

A TWO YEAR CLINICOPATHOLOGICAL STUDY OF NON-GRAVID WOMEN WITH ABNORMAL UTERINE BLEEDING IN A RURAL TERTIARY CARE CENTRE IN TAMILNADU: IN CONCURRENCE WITH THE FIGO RECOMMENDATIONSJonathan Arnold A. P¹, Srivani Saravanan²**HOW TO CITE THIS ARTICLE:**

Jonathan Arnold A. P, Srivani Saravanan. "A Two Year Clinicopathological Study of Non-Gravid Women with Abnormal Uterine Bleeding in A Rural Tertiary Care Centre In Tamilnadu- in Concurrence with The Figo Recommendations". Journal of Evolution of Medical and Dental Sciences 2015; Vol. 4, Issue 63, August 06; Page: 10990-11000, DOI: 10.14260/jemds/2015/1585

ABSTRACT: CONTEXT: Abnormal uterine bleeding (AUB) is a very common symptom in gynecology practice which is associated with a plethora of pathologies. The new definitions, terminology and PALM-COEIN classification helps to standardize and streamline the causative factors of AUB. **AIMS:** To collect clinical and histopathology data based on the new terminologies and definitions for AUB, to stratify the causes of abnormal uterine bleeding based on the PALM-COEIN classification and to correlate the clinical and pathological features. **MATERIALS AND METHODS:** Medical records of all non-gravid women with AUB who underwent hysterectomy were collected from January 2014 to May 2015. Clinical details, coagulation profile, gross and microscopic findings of the hysterectomy histopathology samples were noted. Pregnant women and those who underwent procedures other than hysterectomy were excluded. The PALM-COEIN classification was used to categorize the causes of AUB. The data were analyzed and percentages of each category studied were calculated. **RESULTS:** A total of 174 cases were included in which 49% were in the 41-50 age groups. Heavy menstrual bleeding (HMB) was seen in 43.7% cases while 17.2% and 12.6% had irregular and frequent menstrual bleeding respectively. 53.4% had adenomyosis, 47.1% had leiomyoma, 17.2% had ovulatory disorders, 15% had polyps and 15% had endometrial hyperplasia/carcinoma. 48.9% of patients had a single pathology while 51.1% cases had several combinations of pathologies. **CONCLUSION:** The new standardized terminology, definitions and PALM-COEIN classification for AUB formulated by FIGO helps in uniform conduct of research and international comparison of data which was not possible earlier due to confusing terms. Maximum number of patients was in the 41-50 age groups. The most common clinical presentation was HMB. Adenomyosis was the most common pathology seen (AUB-A) followed by leiomyoma (AUB-L) and ovulatory disorders (AUB-O). Nearly half the patients had only a single pathology while the rest had multiple pathologies. In the latter, the precise cause of AUB could not be ascertained by histopathology alone. Further studies are required in this area.

KEYWORDS: Abnormal Uterine Bleeding (AUB), International Federation of Gynecology and Obstetrics (FIGO), PALM-COEIN Classification, Hysterectomy, Histopathology.

INTRODUCTION: Confusing terminology has hampered the accurate analysis of abnormal uterine bleeding (AUB) aetiology. To sort this out the International Federation of Gynaecology and Obstetrics (FIGO) have updated the terminology, definitions and classification of AUB.^{1,2} Accordingly, Chronic AUB is defined as any bleeding from the uterine corpus that is abnormal in duration, volume, and/or frequency and has been present for the majority of the last 6 months. AUB is a very common symptom in gynaecology practice for which there are multiple causes.

ORIGINAL ARTICLE

The PALM-COEIN Classification System is the new classification for Causes of AUB and is composed of PALM: Visually objective structural criteria; COEI: unrelated to structural anomalies; N: entities Not yet classified [refer Table 4]. There are not many studies with the new classification system in our area.

The objectives of our study are to collect clinical and histopathology data based on the new terminologies and definitions for abnormal uterine bleeding put forth by FIGO, to stratify the causes of abnormal uterine bleeding based on the PALM-COEIN classification and to correlate the clinical and pathological features.

MATERIALS AND METHODS: This is a descriptive study which was conducted in the department of pathology, Dhanalakshmi Srinivasan Medical College and Hospital [DSMCH], Siruvachur, Perambalur after obtaining institutional ethical committee clearance. The study population included the medical records of all non-gravid women patients who had symptoms of AUB and had hysterectomy between January 2014 and May 2015. Data assessed included patient age, parity, menstrual and past history and hormonal/coagulopathy treatment. The patients' prothrombin time (PT) and partial thromboplastin time (APTT) were noted. The gross and microscopic findings of the hysterectomy histopathology samples were noted. Women who did not have abnormal uterine bleeding, or pregnant or who underwent procedures other than hysterectomy (endometrial & cervical biopsies) were excluded. The PALM-COEIN classification was used to categorize the causes of AUB. The data were analyzed and percentages of each category studied were calculated.

RESULTS:

Age Group	No.	%
30-40	77	44.2
41-50	85	49
51-60	11	6.3
>60	1	0.5
Total	174	100

Table 1: Patient Age Distribution

There were 174 cases of Abnormal Uterine Bleeding (AUB). Table 1 shows that Maximum number of patients was in the 41-50 age groups (49%cases) followed by 30-40 years (44.2% cases).

Parity	No.	%
Para 1	13	7.5
Para 2	66	38
Para 3	67	38.5
Para 4 and above	23	13.2
Nulliparous	5	2.8
Total	174	100

Table 2: Parity

Most were multiparous in which 38% had a parity of 2 and 38.5% with a parity of 3 [Table 2]. This was followed by parity of four (13.2%).

ORIGINAL ARTICLE

Among the patients, 42.5 % (74 cases) had associated complaints of dysmenorrhea while the rest (57.5%/100 cases) did not.

SYMPTOM	No.	%
Heavy menstrual bleeding (HMB) *	76	43.7
Irregular Menstrual Bleeding †	30	17.2
Absent Menstrual Bleeding‡	1	0.6
Frequent Menstrual Bleeding §	22	12.6
Infrequent Menstrual Bleeding	16	9.2
Prolonged Menstrual Bleeding **	24	13.8
Heavy & Prolonged menstrual bleeding	16	9.2
Shortened Menstrual Bleeding ††	31	17.8
Postmenopausal Bleeding (PMB) ‡‡	11	6.3
Irregular Nonmenstrual Bleeding ***	2	1.1

Table 3. Abnormal uterine bleeding symptomatology

Footnote: The definitions of AUB symptoms^{2,3}:

- Excessive menstrual blood loss that interferes with the woman's physical, emotional, social, and material quality of life and can occur alone or in combination with other symptoms.
- † Variation of >20 days in individual cycle lengths over a period of one year.
- ‡ No bleeding in a 90-day period.
- § More than four menstrual episodes in a 90-day period.
- || One or two menstrual episodes in a 90-day period.
- ** Menstrual periods exceeding 8 days in duration on a regular basis.
- †† Bleeding of no longer than 2 days.
- ‡‡ Bleeding occurring >1 year after the acknowledged menopause.
- *** Post-coital or intermenstrual bleeding.

In concurrence with the new terminology and definitions put forth by the FIGO menstrual disorders group,² we sorted the patients based on the type of symptoms they had [Table 3]. The most common clinical presentation was HMB (43.7%) followed by 17% each of irregular menstrual bleeding and shortened menstrual bleeding, while 13.8% and 6.3% had Prolonged Menstrual Bleeding and PMB respectively.

	FINDINGS (NOTATION)	No.	%
P	Polyp (AUB-P)	26	15
A	Adenomyosis (AUB-A)	93	53.4
L	Leiomyoma (AUB-L)	82	47.1
M	Malignancy (AUB-M)	26	15
C	Coagulopathy (AUB-C)	-	-
O	Ovulatory disorder (AUB-O)	30	17.2
E	Endometrial inflammation (AUB-E)	2	1.1
O/E	Ovulatory/endometrial? (AUB-O/E)	15	8.6
I	Iatrogenic (AUB-I)	-	-
N	Not classified (AUB-N)	-	-

Table 4: Palm-coein Classification of AUB cases

ORIGINAL ARTICLE

Table 4 shows the distribution of cases based on the PALM-COEIN classification of AUB. Adenomyosis was the most common structural abnormality seen (53.4%), followed closely by leiomyomas (47.1%). 49 cases with adenomyosis also had dysmenorrhea (52.6%).

	SUBCLASS	No.	%
Leiomyoma	AUB-L _{SM}	4	4.9
	AUB-L _O	77	93.9
	AUB-L _{CX}	1	1.2
	TOTAL	82	100

Table 5: Leiomyoma Sub-classification

KEY:

L_{SM}- Submucosal Leiomyoma.

L_O- Other leiomyoma (subserous/intramural).

L_{CX} -Leiomyoma cervix.

We subclassified leiomyomas based on the location and noted that the most common ones were either subserous or intramural (93.9%). 4.9% of our cases were submucosal leiomyomas [Table 5].

	Type	No	%
Polyp (AUB-P)	Endocervical polyp	12	46
	Benign endometrial polyp	14	54
	Total	26	100

Table 6: Polyp Sub-classification

AUB-M and polyps accounted for 15% of cases each. On subclassifying the polyps [Table 6] seen in our study (26 cases), 54% arose from the endometrium (benign endometrial polyp) while the remainder were from endocervix. The endometrial polyps were composed of benign appearing endometrial glands in a stroma with thick walled vessels and fibrous tissue with no atypia/complexity. Similarly the endocervical polyps were composed of benign appearing endocervical glands with columnar lining with no evidence of atypia.

	Type	No.	%
Malignancy (AUB-M)	Benign Endometrial hyperplasia	17	65.4
	Endometrial adenocarcinoma	3	11.5
	SCC cervix	5	19.3
	Benign Endometrial hyperplasia + SCC cervix	1	3.8
	TOTAL	26	100

Table 7: AUB-M Sub-classification

SCC- Squamous cell carcinoma cervix.

The PALM-COEIN classification includes all endometrial hyperplasias and malignancy into the umbrella of AUB-M. Of our 26 cases of AUB-M, 65.4% were benign endometrial hyperplasia (17 cases) followed by 19.3% of squamous cell carcinoma cervix and endometrial adenocarcinoma in 11.5% of cases [Table7]. Overall, the malignancies (SCC & endometrial adenocarcinoma) accounted

ORIGINAL ARTICLE

for 5% of the 174 cases in our study group, while endometrial adenocarcinoma alone accounted for 1.7% of cases.

Among the non-structural causes, ovulatory disorders were the commonest with 17.2% cases while chronic endometritis (AUB-E) accounted for 1.1% cases [Table 4]. There were 15 cases which had no structural abnormality in uterus or any functional ovarian pathology (all cases had regular menstrual cycles with 11 patients having HMB, 2 patients Shortened menstrual bleed and 2 patients with PMB). In such patients we were unable to pinpoint the exact cause of AUB and thus labelled them as? Ovulatory/endometrial (AUB-O/E)[Table 4]. Basic tests for hemostasis were done in our study (PT and APTT) which were within reference limits in our study population. No cases in our study had any history of use of hormonal drug or intrauterine contraceptive device or drug for coagulopathy.

		PMB*	Reproductive Age/ Premenopausal AUB
AUB-P		1	25
AUB-A		4	89
AUB-L		2	80
AUB-M	SCC†	2	4
	BEH‡	-	18
	EM ADCA§	2	1
AUB-C		-	-
AUB-O		-	30
AUB-E		-	2
AUB-O/E ?			15

Table 8: AUB: PMB VS Reproductive age/Premenopausal bleeding

Footnote:

- *Postmenopausal bleeding
- †Squamous Cell Carcinoma
- ‡Benign Endometrial Hyperplasia
- §Endometrial Adenocarcinoma

Among the 11 AUB cases with PMB [Table 8], the most common structural abnormality was adenomyosis followed by leiomyoma (AUB-L) and malignancy (AUB-M). In our study, AUB appears to be more common in premenopausal/reproductive (93.7% cases) age rather than postmenopausally (6.3% cases).

PALM-COEIN	PATIENT AGE GROUP								TOTAL CASES
	30-40 years		41-50 years		51-60 years		>60 years		
	No.	%	No.	%	No.	%	No.	%	
AUB-P	13	50	12	46.2	1	3.8			26

ORIGINAL ARTICLE

AUB-A	41	44.1	47	50.5	5	5.4			93	
AUB-L	35	42.7	43	52.4	4				82	
AUB-M	SCC*	2	33.3	3	50			1	16.7	6
	BEH†	11	61.1	7	38.9	-				18
	EM- ADCA‡	1	33.3	2	66.7	-				3
AUB-C	-	-	-		-	-	-	-	-	-
AUB-O	13	43.3	13	43.3	4	13.4			30	
AUB-E			2	100					2	
AUB-O/E?	6	40	8	53.3	1	6.7			15	

Table 9: Age Distribution of Various Pathologies in AUB

Footnote:

- *Squamous Cell Carcinoma.
- †Benign Endometrial Hyperplasia.
- ‡Endometrial Adenocarcinoma.

Coming to the age distribution of the structural and non-structural causes of AUB [Table 9], we found that both endometrial and endocervical polyps were seen in almost equal numbers in the thirties and forties age groups, while only a single patient above 50 years of age had a polyp. Adenomyosis was most commonly seen in the 41-50 age group (50.5%) followed by the thirties (44.1%) and it was rare (5.4%) in the 51-60 age group. More than half the leiomyomas (52.4%) were in the 41-50 age group while most of the remainder were in the 30-40 age group (42.7%). Among the AUB-M cases, the benign ones (Benign endometrial hyperplasia) were observed more in the 31-40 age group (61.1%) while the malignant ones (66.7% of endometrial adenocarcinoma and 50% of squamous cell carcinoma) were seen more in the 41-50 age group. 86.6% of patients with ovulatory dysfunction were seen in the 30-50 years age group while those with chronic endometritis were seen in the 41-50 age group. 93.3% of those cases which we could not place in the ovulatory dysfunction or endometrial group were also in the 30-50 years age group.

PALM-COEIN TYPE	No.	Total Number	%	
AUB-P	6	85	48.9	AUB CASES WITH SINGLE PATHOLOGY
AUB-A	36			
AUB-L	32			
AUB-M	8			
AUB-O	3			
AUB-P;A	5	89	51.1	AUB CASES WITH MULTIPLE PATHOLOGIES
AUB-P;L	4			
AUB-P; O	1			
AUB-P;A;L	2			
AUB-P; A; O	1			
AUB-P;L;M	2			
AUB-P;A;L;M	1			
AUB-P; A; L; O	3			

ORIGINAL ARTICLE

AUB-P; A; L; M; O	1			
AUB-A;M	5			
AUB-A;E	1			
AUB-A;L	23			
AUB-A; O	7			
AUB-A;L;M	2			
AUB-A; L; O	4			
AUB-A; M; O	2			
AUB-L;M	4			
AUB-L; O	4			
AUB-M; O	1			
AUB-O; E?	15			
AUB-O;E	1			
TOTAL	174	174	100	

Table 10. Summary of Cases Showing Single/Multifactorial Etiology of AUB

Key:

- P-Polyp.
- A-Adenomyosis.
- L-Leiomyoma.
- M- Malignancy (Includes hyperplasia/scc/endometrial adenocarcinoma).
- O-Ovulatory dysfunction.
- E- Endometrial (Inflammation/infection/hemostatic disorder).

Table 10 summarises all the findings in individual cases. As we can see, 85 cases had a single identified pathology (48.9%), i.e., each patient had only one finding, either polyp or adenomyosis or leiomyoma or malignancy or ovulatory disorder. The remaining 51.1% cases had several different combination of pathologies, for example 5 patients had a combination of polyp and adenomyosis (AUB-P; A); 23 patients had a combination of adenomyosis and leiomyoma (AUB-A; L); 3 cases had a combination of polyp, adenomyosis, leiomyoma and ovulatory disorder (AUB-P; A; L; O) and so on.

DISCUSSION: We undertook this study in light of the new terminologies, definitions and classification put forth by the FIGO.¹⁻³ The Recommended Normal Limits of Menstrual Dimensions includes 3 parameters: frequency, regularity and duration of menstrual blood flow. Based on this, the normal menstrual limits will include a frequency of once every 24-38 days, a variation of <20 days in cycle to cycle variation over 12 months, and a duration of menstrual flow between 4.5 to 8 days.³ A significant step has been the discarding of several obscure, poorly defined and extensively used terms such as menorrhagia, polymenorrhoea and “dysfunctional uterine bleeding”. While menorrhagia and polymenorrhoea were replaced by heavy menstrual bleeding and frequent menstrual bleeding respectively, the disorders previously named as dysfunctional uterine bleeding (DUB) were replaced by coagulopathy/ovulatory disorders/endometrial dysfunction in the PALM-COEIN classification.¹

The most common clinical presentation was HMB which was observed in 43.7% of the cases and is similar to that of Rizvi et al⁴ who found HMB to be more common than irregular menstrual

ORIGINAL ARTICLE

bleeding. PMB was the presenting symptom in 11 cases (6.3%). 13.8% patients had prolonged menstrual bleeding while 12.6% of patients had frequent menstrual bleeding [Table 3].

Ovulatory bleeding, the more common AUB and superimposed on regular cyclic menstruation (24 to 35 days), is usually associated with structural causes [PALM] or sometime by functional cause [AUB-O].⁵ Of the 174 cases presenting with AUB, adenomyosis was the [Table 4] most common structural abnormality seen (53.4%), followed closely by leiomyomas (47.1%). This is in accordance with the study by Rizvi et al who had 46.34% and 41.46% respectively.⁴ There is a strong association between adenomyosis and AUB, with published data stating that 70% of adenomyosis patients have AUB symptoms.³ 49 cases with adenomyosis also had dysmenorrhea (52.6%) while Rizvi et al⁴ found 68% of cases with both findings. which is also in concurrence with literature which states that at least 19% have both adenomyosis and dysmenorrhea.³ Of all the leiomyomas in our study 4.9% were submucosal. Literature³ states that there is a higher association between submucosal leiomyomas and AUB than between subserous/intramural leiomyomas and AUB. In cases with PMB, similar to the study by Rizvi et al,⁴ the most common structural abnormality was adenomyosis followed by leiomyoma and malignancy.

9.8% of our cases were benign endometrial hyperplasia (17 cases), while Doraiswami et al⁶ found 6.1% of hyperplasia causing AUB.

Doraiswami et al⁶ found 11.2% of benign polyps while we obtained 15% [Table 4]. Literatures state that some but not all polyps present with AUB¹ and that AUB in 39% of premenopausal and 21-28% of postmenopausal women are due to polyps.³ Chronic endometritis and endometrial carcinomas was seen in 1.1% and 1.7% of our cases while each of those conditions were seen in 4% of cases of Doraiswami et al.⁶ Overall the malignancies (SCC & endometrial adenocarcinoma) accounted for 5% of the 174 cases in our study group while malignant tumours comprised only 0.72% of cases in the study by Rather et al.⁷

Ovulatory dysfunction (AUB-O) was found in 22.5% of cases by Mohammed et al,⁸ while we found 17.2% who had irregular menstrual bleeding(30 cases)[Table 4]. Anovulatory cycles have unpredictable bleeding, which varies in frequency, regularity, duration, and volume and are characterized by frequent spotting to infrequent, heavy bleeding.⁵ The 15 cases of AUB with regular cycles and no structural abnormality (AUB-O/E?) require more studies like hormone assay, timed endometrial samples and evaluation for endometrial hemostatic disorders.

The ages of patients [Table 1] ranged from 30 to 62 years with maximum number of patients in the 41-50 age groups (49%cases) followed by 30-40 years (44.2% cases) which is similar to the study by Rizvi et al⁴ who found 44.56% in the 41-50 age group. Only 0.5% cases were above 60 years showing that abnormal uterine bleeding is a very common symptom in late reproductive age and perimenopausal age rather than the elderly. Karmarkar et al studying PMB found 87.2% cases in 41-60 age group and rest above 60.⁹ Adenomyosis was most commonly seen in the 41-50 age group (50.5%) followed by the thirties(44.1%), and 95% of leiomyomas as well as polyps were in the 30-50 age group [Table 9] which are comparable to that of Rizvi et al.⁴ 61% of benign endometrial hyperplasias were in the 30-40 age group while 66.7% of endometrial adenocarcinoma were in the 41-50 age group.

In our study [Table 2], 38% of AUB patients had a parity of 2 and 38.5% with a parity of 3 while Mohammed et al⁸ found 65.9% with a parity of 2. Also only 7.5% and 2.8% of AUB patients were uniparous and nulliparous respectively. This shows that AUB as a symptom is more common among multiparous rather than in women with parity 1 or 0.

ORIGINAL ARTICLE

Literature states that one or more entities in a given patient can cause AUB, while it also states that defined entities like leiomyoma, adenomyosis or polyp can be present in a woman without causing the symptom of AUB.¹ 48.9% of our AUB cases [Table 10] had only a single pathology (either AUB-P or AUB-A or AUB-L or AUB-M or AUB-O). That necessarily does not mean that the identified pathology caused the AUB. Also the remaining 51.1% cases had several different combination of pathologies, for example AUB-P; A; L or AUB-P; A; L; O or AUB-P; A; L; M; O. So one of the questions that arise from these findings is "What pathology exactly caused the abnormal uterine bleeding in these cases with multiple pathologies?" All of them or few of them or none of them could have caused the AUB in a given patient. Hence further analysis is required in this area.

CONCLUSION: Confusion regarding the terminology, definitions, and classification of AUB has been put aside by the new standardized terminology, definitions and PALM-COEIN classification for AUB formulated by FIGO.¹⁻³ Several terms were discarded including menorrhagia, polymenorrhea and dysfunctional uterine bleeding (DUB). In light of these developments we undertook this study.

In our study, maximum number of patients was in the 41-50 age groups and most had a parity of 2 or 3 and 42.5% had dysmenorrhea. The most common AUB symptom was HMB. The most common histopathological finding was adenomyosis followed by leiomyoma and 15% each of polyps and AUB-M (Hyperplasia/Carcinoma).

Among the non-structural abnormalities, ovulatory disorder was the foremost. Nearly half the study group had a single identified pathology (48.9%) while the remaining half of the patients had multiple identified pathologies. We do not know which pathology caused the AUB in the latter group. This leaves a great vacuum in the understanding of abnormal uterine bleeding and further research is much needed to help us be able to identify the specific cause of AUB in a given patient who may have multiple pathologies.

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ORIGINAL ARTICLE

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Fig. 1: Adenomyosis composed of endometrial glands and stroma deep in myometrium (H&E 100x).

Fig. 2: Leiomyoma composed of benign smooth muscle bundles (H&E 100x).

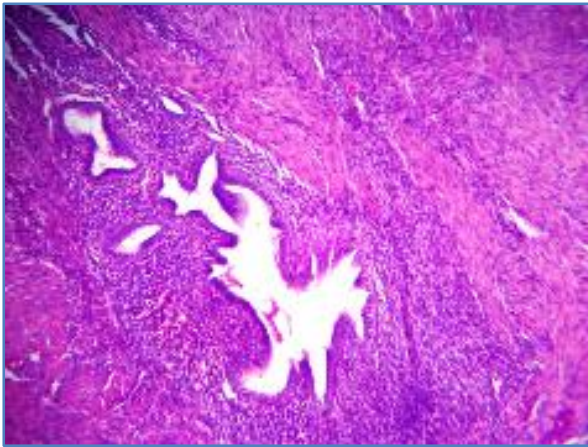


Fig. 1

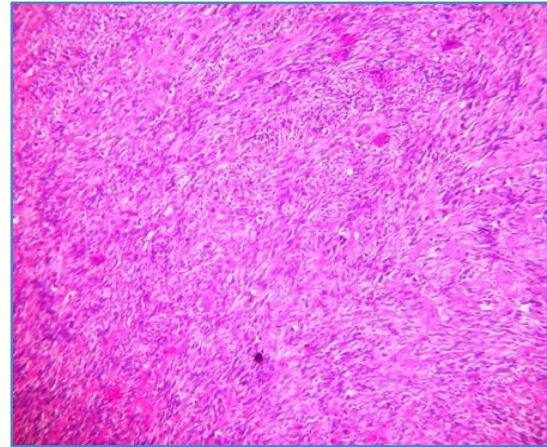


Fig. 2

Fig. 3: Endometrial polyp composed of cystically dilated glands with fibrous stroma and thick walled blood vessels (H&E 100x).

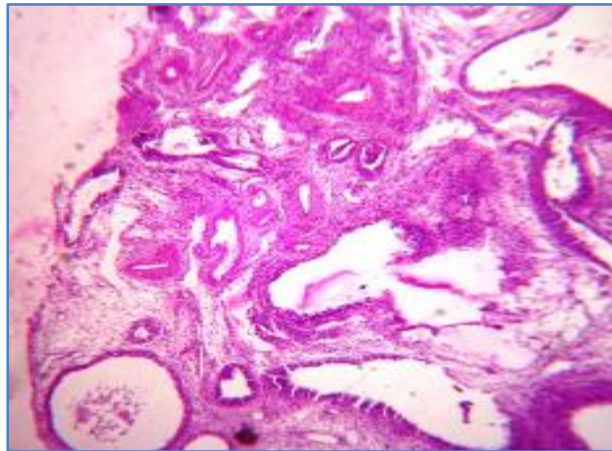


Fig. 3

ORIGINAL ARTICLE

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