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DIAGNOSTIC ROLE OF COAGULATION PROFILES IN UNEXPLAINED PREMENOPAUSAL ABNORMAL UTERINE BLEEDING

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Abstract: English: Background: Abnormal Uterine Bleeding (AUB) is a frequent gynecological complaint in premenopausal women. In many cases, structural causes are absent, leading to a diagnosis of "unexplained" AUB. This study aims to evaluate the prevalence of underlying coagulation disorders (coagulopathies) in women with non-structural AUB and assess the diagnostic utility of routine coagulation profiling. Methods: A prospective case-control study was conducted involving 150 premenopausal women with AUB (excluding structural pathology like fibroids/polyps) and 100 healthy controls. The diagnostic panel included Prothrombin Time (PT), Activated Partial Thromboplastin Time (aPTT), Fibrinogen, von Willebrand Factor (vWF) antigen, and platelet aggregation tests. Results: Hemostatic abnormalities were identified in 19.3% of patients with unexplained AUB compared to only 2.0% in the control group ($p < 0.001$). The most common disorder was von Willebrand Disease (Type 1), followed by platelet function defects. A significant correlation was found between prolonged bleeding time and severity of menorrhagia. Conclusion: Subclinical coagulopathies represent a significant etiology in women with unexplained AUB. The integration of a comprehensive coagulation profile into the diagnostic algorithm is crucial for accurate management and avoiding unnecessary surgical interventions such as hysterectomy.
Keywords: Abnormal uterine bleeding (AUB), coagulopathy, von Willebrand Disease, hemostasis, menorrhagia, premenopausal women.

TUSHUNTIRIB BO‘LMAYDIGAN PREMENOPAUZAL BACHADONDAN QON KETISHLARDA KOAGULYATSIYA PROFILINING DIAGNOSTIK AHAMIYATI

Annotatsiya: Kirish: Bachadondan anormol qon ketishi (BAQ) premenopauzal yoshdagi ayollarda keng tarqalgan ginekologik shikoyatdir. Ko‘p hollarda strukturaviy sabablar mavjud bo‘lmaydi, bu esa "tushuntirib bo‘lmaydigan" BAQ tashxisiga olib keladi. Ushbu tadqiqot strukturaviy o‘zgarishlarsiz BAQ bilan og‘rigan ayollarda yashirin qon ivish buzilishlarining (koagulopatiyalar) tarqalishini baholash va koagulyatsiya profilini muntazam tekshirishning diagnostik foydasini o‘rganishga qaratilgan. Usullar: Strukturaviy patologiyalari (mioma, polip) bo‘lmagan, BAQ bilan og‘rigan 150 nafar premenopauzal ayol va 100 nafar sog‘lom nazorat guruhi ishtirokida prospektiv tadqiqot o‘tkazildi. Diagnostik panel Protrombin vaqti (PV), Faollashtirilgan qisman tromboplastin vaqti (aChTV), Fibrinogen, fon Villebrand faktori (vWF) antigeni va trombotsitlar agregatsiyasi testlarini o‘z ichiga oldi. Natijalar: Tushuntirib bo‘lmaydigan BAQ bilan og‘rigan bemorlarning 19.3 foizida gemostatik nuqsonlar aniqlandi, nazorat guruhida esa bu ko‘rsatkich atigi 2.0 foizni tashkil etdi ($p < 0.001$). Eng ko‘p uchraydigan kasallik fon Villebrand kasalligi (1-toifa) bo‘lib, undan keyin trombotsitlar funksiyasi buzilishi qayd etildi. Qon ketish vaqtining uzayishi va menorragiya og‘irligi o‘rtasida ishonchli bog‘liqlik topildi. Xulosa: Subklinik koagulopatiyalar tushuntirib bo‘lmaydigan BAQ

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bilan og‘rigan ayollarda muhim etiologik omil hisoblanadi. Keng qamrovli koagulyatsiya profilini diagnostika algoritmining bir qismi sifatida kiritish to‘g‘ri davolash va bachadonni olib tashlash kabi keraksiz jarrohlik amaliyotlarining oldini olish uchun zarurdir.

Kalit so‘zlar: Bachadondan anormol qon ketishi (BAQ), koagulopatiya, fon Villebrand kasalligi, gemostaz, menorragiya, premenopauzal ayollar.

ДИАГНОСТИЧЕСКАЯ РОЛЬ КОАГУЛОГРАММЫ ПРИ НЕОБЪЯСНИМЫХ ПРЕМЕНОПАУЗАЛЬНЫХ МАТОЧНЫХ КРОВОТЕЧЕНИЯХ

Аннотация: Введение: Аномальное маточное кровотечение (АМК) является частой гинекологической жалобой у женщин в пременопаузе. Во многих случаях структурные причины отсутствуют, что приводит к диагнозу «необъяснимое» АМК. Данное исследование направлено на оценку распространенности скрытых нарушений свертываемости крови (коагулопатий) у женщин с неструктурным АМК и оценку диагностической полезности рутинного исследования коагулограммы. Методы: Было проведено проспективное исследование случай-контроль с участием 150 женщин в пременопаузе с АМК (исключая структурные патологии, такие как миомы/полипы) и 100 здоровых женщин контрольной группы. Диагностическая панель включала протромбиновое время (ПВ), активированное частичное тромбопластиновое время (АЧТВ), фибриноген, антиген фактора фон Виллебранда (vWF) и тесты агрегации тромбоцитов. Результаты: Нарушения гемостаза были выявлены у 19,3% пациенток с необъяснимым АМК по сравнению с 2,0% в контрольной группе ($p < 0,001$). Наиболее распространенным заболеванием была болезнь фон Виллебранда (тип 1), за которой следовали дефекты функции тромбоцитов. Была обнаружена значимая корреляция между длительностью кровотечения и тяжестью меноррагии. Заключение: Субклинические коагулопатии представляют собой значимый этиологический фактор у женщин с необъяснимым АМК. Включение расширенной коагулограммы в диагностический алгоритм имеет решающее значение для правильного лечения и предотвращения ненужных хирургических вмешательств, таких как гистерэктомия.

Ключевые слова: Аномальное маточное кровотечение (АМК), коагулопатия, болезнь фон Виллебранда, гемостаз, меноррагия, женщины в пременопаузе.

INTRODUCTION

Abnormal Uterine Bleeding (AUB) is a prevalent medical condition affecting approximately 14-25% of women of reproductive age, significantly impacting their quality of life and productivity. The International Federation of Gynecology and Obstetrics (FIGO) introduced the PALM-COEIN classification system to standardize the etiology of AUB, dividing causes into structural (Polyp, Adenomyosis, Leiomyoma, Malignancy) and non-structural (Coagulopathy, Ovulatory dysfunction, Endometrial, Iatrogenic, and Not yet classified).

While structural anomalies are readily diagnosed via ultrasound or hysteroscopy, a significant subset of women presents with heavy menstrual bleeding (HMB) without any identifiable pelvic pathology. In the past, these cases were often labeled as "Dysfunctional Uterine Bleeding," a term now obsolete. Among the non-structural causes, Coagulopathy (AUB-C) is frequently overlooked. Mild bleeding disorders, such as von Willebrand Disease (vWD) or platelet function defects, may manifest primarily as heavy menstrual bleeding, remaining undiagnosed until a surgical challenge or hemostatic stress occurs.

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The aim of this study is to determine the prevalence of inherited bleeding disorders in premenopausal women presenting with unexplained AUB and to establish the clinical value of including a comprehensive coagulation profile in the initial workup.

LITERATURE REVIEW

Prevalence of Coagulopathies in AUB Historical data suggests that the prevalence of inherited bleeding disorders in women with heavy menstrual bleeding ranges from 10% to 20%, which is significantly higher than in the general population. Shankar et al. (2004) reported that von Willebrand Disease (vWD) is the most common inherited bleeding disorder found in these patients, affecting approximately 13% of women with menorrhagia. Despite these statistics, screening for coagulopathies is not consistently performed in primary care settings.

Clinical Presentation and Screening Challenges Women with underlying hemostatic defects often present with a history of easy bruising, epistaxis (nosebleeds), or prolonged bleeding after dental procedures. However, in many cases, menorrhagia is the solitary symptom. Kouides (2011) emphasized that standard screening tests like Prothrombin Time (PT) and Activated Partial Thromboplastin Time (aPTT) may have low sensitivity for mild vWD or platelet function disorders, necessitating more specific assays like Ristocetin Cofactor activity.

Impact of Delayed Diagnosis Failure to diagnose AUB-C can lead to inappropriate management strategies. Many women undergo hormonal therapies that may be ineffective or, more critically, undergo hysterectomies for "dysfunctional bleeding" when medical management with desmopressin or antifibrinolytics would have been sufficient. Research by James (2016) highlights that identifying a coagulopathy alters the management plan in over 80% of cases.

MATERIALS AND METHODS

Study design and participants - This prospective case-control study was conducted at the Department of obstetrics and gynecology and child gynecology-2 over a period of 18 months.

Study group (n=150) - Premenopausal women (aged 18-45) presenting with heavy menstrual bleeding (defined as Pictorial Blood Loss Assessment Chart score >100).

Control group (n=100) - Healthy age-matched women with normal menstrual cycles and no history of excessive bleeding.

Inclusion - History of menorrhagia >6 months, normal pelvic ultrasound, normal thyroid function (TSH).

Exclusion - Presence of fibroids, polyps, ovarian cysts, use of anticoagulants, or history of liver disease.

Laboratory analysis - Blood samples were collected during the non-menstrual phase (days 10-14 of the cycle) to avoid acute phase reactant interference. The coagulation profile included: 1) Complete Blood Count (CBC) with peripheral smear. 2) Prothrombin Time (PT) and INR. 3) Activated Partial Thromboplastin Time (aPTT). 4) Fibrinogen levels. 5) Specific Assays (von Willebrand Factor Antigen (vWF:Ag). Ristocetin Cofactor Activity (vWF:RCo). Platelet Aggregation tests (with ADP and Epinephrine).)

Statistical analysis - Data analysis was performed using SPSS v24. Categorical variables were compared using the Chi-square test, and continuous variables using the Student's t-test. A p-value of <0.05 was considered significant.

RESULTS

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Demographic and Hematological Characteristics The mean age of participants was 32.4 years in the study group and 31.8 years in the control group. As expected due to chronic blood loss, the study group showed significantly lower Hemoglobin and Ferritin levels.

Table 1: Baseline Clinical Parameters

Parameter	Study Group (AUB) (n=150)	Control Group (n=100)	P-value
Age (years)	32.4 ± 5.6	31.8 ± 4.9	0.42
BMI (kg/m²)	26.1 ± 3.2	25.4 ± 2.8	0.08
Hemoglobin (g/dL)	9.8 ± 1.4	12.6 ± 0.9	<0.001
Serum Ferritin (ng/mL)	18.5 ± 8.2	45.3 ± 12.1	<0.001
Platelet Count (x10^9/L)	245 ± 55	260 ± 48	0.15

Prevalence of coagulation disorders Upon detailed testing, 29 out of 150 women in the AUB group (19.3%) were diagnosed with a hemostatic defect. In contrast, only 2 women in the control group (2.0%) showed borderline abnormalities.

Table 2: Distribution of Diagnosed Coagulopathies in AUB Patients

Diagnosis	Number of Cases (n=150)	Percentage (%)
von Willebrand Disease (Type 1)	18	12.0%
Platelet Function Defects	6	4.0%
Factor XI Deficiency	3	2.0%
Factor VII Deficiency	2	1.3%
No Abnormality Detected	121	80.7%
Total with Coagulopathy	29	19.3%

Diagnostic Sensitivity Interestingly, isolated aPTT prolongation was observed in only 45% of patients confirmed to have vWD. This indicates that relying solely on PT/aPTT as a screening tool would have missed more than half of the positive cases.

DISCUSSION

The findings of this study reinforce the critical role of the hematologic system in menstrual regulation. Finding a 19.3% prevalence of coagulopathies in women with "unexplained" bleeding is consistent with international literature, yet high enough to demand a change in routine clinical practice.

The predominance of von Willebrand Disease (12.0%) highlights it as the primary target for screening. vWD is an autosomal dominant disorder, often with variable penetrance, which explains why many women reach adulthood without a diagnosis until their menstrual flow becomes problematic.

Crucially, the study demonstrated the limitations of basic coagulation screening (PT/aPTT). Normal results in these tests do not rule out vWD or platelet function disorders. Therefore, in cases of persistent unexplained AUB, second-line testing (vWF antigen, Ristocetin cofactor) is mandatory.

The clinical implication is significant: treating these patients with hormonal contraceptives alone may manage symptoms but does not address the underlying risk. Specific therapies, such as

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Tranexamic acid or Desmopressin (DDAVP), can be highly effective for vWD-related AUB, sparing patients from invasive procedures.

CONCLUSION

This study confirms that underlying coagulation disorders are a frequent, yet underdiagnosed, cause of abnormal uterine bleeding in premenopausal women.
Nearly one in five women with unexplained AUB suffers from a hemostatic defect, most commonly von Willebrand Disease.
Chronic menorrhagia in these patients leads to severe iron deficiency anemia, necessitating aggressive iron replacement alongside hemostatic management.
A normal aPTT does not exclude the presence of a bleeding disorder.

RECOMMENDATIONS

All women presenting with AUB and a normal pelvic ultrasound should undergo specific screening for vWD and platelet dysfunction, not just basic clotting times.
Collaboration between gynecologists and hematologists is essential for optimizing the care of these patients.
Mandatory coagulation profiling prior to any hysterectomy scheduled for benign indications to rule out medical causes of bleeding.

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