due to some hemostatic imbalance in the endometrium.

Menorrhagia may be the first and only clinical manifestation of an inherited bleeding disorder [3]. Yet coagulopathies are not appreciated as etiology of menorrhagia by gynecologists and unintentional surgical intervention is done without getting the patients investigated for coagulopathies [8]. Our study emphasizes the importance of careful history taking since certain factors significantly predict menorrhagia viz., menorragia since menarche, presence of other bleeding symptoms like bruising, epistaxis, gum bleeding and history of postoperative bleeding and postpartum hemorrhage. Clinical suspicion for an underlying bleeding disorder in menorrhagic patients will not only help in its early diagnosis but will also have important implications in management of antepartum and postpartum hemorrhage of future pregnancies [8].

This study shows that search for systemic diseases including endocrine and hemostatic disorders in menorrhagic patients with no pelvic cause reveals the underlying cause in most cases.

Conclusion

A gynecologist's awareness and inclusion of detailed history, clinical examination and simple laboratory tests in day-to-day practice can prevent unnecessary hysterectomies in women with menorrhagia.

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