

An analytical study of abnormal uterine bleeding in women of child bearing age group

Dr. Radhika Parmar¹, Dr. Aditi Atodaria², Dr. Tulsi Patel³, Dr. Kishor Chauhan^{4*}

¹M.D (Obstetrics and gynecology), AssociProfessor, Department of obstetrics and gynecology , Smt.B.K.Shah Medical Institute & Research Centre, Sumandeep Vidyapeeth Deemed to be university, waghodia, Vadodara. District 391760, Email:radhikaparmar2105@gmail.com Contribution: Concept, Planning, Literature review, Manuscript preparation.

²second year Resident doctor (obstetrics and gynecology) , Department of obstetrics and gynecology, Smt.B.K.Shah Medical Institute & Research Centre, Sumandeep Vidyapeeth Deemed to be university, waghodia, Vadodara. District 391760, Email:aditiatodaria16@gmail.com Contribution: Data Collection.

³Second year Resident doctor (obstetrics and gynecology) , Department of obstetrics and gynecology, Smt.B.K.Shah Medical Institute & Research Centre, Sumandeep Vidyapeeth Deemed to be university, waghodia, Vadodara. District 391760, Email:tulsip1510@gmail.com Contribution: Data Collection.

^{4*}M.D (Obstetrics and gynecology), Professor and head of Department, Department of obstetrics and gynecology , Smt.B.K.Shah Medical Institute & Research Centre, Sumandeep Vidyapeeth Deemed to be university, waghodia, Vadodara. District 391760, Email:kishorchauhan52@yahoo.com Contribution: Literature review and Data Collection.

***Corresponding author:** Dr. Kishor Chauhan
Email:kishorchauhan52@yahoo.com

ABSTRACT INTRODUCTION

AUB is defined as any variation from the normal menstrual cycle. It includes alteration in its frequency, regularity of menses, duration of flow and amount of blood loss AUB can further be divided based on regularity, volume, frequency, duration, chronicity and timing in relation to the reproductive status.

In India, the reported prevalence of AUB is 17.9%. It can occur any time between menarche to menopause.

A good clinician tries to recognize and identify the causative factors responsible for the disease, reverse the abnormality and induce or restore the cyclic predictable menses which should have normal volume and duration.

MATERIALS AND METHOD

SOURCE OF DATA: 200 cases of AUB were taken for our study from the Department of Obstetrics and Gynecology, in our institute between November 2017 to May 2019. Patients coming in the O.P.D. or the ones that were admitted in the Gynecology ward for the complaints of AUB, fitting the selection criteria were included in the study.

SELECTION CRITERIA:

INCLUSION CRITERIA:

Women aged 15-45 yrs.

Cases of Abnormal uterine bleeding, attending the gynecology OPD with complaints of heavy menstrual bleeding, heavy and frequent bleeding, frequent bleeding, infrequent bleeding

EXCLUSION CRITERIA:

Pregnancy and related complications. Women with normal menstrual cycles

Women taking drugs like anticoagulants, glucocorticoids or tamoxifen, which can cause abnormal uterine bleeding

Women with Pelvic inflammatory diseases Women who have IUD inserted.

RESULT AND DISCUSSION:

After applying the inclusion and exclusion criteria, 200 cases were selected for my study. A/B is more common in the age group 41-45 years, suggesting it is more towards the perimenopausal age group. It is seen more in multiparous women and women with previous surgeries on uterus and adnexa. Heavy Menstrual Bleeding is the most common complaint. Endometrial Hyperplasia was the most common finding on ultrasound examination. Medical therapy was beneficial in some patients, rest had to undergo surgical intervention later. Hysterectomy is used as a final measure. Vaginal Hysterectomy is preferred.

CONCLUSION:

It is observed that AUB is more common towards the end of 4th decade of life, in the peri-menopausal age group, that too more in multiparous women. Surgical intervention on the uterus and adnexa are also associated with AUB. Heavy Menstrual Bleeding is the most common presenting complaint. Clinical examination correlates well with the ultrasound findings, however, transvaginal sonography is very accurate in assessing the endometrium as well as uterus and adnexa and diagnosing their abnormalities.

Medical Therapy is still the first line of management in most cases which includes progestogens, combined oral contraceptive pills or a combination of tranexamic acid and mefenamic acid.

Dilatation and Curettage still holds a role in diagnosis and has therapeutic effect as well. But should be used along with hysteroscopy for better results. LNG-IUS gives very good result in suitable cases.

Hysterectomy is the final measure if everything else fails. Vaginal hysterectomy is preferred wherever possible.

INTRODUCTION

Menstrual disorders are a common indication for medical visits among women of reproductive age group, among which abnormal uterine bleeding (AUB) is the most common condition. AUB is defined as any variation from the normal menstrual cycle, including alteration in its regularity, frequency of menses, duration of flow, and amount of blood loss. AUB is further subdivided based on volume of menstruation, regularity, frequency, duration, chronicity, and timing related to reproductive status.

AUB is reported to occur in 9-14% women between menarche and menopause. In India, the reported prevalence of AUB is 17.9%. However, the accurate prevalence is very difficult to estimate.

AUB can occur at any age in various forms and has different modes of presentation. Abnormal uterine bleeding during reproductive age can result from a broad spectrum of conditions ranging from physiological process to malignant lesions involving organic, systemic, and hormonal responses.

Heavy menstrual bleeding is the most common complaint of AUB. It has been defined as "excessive menstrual blood loss which interferes with the women's physical, social, emotional, and/or quality of life [that] can occur alone or in combination of other symptoms.*"

Abnormal uterine bleeding is a symptom and not a disease. It occurs in various forms, which may be categorized in two broad categories'.

- 1) Due to organic causes
- 2) Dysfunctional uterine bleeding - Anovulatory and ovulatory

Acute AUB

"An episode of bleeding in a woman of reproductive age, who is not pregnant, that is of sufficient quantity to require immediate intervention to prevent further blood loss

Chronic AUB

"Bleeding that is abnormal in duration, volume and/or frequency and has been present of most of the last 6 months.

Earlier, increased amount, duration or flow of menses in absence of structural etiology was called "dysfunctional uterine bleeding". However, after 2011, the FIGO classification system (PALM-COEIN) was published. This included DUB as a part of AUB. DUB affects 20-30% of all women and 12% of them are referred to gynecologist.

Abnormal uterine bleeding is one of the most common complaints that the patient presents with in the OPD. During transitions in the puberty to adulthood, perimenopause and menopause, cycles become irregular.

The key to successful clinical management is to recognize or identify the causative factors responsible. This can be achieved by clinical examination and various imaging modalities such as ultrasonography, hysterosalpingography, CT scan and MRI. The aim of the clinician is to reverse the abnormality and induce or restore the cyclic predictable menses of normal volume and duration. By operative procedure such as Hysteroscopy, D & C, Endometrial Biopsy, Hysterectomy, it is possible to do the histopathological examination. This gives the diagnosis. It is possible to treat it by various medical therapies and operations.

AIM AND OBJECTIVES AIM:

Analytical study of various etiopathological factors responsible for AUB in women aged 15-45 years.

OBJECTIVES:

1. To study the various abnormal patterns of bleeding presenting in reproductive age group.
2. To study the etiology, pre-disposing and associated factors of AUB.
3. To study the various histopathological changes in the uterus, and their subsequent treatment in cases of AUB,
4. To study the various treatment options available for AUB.
5. To assess the outcome and effect of each treatment modality for AUB.

MATERIALS AND METHOD

This prospective, analytical and observational study was carried out in the Dhiraj General Hospital, Piparia, Vadodara. It is a tertiary health care centre serving the people of rural area primarily. We enrolled patients of O.P.D. and the patients that were admitted in the gynecology ward. 200 cases of AUB who met all the inclusion and exclusion criterias, were taken for our study from the Department of Obstetrics and Gynecology of Dhiraj Hospital, between November 2017 to May 2019. Informed Consent for participation was taken from the subjects. Only those who gave consent were enrolled in the study.

INCLUSION CRITERIA:

Women aged 15-45 yrs.

Cases of Abnormal uterine bleeding, attending the gynecology OPD with complaints of heavy menstrual bleeding, frequent menstrual bleeding, prolonged bleeding, heavy and frequent bleeding, infrequent bleeding.

EXCLUSION CRITERIA:

Pregnancy and related complications. Women with normal menstrual cycles.

Women taking drugs like anticoagulants, glucocorticoids or tamoxifen, which can cause abnormal uterine bleeding

Women with Pelvic inflammatory diseases

- Women who have IUD inserted.

STUDY PERIOD:

The study was conducted for a period of one and half year ie. November 2017 to May 2019. **SAMPLE SIZE:**

The sample size was calculated by the formula given below: $n = (Z^2 * P(1 - P)) / (d^2)$

where n = Sample size.

Z = Z statistic for a level of confidence,

P = Expected prevalence or proportion (If the expected prevalence is 20%, then P = 0.2) and d

= (If the precision is 5%, then d = 0.05)

Sample size came out to be 200 patients by considering the prevalence as 17.9%.

Once the subjects were found eligible for participation in the study and were willing to participate, they were explained in detail about the purpose and their role in the study in the language they understood. They were explained that they will not bear any extra expenditure for the purpose of the study. Patients were given an opportunity to clarify any issue related to the study and were encouraged to ask questions. Confidentiality of the patients was maintained at all levels.

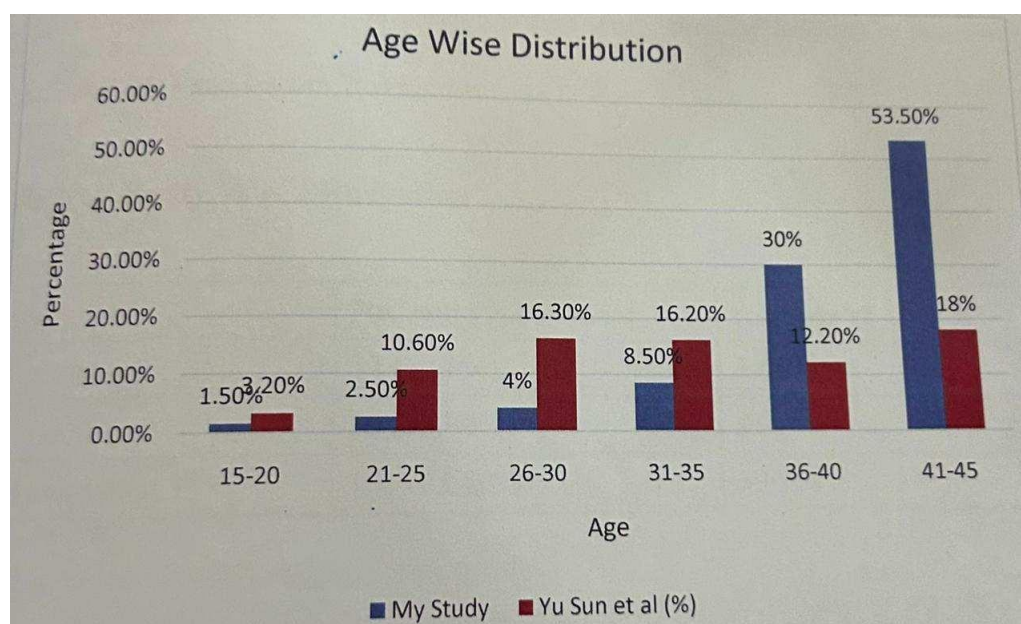
Participant Information Sheet, Informed Consent Form and Informed Assent form in all languages can be found in the Annexures.

Observation, Results & Discussion OBSERVATIONS, RESULTS AND DISCUSSION INCIDENCE:

The accurate incidence of AUB is difficult to establish because even the normal variation in menstrual cycle during the transition phase may be considered as abnormal bleeding by the patient. In this study, 200 cases of AUB, that fitted the inclusion criteria were taken.

Age distribution in patients in our study and comparison with a study done by Yu Sun et al is shown in the Table 1 and Figure 1 below:

Age wise distribution	No and% of cases	Yu sun et al 61(%)
15-20	3(1.50%)	3.20%
21-25	5(2.50%)	10.60%
26-30	8(4.00%)	16.30%
31-35	17(8.50%)	16.20%
36-40	60(30.00%)	12.20%
41-45	107(53.50%)	18%



15% of AUB cases in Yu Sun et al were between 46-55 years of age. But our study is restricted to the reproductive age

group, and thus women between age group 16.55 years are excluded from our study,

The maximum number of the patients were in the age group 41-45 years (53.5%), Followed by 36-40 years (30%). This shows that AUB is more common in the early 40s and late 30s, the later spectrum of the reproductive age group.

These findings are consistent with a study done by Yu Sun et al, which showed 23.5% in the age group 46-55 years, followed by 18% in the 41-45 years age group

Epidemiological Factors Influencing AUB

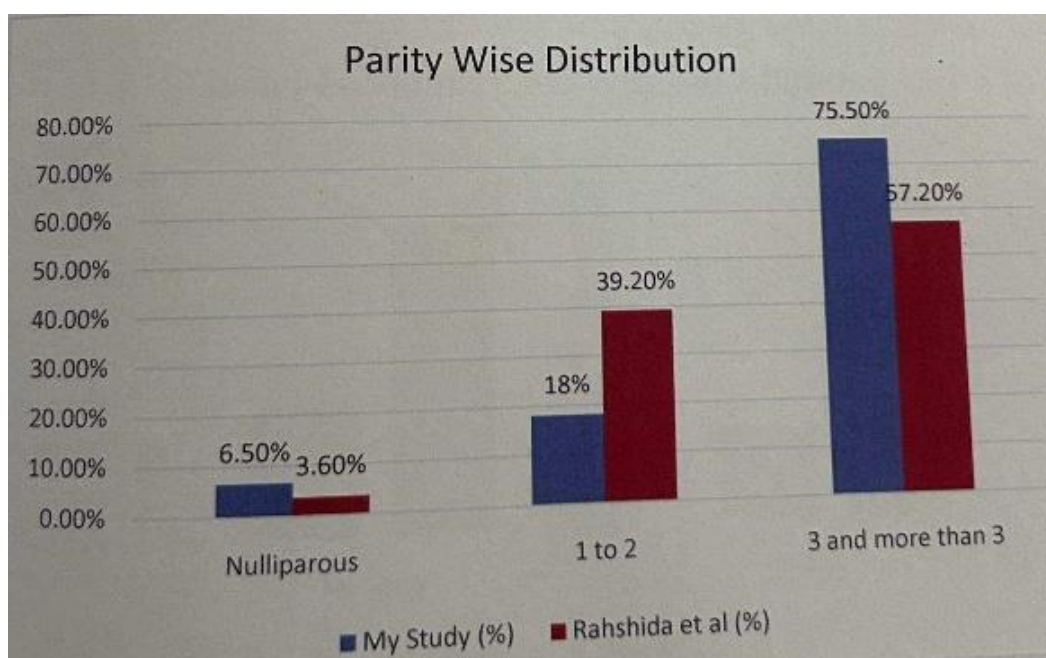
Epidemiological factors that appear to be associated with AUB are parity, socio economic class, previous history of any pelvic surgeries including tubal sterilization.

Parity wise

Table 2(a)) and Figure 2(a) below Table 2(a): Parity Wise Distribution

Parity	No.and(%) of cases	Rashida et al 62 (%)
Nulliparous	13 (6.50%)	3.6%
1-2	36(18.00%)	39.2%
3 and more than 3	151(75.50%)	57.2%

distribution and comparison with a study done by Rashida et al is shown



Maximum number of patients were multiparous, of higher parity (75.5%), having 3 or more than 3 children. Similar results were found by Rashida et al (57.2%). Also, 77 out of the 200 patients had history of one or more abortions (spontaneous or induced).

Observation, Results & Discussion

Traditionally, it is believed that nulliparity predisposes to endometrial hyperplasia, leading to AUB). However, our results contradict that and show that most patients of AUB are of higher parity.

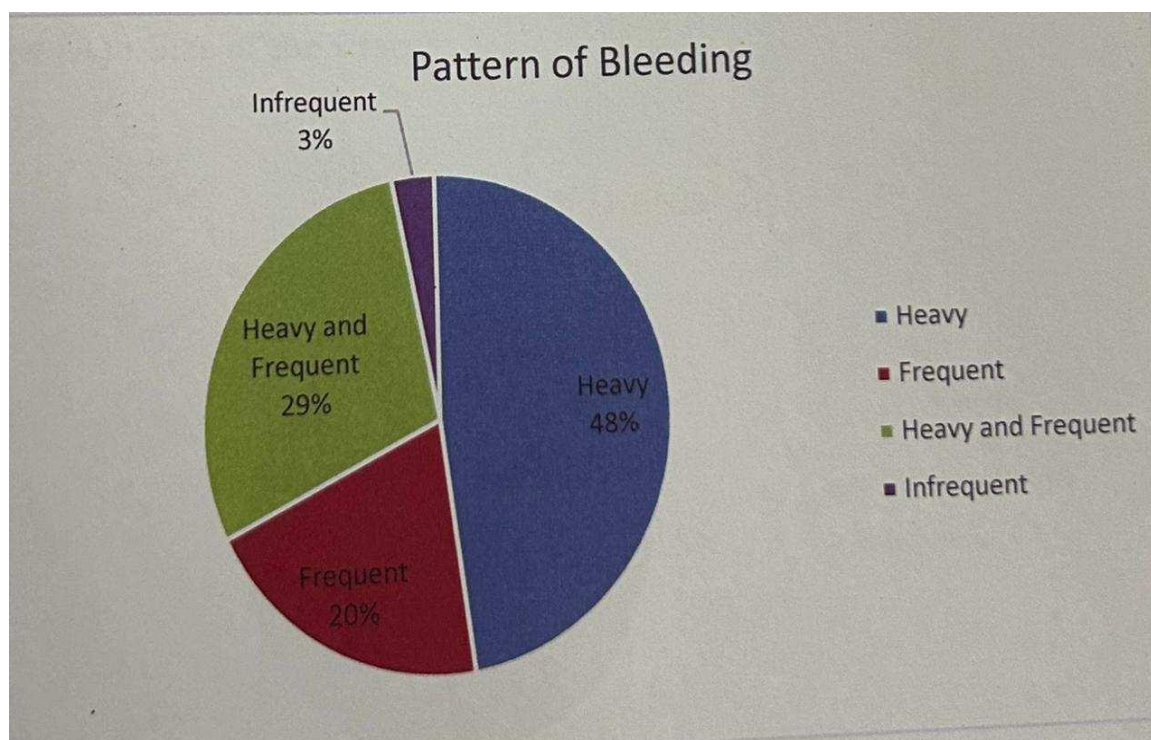
A Modified Prasad scale was used for assigning the socioeconomic class Table 2(B): Socio-Economic Class Wise Distribution

Socio economic class	No and% of cases	Rashida et al 62
III	58(29.00%)	21.56%
IV	142(71.00%)	78.44%

Patients belonging to lower socio-economic class were maximum (71%), signifying the importance of its association to AUB. Rashida et al also shows similar results.

Our hospital, being a general tertiary care hospital in a rural locality providing free services to the people and operations are free of cost as well, caters mainly to a lower socio-economical class society.. Table Patterns of Uterine Bleeding

Pattern of bleeding	No. and % of cases
Heavy	96(48.00%)
Frequent	40(20.00%)
Heavy and frequent	58(29.00%)
Infrequent	06(03.00%)

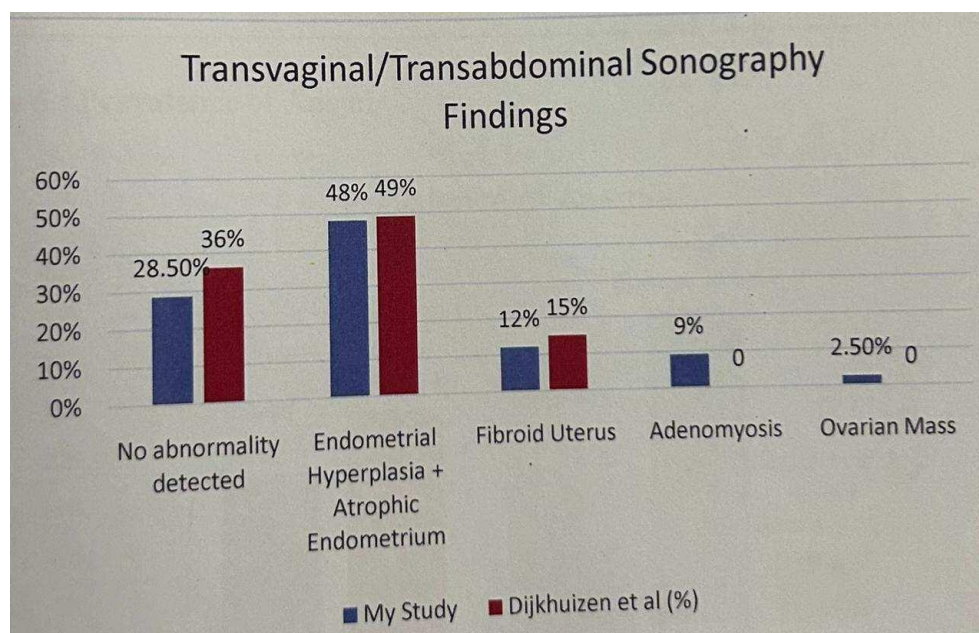


Heavy Menstrual Bleeding (48%) was the most common presentation in women. Patients presenting with heavy and frequent bleeding (29%) were next, followed by frequent bleeding (20%).

Patients with infrequent bleeding (3%) were the least. Infrequent bleeding was probably due to immature development of the Hypothalamo-pituitary ovarian axis of the women in the early reproductive age group. Since the women in our study are from lower socio-economic class, they are more likely to be malnourished and anemic.

Table : Transvaginal/Transabdominal Sonography Findings

TVS/TAS Findings	No. And % of cases	Dijkhuizen et al (%)
No abnormality detected	57(28.50%)	36%
Endometrial hyperplasia+atrophic endometrium	93(46.50%)+03(1.50%)	49%
Fibroid uterus	24(12.00%)	15%
Adenomyosis	18(09.00%)	-
Ovarian mass	05(2.50%)	-;



All 200 women underwent either transabdominal or transvaginal sonography, out of which 57(28.5%) had no abnormality at all. USG findings of a bulky uterus in 42 (21%) patients were already clinically detected by bimanual examination. USG was very accurate in detecting endometrial abnormalities and 93 (46.5%) patients had endometrial hyperplasia while 3 (1.5%) had atrophic endometrium. These findings are similar to a study done by Dijkhuizen et al. In his study, 36% of the patients had no abnormalities while in our study 27.5% patients had the same finding. Endometrial hyperplasia atrophic endometrium was seen in 48% patients in our study, while it was 49% in his study. 15% patients had Fibroid Uterus in study. while in our study 12% patients had fibroid uterus. "

These findings are similar to a study done by Dijkhuizen et al. In his study, 36% of the patients had no abnormalities while in our study 27.5% patients had the same finding. Endometrial hyperplasia atrophic endometrium was seen in 48% patients in our study, while it was 49% in his study. 15% patients had Fibroid Uterus in study. while in our study 12% patients had fibroid uterus. "

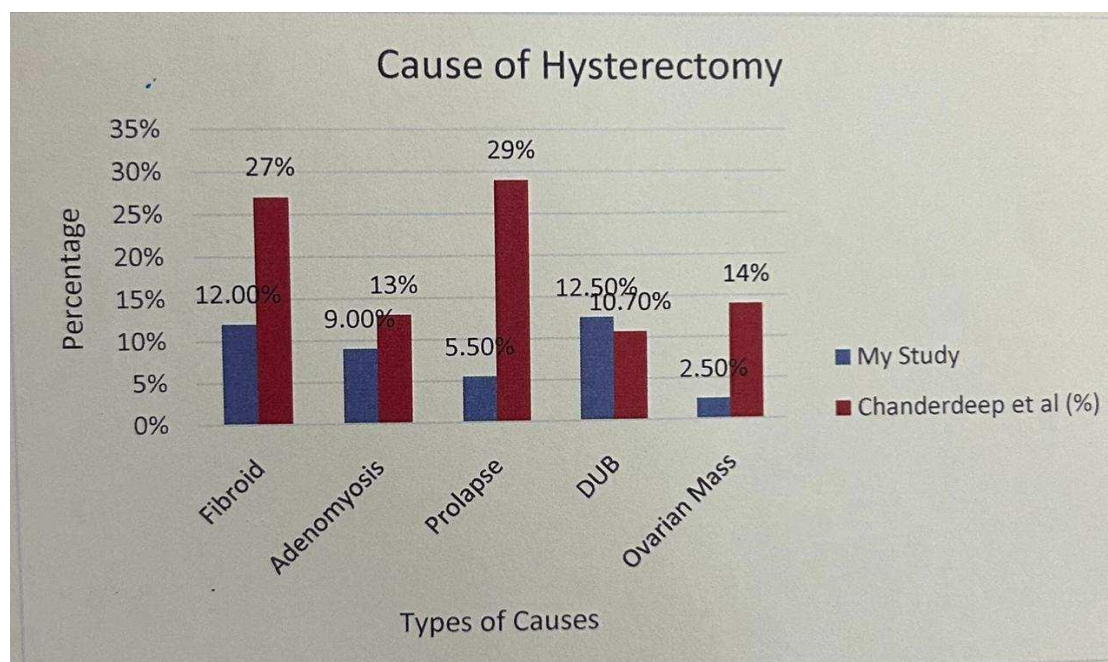
Table 10: Histopathology of D & C Material

Endometrial pattern	No. and % of cases	Nadia et al (%)
Proliferative	65(32.50%)	45%
Secretory	31(15.50%)	21.6%
Hyperplasia	26(13.00%)	30.6%
Irregular Ripening	7(3.50%)	1.96%
Atrophic	03(1.50%)	0.98%

Endometrial Sampling was done in 132 (66%) women. D & C was done in 108 patients as a therapeutic as well as diagnostic procedure for an acute episode of bleeding and 24 patients were offered curettage for endometrial biopsy. 65(32.5%) of the women had a proliferative endometrium, which suggests that the cycles were anovulatory. In 26 (13%) women, endometrial hyperplasia was seen indicating unopposed action of the estrogen. 3 cases of endometrial hypoplasia were also seen. In a study conducted by Nadia et al, similar results were seen. In that study, 45% of the cases had proliferative endometrium and 30.6% had endometrial hyperplasia, while in our study 32.5% women had proliferative endometrium while 13% women had endometrial hyperplasia.

Table 12(b): Individual Causes of Hysterectomy

Histopathology in hysterectomy	No. and % of cases	Chanderdeep et al 72(%)
Fibroid	24(12.00%)	27%
Adenomyosis	18(9.00%)	13%
Prolapse	11(5.50%)	29%
DUB	25(12.50%)	10.7%
Ovarian mass	5(2.50%)	14%



25 (12.5%) women underwent hysterectomy for DUB which was maximum out of all the causes. This is mostly seen in the perimenopausal age group. All other causes like Fibroid (12%), Adenomyosis (9%) and Prolapse (5.5%) have similar numbers.

In a study done by Chanderdeep et al, these findings are different. More hysterectomies were done for cases of prolapse (29%), while in our study only 5.5% hysterectomies were done for prolapse. 27% women underwent hysterectomy for fibroid in study by Chanderdeep et al, while in our study only 12% underwent hysterectomy for the same.

CONCLUSION

AUB is a fairly common condition in the reproductive age-group and needs to be tackled tactfully. It contributes significantly to the ill health of the woman and affects the quality of life.

It is observed that AUB is more common towards the end of 4th decade of life, in the peri-menopausal age group, that too more in multiparous women. Surgical interventions on the uterus and adnexa like Caesarean Section, Tubal Sterilization or D and E, is a strong contributing factor to the occurrence of AUB. Hence, reducing the number of conceptions and surgical interventions may contribute to decrease in the prevalence of AUB.

Heavy Menstrual Bleeding is the most common bleeding pattern.

Clinical examination correlates well with the USG findings and is a reliable method of evaluation. There is a poor correlation between the size of the uterus and severity of AUB. Most of our patients had normal sized uterus on examination.

Trans-vaginal Sonography (TVS) is a fairly effective procedure to detect the cause and hence should be used as a first line imaging procedure in all patients, when available. Proper diagnosis should be made before starting the treatment for better results.

Medical Therapy is still the first line of management in most cases of AUB. Hormonal therapy depends on the age of the patient, other risk factors and regularity of the cycle. Usually, in the later age group, progestogens are used as the first line therapy. Both progestogens and combined OC pills have similar efficacy in reduction of bleeding, COCs have the advantage of cycle regulation as well as contraception.

Tranexamic Acid reduces menstrual blood loss, but it does not affect the underlying cause of bleeding. However, they are not preferred in acyclical bleeding.

Endometrial ablation techniques can be used as an alternative to hysterectomy. They are patient friendly and reduces hospital stay. However, these techniques require expertise and high cost instruments. These are not available in our institute, so they could not be used.

LNG-IUS has an advantage of being reversible and has excellent results. However due to high cost, it is less popular especially in our setup.

Hysterectomy may be used as a final measure, but like with any other major surgery, it has its own complications and sequelae. Vaginal hysterectomy should be undertaken as far as possible as it is associated with less morbidity and mortality. Several factors are to be considered before choosing any treatment modality. Involving patients in the decision making is imperative to increase the success rate of any treatment. All pros and cons of a treatment modality must be explained to

the patient, helping them to choose what is in the best interest of the patient. Best treatment should be offered to the patient.

BIBLIOGRAPHY

1. Munro MG. Abnormal uterine bleeding. Cambridge: Cambridge University Press; 2010.
2. Fraser IS, Langham S, Uhi-Hochgraeber K. Health-related quality of life and economic burden of abnormal uterine bleeding. *Expert Rev Obstet Gynecol.* 2009;4:179-89.
3. Sharma A, Dogra Y. Trends of AUB in tertiary center of Shimla hills. *J Midlife Health* 2013;4:67-68
4. National Collaborating Centre for Women's and Children's Health, National Institute for Health and Care Excellence. NICE guidelines CG44: heavy menstrual bleeding London: Royal College of Obstetricians and Gynaecologists, 2007.
5. Jeffcoate's principles of Gynaecology 8th Edition Chapter 38 Page 560.
6. Jeffcoate's principles of Gynaecology 8th Edition Chapter 38 Page 566.
7. Progress 16th Alexander Taylor, Management of DUB
8. Cochrane database of systematic reviews 2005.
9. Jeffcoate's principles of Gynaecology 8th Edition Chapter 4 Page 72
10. Widmaier, Eric P.; Raff, Hershel; Strang, Kevin T. (2010). *Vander's Human Physiology: The Mechanism of Body Function* (12th ed.). New York, NY: McGrawHill. pp. 555-631
11. Silverthorn, DeeUnglaub (2013). *Human Physiology: An Integrated Approach* (6th ed.). Glenview, IL: Pearson Education, Inc. pp. 850-890
12. Mark A Fritz and Leon speroff/clinical gynaecology endocrinology and fertility/8th edition/15th chapter/pg 593.
13. Munster K, Schmidt L, Helm P. Length and variation in the menstrual cycle a cross-sectional study from a Danish county, *BJOG: An International Journal of Obstetrics and Gynaecology*, 99(5), 422-429.
14. Belsey EM, Pinol APY, and Task Force on Long-Acting Systemic Agents for Fertility Regulation, Menstrual bleeding patterns inuntreated women, *Contraception* 55:57, 1997.
15. Treloar AE, Boynton RE, Behn BG, Brown BW, Variation of thehuman menstrual cycle through reproductive life, *Int J Fertil* 12:77,

Bibliography BIBLIOGRAPHY

1. Munro MG. Abnormal uterine bleeding. Cambridge: Cambridge University Press; 2010.
2. Fraser IS, Langham S, Uhi-Hochgraeber K. Health-related quality of life and economic burden of abnormal uterine bleeding. *Expert Rev Obstet Gynecol.* 2009;4:179-89.
3. Sharma A, Dogra Y. Trends of AUB in tertiary center of Shimla hills. *J Midlife Health* 2013;4:67-68
4. National Collaborating Centre for Women's and Children's Health, National Institute for Health and Care Excellence. NICE guidelines CG44: heavy menstrual bleeding London: Royal College of Obstetricians and Gynaecologists, 2007.
5. Jeffcoate's principles of Gynaecology 8th Edition Chapter 38 Page 560.
6. Jeffcoate's principles of Gynaecology 8th Edition Chapter 38 Page 566.
7. Progress 16th Alexander Taylor, Management of DUB
8. Cochrane database of systematic reviews 2005.
9. Jeffcoate's principles of Gynaecology 8th Edition Chapter 4 Page 72
10. Widmaier, Eric P.; Raff, Hershel; Strang, Kevin T. (2010). *Vander's Human Physiology: The Mechanism of Body Function* (12th ed.). New York, NY: McGrawHill. pp. 555-631
11. Silverthorn, DeeUnglaub (2013). *Human Physiology: An Integrated Approach* (6th ed.). Glenview, IL: Pearson Education, Inc. pp. 850-890
13. Mark A Fritz and Leon speroff/clinical gynaecology endocrinology and fertility/8th edition/15th chapter/pg 593.
14. Munster K, Schmidt L, Helm P. Length and variation in the menstrual cycle a cross-sectional study from a Danish county, *BJOG: An International Journal of Obstetrics and Gynaecology*, 99(5), 422-429.
15. Belsey EM, Pinol APY, and Task Force on Long-Acting Systemic Agents for Fertility Regulation, Menstrual bleeding patterns inuntreated women, *Contraception* 55:57, 1997.
16. Treloar AE, Boynton RE, Behn BG, Brown BW, Variation of thehuman menstrual cycle through reproductive life, *Int J Fertil* 12:77,

Bibliography

1. Fraser IS. Critchley HOD, Munro MG, Broder M, Writing Group for this
2. Menstrual Agreement Process. A process designed to lead to international agreement on terminologies and definitions used to describe abnormalities of menstrual bleeding. *Fertil Steril* 2007;87(3):466-476
3. Mark A Fritz and Leon speroff clinical gynaecology endocrinology and fertility/8th edition/15th chapter/pg 595
4. Munro MG, Critchley HO, Border MS, Fraser IS, FIGO Working Group on menstrual disorders. FIGO classification system (PALM-COEIN) for causes of abnormal uterine bleeding in nongravid women of reproductive age. *Int J Gynaecol Obstet* 2011;113:313.
5. American College of Obstetricians and Gynecologists. ACOG Practice Bulletin. Clinical management guidelines for obstetrician-gynecologists number 34, February 2002. Management of infertility caused by Gynecol. 2002, 99: (2): 347-358.



6. Jeffcoate's principles of Gynaecology 8th Edition Chapter 4 Page 80.
7. Telinde's operative gynecology/10th edition/26th chapter/pg 589.
8. Mark A Fritz and Leon speroff/clinical gynaecology endocrinology and fertility/8th edition/15th chapter/pg 593.
9. Jeffcoate's principals of gynaecology/8th edition/chapter 38/pg 566-567.
10. Mark A Fritz and Leon speroff/clinical gynaecology endocrinology and fertility/8th edition/17th chapter/pg 681.
11. National Center for Complementary and Alternative Medicine. Menopausal Symptoms and Complementary Health Practices Accessed 1/16/2015.
12. Pekker, M.and profile, V. my complete (2013) Indian women and menopause. Available at: <http://menopause-aid.blogspot.in/2013/07/indian-women-andmenopause.html> (Accessed: 11 January 2017).
13. Vollman RF. The Menstrual Cycle. Philadelphia, PA: W.B. Saunders; 1977
14. Soules MR, Sherman S, Parrott E, et al. Executive summary: Stages of Reproductive Aging Workshop (STRAW). Climacteric 2001;4:267-272
15. NICE quality standards. <http://www.nice.org.uk/guidance/QS47> Heavy menstrual bleeding.
16. Vercellini P, Cortesi I, Oldandi S, Moschetta M, DeGiorgi O, Crosignani PG. The role of transvaginal ultrasonography and outpatient diagnostic