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The INFLUENCE OF DIFFERENT PHASES OF MENSTRUAL CYCLE ON THE DIAGNOSIS OF ACUTE APPENDICITIS, A PROSPECTIVE STUDY

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Abstract

A prospective study was conducted to assess the frequency of acute appendicitis at different phases of menstrual cycle, 508 patients presented with acute right lower abdominal pain diagnosed as acute appendicitis and submitted to appendectomies at Basrah Teaching Hospital during a two years period from October 2000 to October 2002. There were 263 females with mean age of 25 years and 245 males as a control with the mean age of 27 years. The study reveals a higher incidence of normal appendixes were removed among females 46 patients (17.5%) as compared to 12 (4.9%)in males. Most of normal appendixes occurred during follicular phase 27 patients (58.7%) as compared to other phases. There were 23 females with normal appendixes have no any associated pathology, 20 patients (86.95%) of them were occurred around the mid cycle (day 12-16). There was difference in the incidence and the severity of acute appendicitis among different phases of menstrual cycle. It appears that the frequency of acute appendicitis was highest in the luteal phase 105 patients (61.77%) compared to other phases, while most of perforated and gangrenous appendixes occurred during menstrual and follicular phases, 13 patients (36.11%), 15 patients (41.66%) respectively.

Introduction

Acute appendicitis is a major surgical problem in terms of both incidence and potential complications[1]. It has been estimated that the lifetime risk that a person will develop appendicitis is about 15-20%[2].

The incidence of appendicitis is equal amongst males and females before puberty. In teenagers and young adults the male to female ratio increase to 2:1 at the age of 25 years and there after the greater incidence in males declines until these related incidence is again equal[3].

Appendicitis should be suspected in individuals of any age who have lower or right lower quadrant abdominal pain. Although the pain may vary with location of the appendix right lower quadrant pain always present[4]. Other symptoms such as nausea, vomiting and bowel motion disturbances, although common, are not constant occurrence in every case. Likewise, elevation in core body temperature is a variable finding. Physical examination generally discloses localized right lower quadrant tenderness with or without local peritoneal signs[5].

Laboratory tests are only modestly useful in acute appendicitis. It is reported that at least 1/4th of all patients with acute appendicitis will have a normal leukocyte count. The rest develops mild to moderate leukocytosis. In addition as many as 20% of patients may have either erythrocyte or leukocyte during general urine examination[6].

The sonographic diagnosis of acute

appendicitis has a reported sensitivity of 78% to 96% and specificity of 85% to 98%, although it has definite limitation and results are operator dependent[7].

Most investigators report that some normal appendixes will be encountered in operations for acute appendicitis. Although the rate of inaccurate diagnosis is generally in the range of 10-20%, it may be twice as high in women of reproductive age[8].

When a normal appendix is found during operation on a patient believed to have acute appendicitis, most surgeons agree that appendectomy should be performed[9].

In one series, 19% of patients with clinical feature of acute appendicitis, who had grossly normal appendix, had acute appendicitis histologically. On the other hand, 8% of the patients believed during operation to have acute appendicitis would show a normal histology[10].

Because appendicitis and gynecological disorders are both common conditions, it is not surprising that the high negative appendectomy rate especially in young women is attributed to misdiagnosis of the gynecological disorders[11].

It is in women of childbearing age that pelvic disease most often mimics acute appendicitis. A careful gynecological history should be taken in all women with suspected appendicitis concentrating on menstrual cycle, vaginal discharge, and possible pregnancy[12].

It has been found that there is a higher incidence for removal of obviously normal appendix in females. The frequency for removal of such normal appendix was highest in certain phases of menstrual cycle. In many instances the abdominal pain which the female patients have and for which appendectomy was planned is due to a cause in the female reproductive organs. This explains that many normal appendixes are removed for gynecological reasons[13].

On other hand recurrent monthly pain of genital organ origin might cause delay in seeking medical care for what is in reality due to mild acute appendicitis which might lead to a high proportion of gangrenous and perforated appendix in certain phases of menstrual cycle [14].

The concept that acute appendicitis is more common during certain phases of the menstrual cycle might not contribute substantially to the diagnosis, but provides an indication for early surgical intervention. It is also important in understanding the etiology of the disease and could explain the lower incidence of acute appendicitis in female[15].

It has been mentioned that the incidence of operations for uninflamed appendixes may be higher during follicular and menstrual phases and more negative laparotomies are done during these phases, this may point to the existence of functional (gynecological) disorders that mimic acute appendicitis[16].

It can be concluded that there is a difference in the frequency of acute appendicitis and number of appendectomies performed in different phases of menstrual cycle[17].

The aim of this study is to assess the frequency of acute appendicitis in different phases of menstrual cycle.

Patients and Methods

This prospective study was carried out on 508 patients presented with acute right-sided lower abdominal pain diagnosed as acute appendicitis and submitted to appendectomies at Basrah Teaching Hospital for two years period from October 2000 to October 2002. There were 263 females (51.77%) with age ranging from 10-55 years (mean 25 years) and 245 males (48.22%) with age ranging from 10-55 years (mean 27 years) with female to male ratio of (1.07:1).

Forty-seven female patients have been excluded from the study because in 27 of them the menstrual cycle was irregular,

the other 13 patients had amenorrhoea due to different reasons, and 7 patients were pregnant.

The incidence of acute appendicitis during different phases of menstrual cycle was studied and analyzed. The male patients were included in this study as a control group.

Preoperative assessment and preparation: Each patient in this study was submitted to a detailed clinical assessment and was investigated according to formulated questionnaire. This included detailed history, thorough clinical examination and the relevant investigations.

For females, details of normal cycles were taken carefully. These included the duration (in days) since last menstrual period, any spotting at presentation, history of contraception and obstetric history.

Each patient was examined carefully. Vital signs were measured for each patient. Abdominal tenderness, rebound tenderness, rigidity and bowel sound were recorded. Positive findings on per rectal and/or per vaginal examinations were also reported.

Most of the patients in this study have had preoperative investigations, which include (white blood cell count and general urine examination). Ultrasonic examination of the abdomen and pelvis were not carried out for all patients, because the urgency of patient's condition and unavailability of ultrasonic examination at certain times limited this type of examination. When the clinical diagnosis of acute appendicitis is considered, the patients were prepared and submitted to surgery by different surgeons (seniors and residents).

Results

Most appendectomies performed for patients with right lower quadrant pain diagnosed as acute appendicitis were in the age group (15-30 years) (49.21%) followed by age group (31-45 years)(32.87%). The least number of appendectomies were among patients more than 45 years age group (4.72%) this is demonstrated in table I.

Table I: Age and sex distribution

Age / Sex	<15 years	15-30 years	31-45 years	>45 years	Total
Male	32	130	88	13	263 (51.77%)
Female	35	120	79	11	245 (48.23%)
Total	67 (13.19%)	250 (49.21%)	167 (32.87%)	24 (4.72%)	508 (100%)

Table II: Distribution of normal and inflamed appendix in male and female patients

State of appendix / Sex	Normal appendix		Inflamed appendix		Total	
	No.	%	No.	%	No.	%
Females	46	17.5	217	82.5	263	51.77
Males	12	4.9	233	95.1	245	48.23
Total	58	11.42	450	88.58	508	100

Table II shows that higher occurrence of normal appendixes were among females (17.5%) compared to (4.9%) in males. The overall of normal appendixes is (11.42%) (n=58).

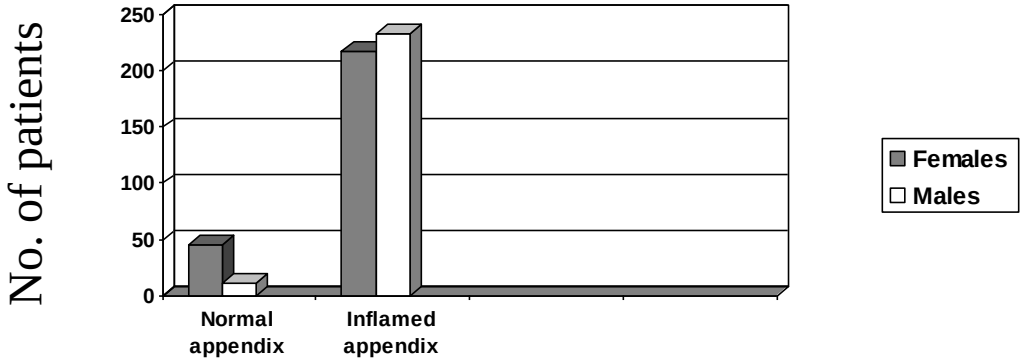

Fig. 1: Distribution of normal and inflamed appendicitis in male and female patients

Table III: Distribution of normal and inflamed appendixes in females according to phases of menstrual cycle.

Menstrual phase / State of appendix	Menstrual		Follicular		Luteal		Total	
	No.	%	No.	%	No.	%	No.	%
Normal	3	6.52	27	58.7	16	34.78	46	21.3
Inflamed	22	12.94	43	25.29	105	61.77	170	78.7
Total	25	11.57	70	32.4	121	56.02	216	100

Table III includes female patients with regular menstrual cycle (47 female patients were excluded because of their irregular menstrual cycle or amenorrhoea). According to this table most of normal appendixes were occurred during follicular phase (58.70%). On other hand most of inflamed appendixes were found during luteal phase (61.677%).

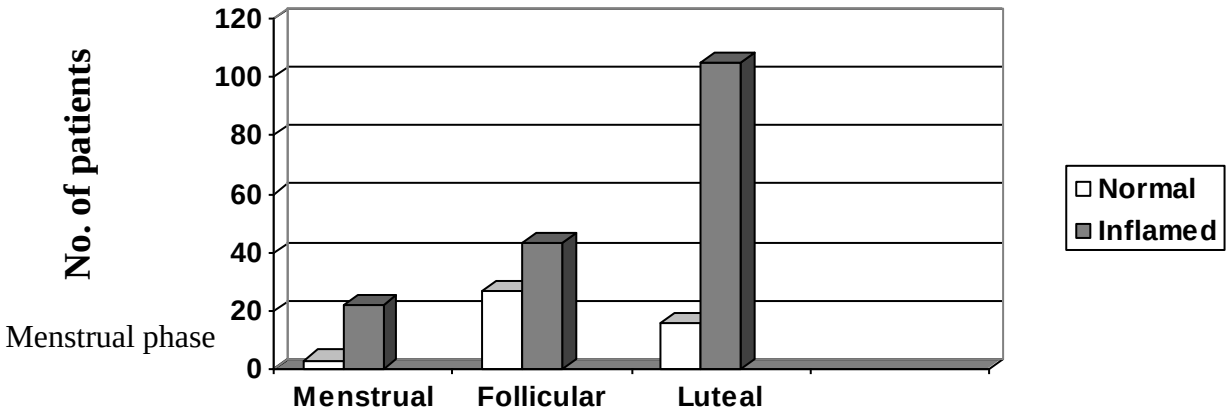

Fig.2: Distribution of normal and inflamed appendixes in females according to phases of menstrual cycle.

Table IV: Per-operative findings during different phases of the menstrual cycle.

Cycle phase / Degree of inflammation	Menstrual		Follicular		Luteal		Total	
	No.	%	No.	%	No.	%	No.	%
Normal looking appendix	3	6.52	27	58.7	16	34.78	46	21.3
Catarrhal appendicitis	3	5.08	13	22.03	43	72.88	59	27.3
Obstructed appendicitis	6	8	15	20	54	72	75	34.73
Gangrenous or perforated appendicitis	13	36.11	15	41.7	8	22.22	36	16.67
Total	25	11.57	70	32.40	121	56.02	216	100

Table IV includes females who had regular menstrual cycle and were subjected to appendectomies (n=216). There was a high proportion of gangrenous and perforated appendixes in menstrual and follicular phases compared with the luteal phase (77.81% versus 22.22%) and this difference was statistically significant (P<0.001). Catarrhal appendicitis, on other hand was higher in the luteal phase (72.88%) in comparison with other phases (27.11%). The difference is statically significant (P<0.001).

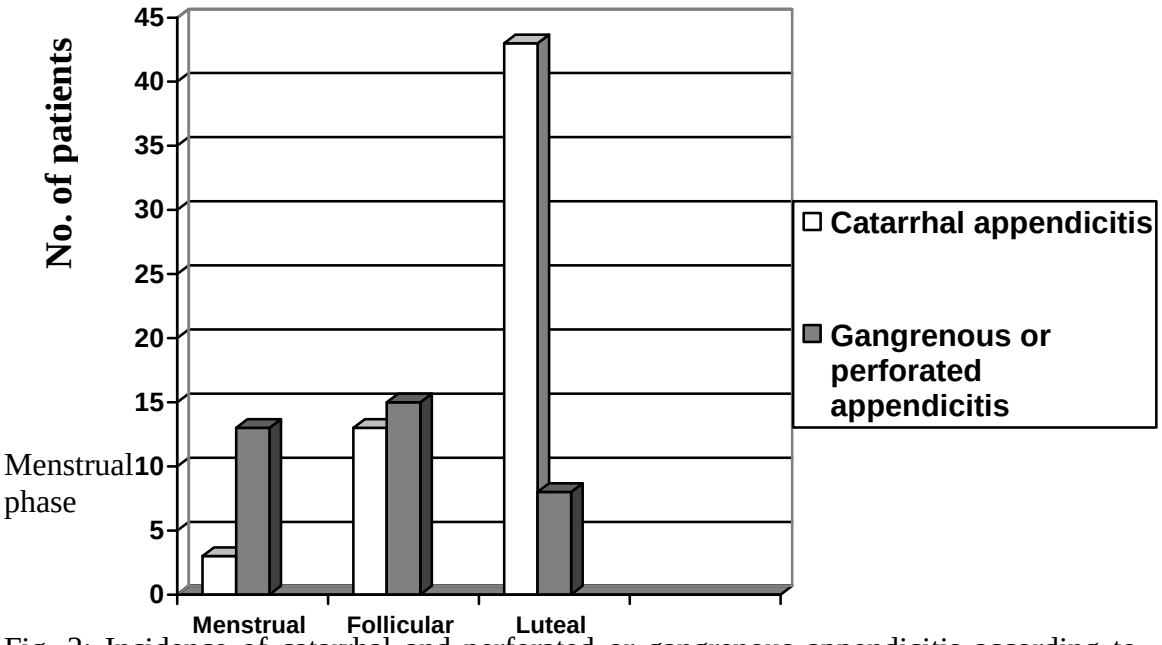

Fig. 3: Incidence of catarrhal and perforated or gangrenous appendicitis according to phases of menstrual cycle.

Table V: Per-operative findings in female patients diagnosed clinically as acute appendicitis.

Peroperative finding	Normal appendix				Inflamed appendix	Total
	Ov. cyst	PID	Ectopic pregnancy	No pathology		
Patients No.	16	5	2	23	217	263

Table V shows the operative findings in all female patients diagnosed clinically as having acute appendicitis. Of the 263 patients who underwent appendectomies, only 217 proved to have acute appendicitis. Other findings include, no pathology 23 patients, complicated ovarian cyst 16 patients, pelvic inflammatory disease (PID) 5 patients, ectopic pregnancy 2 patients.

Table VI: Distribution of negative appendectomies during menstrual cycle.

Duration from last menstrual cycle	Around mid cycle					Away from mid cycle	Total
	12	13	14	15	16		
No. of patients	3	5	7	3	2	3	23
Total	20 (86.95%)					3 (13.05%)	

Table VI shows the distribution of negative appendectomies(with no any pathological finding) during menstrual cycle. Of 23 patients 20 of them were around mid cycle (day 12-16) compared to 3 patients who were away from mid cycle (86.95% versus 13.05%).

Table VII: Histopathological findings

Sex	**Catarrhal**	**Follicular hyperplasia**	**Suppurative**	**Carcinoid**	**Adeno-carcinoma**	**Nor mal**	**Total**
Female	75	84	56	1	1	46	263
Male	120	88	25	0	0	12	245
Total	195	172	81	1	1	58	508

Table VII shows the histopathological findings of all patients (females and males) who underwent appendectomies. It reveals that catarrhal appendicitis is more common among males while suppurative ones are more common among females.

Discussion

Acute appendicitis is the most common surgical condition of the abdomen occurs at all ages but is more frequent in the second and third decades of life, it is quite rare in the very young[18]. Although the sex ratio of acute appendicitis in general is about 1:1 but at puberty the frequency in the males increases gradually so that the male to female ratio in those between 15 and 25 year of age is about 2:1. After that, the male incidence gradually declines until the sex ratio is again equal[19].

In our study, it was found that acute appendicitis more frequent in the age group (15-45 years) (49.21%). The least incidence of acute appendicitis was observed in the patients above 45 years (4.72%).The female to male ratio was about 1.07:1, so these results are in agreement with those reported by Noer[20].

The accuracy of the preoperative diagnosis should be about 85%. If it is found to be less than this, it means that some unnecessary operations were probably done. On the other hand

accuracy greater than 90% must also cause some concern, since this may means that some patients with acute appendicitis are being observed when they should have prompt surgical intervention[3].

The rate of erroneous diagnosis of acute appendicitis is highest in young adult females. Negative appendectomy rate of 32-45% have been reported in women in the age range 15-45 years. This is because diseases of the female internal genital organs may be mistakenly diagnosed as appendicitis, in addition to rupture graafian follicle[21].

We found in the present study that the accuracy for pre-operative diagnosis was higher among males (95.1%) compared with that among females (82.5%), resulting in a higher false positive was among females than males (17.5% versus 4.9%).

The over all preoperative diagnostic accuracy was about (88.58%). Bergeron-E et al[22], reported in their study a negative appendectomies range from 9-40%, and more negative appendectomies were occurring in females of a child bearing age (32.2% compared with 8.4% in males).

Similar results were obtained from Korner et al[23], who found that most of negative appendectomies also occur in female patients age 13-40 year and they found a diagnostic accuracy of about 84% (false positive 16%) compared to that found in males of 92% which are more or less similar to our result.

So in the present study it was found that there was a higher negative appendectomies in females which is statistically significant, but the occurrence of such findings differed in various phases of menstrual cycle.

From the results of 216 female patients with regular menstrual cycle, we found that the frequency of acute appendicitis was highest in the luteal phase (105 patient) (61.77%) as compared with follicular phase (43 patients) (25.29%) and menstrual phase 22 patients (12.94%).

It was found also that most of normal appendixes were removed during follicular phase 27 patients (58.7%) as compared with luteal phase 16 patients (43.78%) and menstrual phase 3 patients (6.52%).

There was a high proportion of gangrenous and perforated appendixes in the menstrual and follicular phases compared with the luteal phase (77.81% versus 22.22%), and this difference is statistically significant ($P<0.001$).

It is reasonable to say that in many cases, the abdominal pain which the patient has is due to causes in the female reproductive organs and that many normal appendixes are removed for gynecological reasons. On the contrary, recurrent monthly pain, originating in the genital organs, might causes delay in seeking medical care for suspected acute appendicitis. This might explain the findings in the present study of a high proportion of gangrenous and perforated appendixes in the menstrual and follicular phases.

The same results were reported by Einar et al[17] who stated that the frequency of acute appendicitis differs in different phases of menstrual cycle. There is also a difference in the degree of inflammation of appendix, and he noticed a high incidence of acute appendicitis in the luteal phase and more gangrenous and perforated appendixes in menstrual and follicular phases.

In their study on 208 patients with regular menstrual cycle, Evgenikos et al[24] showed that acute appendicitis is less common among women during menstruation and follicular phases of the cycle, with high incidence in the luteal phase and the difference was significant in his study.

Eldar[16] et al. reported 144 women of childbearing age operated on for suspected acute appendicitis and subdivided them according to menstrual

phase during which they presented. They found that acute appendicitis occurred randomly during various phases of menstrual cycle. On the other hand, they found that the incidence of the operations for uninflamed appendix was higher during menstrual phase and early follicular phase. This was explained by existence of functional disorders of female genital organs that mimic acute appendicitis.

Despite various sophisticated investtigations aimed at the diagnosis of acute appendicitis clinical evaluation is still an invaluable diagnostic tool. So the diagnosis of acute appendicitis remains clinical entity provided that the clinician is aware of many gynecological conditions as parts of the differential diagnosis of acute appendicitis particularly in females of active reproductive age[25].

In our study the clinical preoperative diagnosis of acute appendicitis was made in 263 females. Acute appendicitis was proved histopathologically in 217 only. This resulted in 46 patients being clinically false positive.

In 23 patient the appendix was normal and the true causes of symptoms was PID in 5 patients, ectopic tubal pregnancy in 2 patients, and in another 16 patients due to ruptured and/or twisted ovarian cysts. In the remaining 23 female patients with false positive picture no peroperative abnormality could be detected.

In female patients with right lower quadrant abdominal pain,a detailed gynecological aspect of the history such as the last menstrual period (LMP), regularity of menstrual cycle and abnormal vaginal bleeding and discharge is very essential. However these relevant data in the history are usually over looked because of the surgical bias toward the clinical impression of acute appendicitis[26].

Eric et al[27] emphasized on the need for the gynecological review of the female patients of a child bearing age presented with lower abdominal pain. They also stressed the use of ultrasonography as an important adjunct in improving the diagnostic accuracy in such case as this helps to avoid unnecessary appendectomies and may show other pathology.

Ultrasound were not performed to all patients due to urgency of the conditions and this type of examination is not available in all times and even those patients who were examined by ultrasound, the results were not conclusive.

Our results showed that most of negative appendectomies were distributed around mid cycle (from day 12-16) for the 23 female patient whose appendixes were normal without any other pathology during exploration: 7 patients presented at day (14) of their menstrual cycle, 5 patients at day (15), 3 at day (12), 2 at day (16), 3 patients during other days away from mid cycle.

Although these female patients presented with a right iliac fossa pain and gave picture similar to that of acute appendicitis, it could be explained by ovulatory pain around mid cycle. Most females with regular 28 days menstrual cycle will experience this pain around day 14 of their cycle, which mimics the pain of acute appendicitis[27].

Vlahakis et al[28] found that most of the negative appendectomies in females of childbearing age when no gynecological disorder discovered were failed around mid cycle and they emphasized on thorough menstrual history.

The same finding was obtained from Einar[17] who showed that there is a higher statistically significant incidence for the removal of normal appendix in females and that the highest incidence was during mid cycle period.

Grossly, an appendix with well-developed acute inflammation shows a fibrinous or purulent coating of the serosa with engorgement of the vessels.

The mucosa shows areas of ulceration against a markedly hyperemic back-ground. Obstruction of the lumen by a fecolith or some other agent is found in about one third of cases[29].

Microscopically the changes range from minimal catarrhal inflammation to total necrosis of appendiceal wall. The degree of abnormalities is being partially dependent on the interval between the onset of symptoms and the timing of operation[30].

In this study we found 195 catarrhal appendicitis, 172 follicular hyperplasia, 81 acute suppurative, 1 carcinoid and 1 adeno carcinoma.

We noticed that catarrhal inflammation was more among males (120 patients) while suppurative inflammation was more among females (56 patients) and this may again reflect the idea of delayed presentation or diagnosis of the females.

There is close correlation between the gross and microscopic findings in acute appendicitis. Therkelsen[31] reviewed 154 organs with microscopic evidence of acute appendicitis, grossly evidence of inflammation was evident in 125, equivocal in 25, and absent in 4.

Carcinoid tumours are found in about 1 of every 300 routine appendectomies and represent the most common tumour of the appendix[32]. In our study there is only 1 reported among 508 cases.

It is concluded that there was a high incidence of a normal appendixes removed in female patients compared to males, and most of a normal appendixes (unnecessary appendec-tomies) were found to occur around mid cycle, acute appendicitis in females occurs through out various phases of menstrual cycle with high frequency found in the luteal phase, perforated and gangrenous appendicitis were found more frequently during menstrual and follicular phases, while catarrhal appendicitis was higher in the luteal phase.

We recommend that careful and detailed gynecological history for a female of a child bearing age with a lower quadrant abdominal pain is mandatory, this include menstrual history last menstrual period (LMP) and intake of oral contraceptive. In order to avoid unnecessary appendectomies, thorough examination and relevant investigations especially white blood cell count, general urine examination, pregnancy test and modern imaging techniques (e.g. ultrasonography) will reduce the frequency at which gynecological conditions misdiagnosed as acute appendicitis, recurrent monthly right lower quadrant abdominal pain originally in the female genital organs should not cause a delay in making a diagnosis of acute appendicitis in order to reduce the proportion of perforated and gangrenous appendixes.

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