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A study on various treatment modalities in Abnormal uterine bleeding.

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Abstract:
Background: *Abnormal uterine bleeding (AUB) is defined as any type of bleeding in which the amount, duration, frequency and cyclicity is abnormal for a patient.1 In order to treat the condition, it is important to identify the cause of bleeding. Treatment must remain individualised and encompass the impact of pressure symptoms, desire for retention of fertility and contraceptive needs, as well as address the management of their AUB in order to achieve improved quality of life. This study was conducted to study the various treatment modalities in AUB with a detailed analysis of medical management which may effevtively avoid surgical approach in such patients and thereby decrease morbidity and improve quality of life.* ***Materials and Methodology:*** *This study was conducted in the department of gynaecology and obstetrics at LallaDed hospital from September 2020 to December 2021. Relevant data was collected from the OPD records and analysed in a microsoft excel sheet. A retrospective observational study was conducted, based on convienience sampling, 100 cases were selected for the study as per the inclusion criteria.****Results:*** *Most common type of AUB among the women presenting with abnormal uterine bleeding was due to ovulatory dysfunction and accounted for 49%. AUB M had the highest iron therapy requirement=42.85%., and blood transfusion = 28.57%. Tranexemic acid was the first line treatment for control of bleeding where as far as hormonal treatment is concerened, norethisterone emerged as the main stay in control of bleeding due to varied etiologies. Total number of patients who requiredsurgical management were only 15%..* ***Conclusion:*** *Patients having AUB M were found to have required most treatment, be it in terms of parenteral iron therapy, blood transfusions, or surgery, however LNG IUS may be a better option in AUB M (endometrial hyperplasia without atypia)than hysterectomy. Medical management, especially with norethisterone is the main say of treatment in case of AUB with non structural causes, and has shown excellent results.In case of AUB with structural cause , surgical management is a significant treatment modality.*

Key Words: *Adenomyosis, menorrhagia, ovulatory dysfunction, uterine bleeding*

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I. Introduction

Abnormal uterine bleeding (AUB) is defined as any typeof bleeding in which the amount, duration, frequency andcyclicity is abnormal for a patient[1]. In order to treat the condition, it is important to identify the cause of bleeding. The International Federation of Gynaecology and Obstetrics (FIGO) in 2011, introduced a classification for AUB called PALM-COEIN[2]. PALM holds for the pathologies related to the uterine structural anomalies (polyp, adenomyosis, leiomyoma, malignancy and endometrial hyperplasia). COEIN holds for the pathologies unrelated with uterine structural anomalies (ovulatory dysfunction, coagulopathy, endometrial, iatrogenic, and unclassified).Treatment must remain individualised and encompass the impact of pressure symptoms, desire for retention of fertility and contraceptive needs, as well as address the management of their AUB in order to achieve improved quality of life.The definitive treatment of AUB is hysterectomy; however, the less invasive options are also available which include medical therapy and endometrial ablation[2,3]. This study was conducted to study the various treatment modalities in AUB with a detailed analysis of medical management which may effevtively avoid surgical approach in such patients and thereby decrease morbidity and improve quality of life.

II. Material And Methods

This study was conducted in the department of gynaecology and obstetrics at LD hospital from September 2020 to December 2021. Relevant data was collected from the opd records and analysed in a microsoft excel sheet. A retrospective observational study was conducted, based on convienience sampling, 100 cases were selected for the study as per the inclusion criteria.

Study design: retrospective observational time based study
Location: This was a tertiary care teaching hospital based study done in Department of Obstetrics and Gynaecology, at LallaDed Hospital, Srinagar, Kashmir.
Study duration: September 2020 to December 2021
Sample size: 100 patients
Sample size calculation: Time based study
Subjects and selection method: The study population was the women in the reproductive age group, who visited the gyanecological OPD with complaints of abnormal uterine bleeding as per the inclusion criteria.

Inclusion criteria:
1. Age15-55 years
2. Abnormal uterine bleeding with complete hospital records

Exclusion criteria:
1. Pregnancy
2. Vaginal bleeding caused due to cervical or vaginal cause
3. Chronic liver disease
4. Chronic renal disease
5. Non endometrial malignancy
6. Post menopausal women

Procedure and Methodology:
All the relevant data regarding the etiology of AUB and various treatment modalities was collected from the OPD records. AUB was classified according to PALM COEIN classification. The treatment received by the patients was analysed according to the type of AUB as per the classification. The need for iron therapy, oral or parental, need for blood transfusion, antibiotics, hormonal and non hormonal medical management as well as surgical management was recorded and classified according to the type of AUB.

Statistical Analysis: All the relevant data was analysed on Microsoft excel sheet . The results were expressed in percentages in the relevant tables.

III. Result

Table no 1: Shows the type of AUB according to PALM COIEN classification

AUB	AUB P	AUB A	AUB L	AUB M	AUB C	AUB O	AUB I	AUB E	AUB N
Number of cases	6	9	12	6	0	49	7	8	0
Percentage	6%	9%	12%	6%	0%	49%	7%	8%	0%

AUB **A**+P=1%
AUB **L**+A= 1%
AUB **L**+ M=1%
Most common type of AUB among the women presenting with abnormal uterine bleeding was due to ovulatory dysfunction and accounted for 49% followed by AUB L (12%).

Table no 2: Shows the pattern of prescription of iron therapy according to PALM COEIN classification.

TYPE OF AUB	ORAL	PARENTERAL	BOTH	TOTAL	PERCENTAGE %
P	1			1	16.66%
A	3			3	30%
L	2	2		4	28.57%
M	0	1	2	3	42.85%
C	0			0	0%
O	6	3	1	10	20.40%
I	2			2	28.57%
E	0			0	0%
N	0			0	0%

Iron therapy was given according to the type of anaemia, patient compliance and affordability. Patients with mild anaemia were not given iron therapy in order to ensure proper compliance with medical management. However moderate anaemia was treated with both oral as well as parenteral iron therapy, although patients with Hb less than 8 were generally given parenteral iron therapy.
Among the 2 patients with AUB L, one was given blood transfusion along with parenteral iron, to build up for surgery. One case of AUB M , was given 3 blood transfusions, 500 mg FCM before surgery and oral iron

therapy after surgery, while another required 5blood transfusions and 400 mg iron sucrose followed by oral iron therapy prior to surgery.
AUB M had the highest iron therapy requirement=42.85%

Table no 3: Shows the type of parenteral iron therapy prescribed for patients with AUB O

Iron sorbitol (IM) 10 doses	Ferric carboxy maltose infusion(FCM) 500mg f/b oral	FCM followed by iron sucrose
2	1	1

Patient who received FCM followed by iron sucrose also received one blood transfusion prior due to severe anaemia.

Table no 4: Shows the need for blood transfusion according to the etiology of AUB

AUB	P	A	L	M	C	O	I	E
No. Of patients	1	0	1	2	0	2	0	0
Percentage	16.66%	0	7.14%	28.57%	0	4.08%	0	0

AUB M has the highest percentage of women who required blood transfusion = 28.57%

Table no 5: Shows the antibiotic therapy prescribed to patients with AUB

AUB	DOXYCYCLINE	METRONIDAZOLE	KIT 6
P		1	
A	1		
L	0		
M	2		
C			
O	3		2
I			1
E			2
N			

KIT 6 was given to patients having features of PID on examination, while metronidazole and doxycycline were given in patients with genital tract infections in accordance with the clinical findings during examination.

Table 6 : Shows the Medical management given in AUB according to PALM COEIN classification

AUB	Tranexemic acid + norethisterone	Tranexemic acid +medroxy progesterone		Tranexemic acid	Noreth controlled release	LNG IUS	Tranexemic acid +Combined oral pills	Tranexemic acid+ mifepristone	Combined oral pills	Norethisterone f/b combined oral pills
P	0	0		2	0	0	0	0		
A	3	0		2	2	1	1	0		
L	2	1		5	0	1	0	1		
M	1	0		0	0	2	0	0		
C	0	0		0	0	0	0	0		
O	5	0		2	1	2			5	
I	1			3			1		2	1
E				1	4	1			2	
N	0	0		0	0	0	0	0		

AUB O:

Cabergolin	Norethisterone + cabergolin	Medroxy progesterone acetate + thyroxin	Levo thyroxin	Tranexemic acid + thyroxin	Tranexemic acid + norethisterone + thyroxin	Norethisterone + thyroxin	Thyroxin + combined oral pills	Medroxy progesterone f/b combined oral pills	N-Acetlycystine + myoinositol +/- metformin
2	1	1	3	1	2	2	1	1	4

N –Acetlycystine + myoinositol+/- metformin were used along with other medicines as per the clinical condition of the patients.

Cabergolin	Combined oral pills	Thyroxin	Cabergolin + thyroxin	Combined pills +thyroxin
1	11	1	1	1

AUB P were inevitably treated with polpectomy in all the cases, however, in 2 cases they were also given tranexemic acid to control bleeding pv, thus accounting for mention in medical management as well.
In a case of AUB M , patient was advicedmedroxy progesterone acetate till surgery as definitive management.
With the wide range of medicines available, it is possible to treat all the causes of AUB, except in few cases.Tranexemic acid was the first line treatment for control of bleeding where as far as hormonal treatment is concerened, norethisterone emerged as the main stay in control of bleeding due to varied etiologies.

Table no 7: Shows the Surgical management in patients with AUB according to etiology

AUB	Polypectomy	Hysterectomy	Laparotomy	Percentage among each type of AUB
P	6			100%
A+(A+P)		2		20%
L + (L+M)		2		14.28%
M		4		66.66%
O		0	1	2.04%

Total number of patients who requiredsurgical management were only 15%. AUB P was inevitably associated with surgical management with all patients requiring polypectomy as definitive management. However AUB M was the second highest category that required hysterectomy , even though medical management options are available. This was found mainly due to the perimenopausal age group of such patients along with severe anaemia which had to be treated with multiple blood transfusions and parenteral iron therapy, adding to the reluctance of both patient and doctor to advice medical management in such patients.Surgical management of AUB L depends on various factors, including age, presenting complaints , size of fibroids etc. Total abdominal hysterectomy was opted in patients who were perimenopausal and had completed their family.

IV. Discussion

AUB is the most common condition for which females approach their gynaecologists [4] . AUB is defined as any abnormality from normal menstrual cycle and includes any bleeding that is abnormal in volume, cycle, timing and continues in the majority for the past 6 months[5]. Although the definitive treatment of AUB is hysterectomy but non invasive options are also available. For deciding a patient appropriate treatment, it is first important to classify AUB which can be done using PALM COEIN classification. The present study was conducted to analyse the various treatment modalities of AUB with main focus on medical management. After obtaining ethical clearance from Institutional Ethics Committee, 100 cases were selected for the study.

As far as the type of AUB was concerned, majority patients in our study had AUB O (49%) followed by AUB L (14%). None of the cases had AUB C and AUB N (table 1). Ovulatory disorders accounted for majority of patients in the functional group while leiomyoma was the main aetiology in structural group. Our findings were supported by the study conducted bySingh PB et al.[6] where AUB O was the most common cause with the prevalence of (55.2%) followed by AUB L which accounted for (18.6%). On the other hand Mishra D and Sultan S et al.[7] found that leiomyoma was the leading cause of AUB in their study (41.1%) followed by ovulatory disorders (37.28%).

Anaemia is a major complication of AUB which can be corrected either by giving iron therapy or blood transfusions. In our study more patients were given iron therapy (23%) while only (6%) received blood transfusions. Similar findings were reported by Suseela TL et al.[8] from her study where maximum patients had received iron therapy (85%) while only (70%) received blood transfusions. Apart from iron therapy these (85%) cases were also given vitamin B, C, A and D, calcium supplements. In another study conducted by Govindaswamy D, Karunakaran P et al.[9] majority patients (90%) were prescribed ferrous sulphate for the correction of anaemia. In our study decision regarding the type of iron therapy was governed by certain factors like type of anaemia, affordability and patient compliance. Among various types, requirement of iron therapy was maximum in case of AUB M (42.8%) followed by AUB A (30%). Among 3 AUB M cases who required iron therapy, one received parenteral therapy while two received both oral and parenteral therapy. Patients with moderate anaemia were given both oral and parenteral iron therapy while those with severe anaemia received only parenteral therapy(table 2).Four AUB O caseshadreceived iron therapy. Among them three had received parenteral while one received both oral and parenteral therapy.Two among them were given iron sorbitol 10 doses, one received ferric carboxy maltose (FCM) followed by oral therapy and another one received FCM followed by iron sucrose and additionally one blood transfusion due to severe anaemia. With regards the requirement of blood transfusion AUB M cases had maximum requirement (28.5%)followed by AUB P (16.6%) .

As far as the requirement of antibiotic therapy is concerned KIT 6 was given to AUB O, I, E cases as patients had features of PID while only AUB P received metronidazole. Doxycycline was given to AUB A, M, O (table 5). Doxycyline was the most commonly prescribed antibiotic followed by KIT 6. Antibiotics were prescribed for prophylaxis and to treat infections like PID. In a study conducted by Suseela TL, Parveen S et al.[8], cephalosporins (44%) and nitroimidazole (44%) were the most commonly prescribed antibiotics. Among cephalosporins, cefixime (35%) was used most commonly followed by ceftriaxone (9%). In the study conducted byGovindaswamy D, Karunakaran P et al.[9], antibiotics were prescribed in (80%) patients. Most commonly used antibiotics were mebendazole (83%),doxycycline (63%), metronidazole (63%), cefixime (10%), ornidazole (6.6%).

Various medical options are available for AUB. Tranexemic acid can be used alone or in combination with norethisterone, medroxyprogesterone, combined pills, mifepristone. Our study concluded that tranexamic acid was the most commonly prescribed drug in all types of AUB.Tranexemic acid controls blood loss within short period of time with less side effects. In majority of patients tranexamic acid was used with hormonal therapy as they provide additional benefit of correcting irregular menstrual cycles by regulating hormonal balance in the body. Our finding was supported by Shobha Rani MS et al.[10] , Suseela TL et al.[8] and Govindaswamy D et al.[9] Suseela S et al reported from her study that out of 100 patients, 23 were prescribed tranexamic acid and mefenamic acid, 14 were prescribed only tranexamic acid, 12 patients were given cyclopam, 8 were given tranexamic acid, mefenamic acid and nor ethisteronewhile 6 patients were given tranexamic acid and norethisterone. On the other hand Shoba Rani et al.[10], stated from her study that tranexemic acid was given to 8 patients with AUB O,out of which 7 (87.5%) responded while 1 (12.5%) did not respond to it. Govindaswamy D et al.[9] also reported from his study that tranexamic acid was the most commonly prescribed anti-fibrinolytic agent. A contradictory result was reported by Bhuvanaswari et al.[11], where they found mefenamic acid is most prescribed anti-fibrinolytic agent. Another study conducted by Ramalingam k et al.[12] reported that anti fibrinolytics were the most commonly prescribed class in AUB and among them tranexamic acid was most commonly used (88.6%). In a study conducted by Bhubaneshwari S, Balasubramaniyam V et al.[11] the authors reported that NSAIDS were the most commonly used drug (61%) followed by progesterone derivatives and oral contraceptive pills. Among NSAIDs commonly used was mefenamic acid alone or in combination with tranexamic acid or dicyclomine. Among progesterone derivatives (64%) cases were treated with medroxy progesterone while (36%) received norethisterone.

AUB O,the most common type found in puberty and peri menopausal age results due to hypothalamic pituitary dysfunction. Main factors which influence HPO axis include PCOS, thyroid disorders, hyperprolactinemia, obesity, weight loss, stress[13]. Since multiple factors contribute to AUB O, the medical management consisted of drugs like cabergoline alone or in combination with norethisterone and thyroxin, OCPs, tranexamic acid, N-acetyl cysteine, myoinositol, metformin.

Out of 100 cases only 15% cases required surgical treatment(table 7). Polypectomy was done in all cases of AUB P. Majority AUB M cases underwent TAH (total abdominal hysterectomy). This was because maximum patients with AUB M were peri menopausal and presented with severe anaemia. Similarly only 32% cases underwent surgical treatment in the study conducted by Suseela TL et al.[8] This was because removal of uterus leads to surgical menopause which inturn is responsible for many cardiovascular and bone related problems.

Most commonly performed surgery in our study was TAH (8%). This was supported by the study conducted bySuseela TL et al.[8] In our study maximum TAH were performed in case of AUB M (66.6%) which is in contrast to the study conducted by Suseela TL et al.[8] were maximum TAH were done in patients with leiomyoma (41.46%). Mostly the patients were above 40 years of age and did not improve on medical management. Similar results were reported byKahveci B et al.[14] in their study with hysterectomy (90%) being the most commonly performed surgery followed by polypectomy (5%) and myomectomy (4.7%).k MS et

V. Conclusion

Patients having AUB M were found to have required most treatment, be it in terms of parenteral iron therapy, blood transfusions, or surgery, however LNG IUS may be a better option in AUB M (endometrial hyperplasia without atypia)than hysterectomy. Medical management, especially with norethisterone is the main say of treatment in case of AUB with non structural causes, and has shown excellent results. .In case of AUB with structural cause , surgical management is a significant treatment modality.

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