Review of Histopathological Diagnoses of One Year Appendectomy Specimens in Sulaimani City

مراجعة نسجية مرضية لعينات الزائدة الدودية المستأصلة في سنة واحدة في مدينة السليمانية

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المستخلص:

الهدف: تهدف الدراسة الحالية لمراجعة تشخيصات الزرع النسجي لكافة حالات استأصال الزائدة الدودية لمدة عام كامل.

المنهجية: هذه الدراسة اجريت في المستشفى التعليمي في السليمانية ولمدة سنه كاملة ابتداءاً من الأول من كانون الثاني ولغاية الحادي والثلاثين من كانون الأول لعام ٢٠٠٩. وفيها تم مراجعة كافة تقارير الزرع النسجي لحالات استأصال الزائدة الدودية لكلا الجنسين ولكافة الأعمار وتسجيل كل الملاحضات الطبية العمليات المرافقة للأستأصال (ان وجدت). تم تصنيف التشخيصات الى موجبة وسالبة نسبة لوجود أو عدم وجود الألتهابات الحادة. وكذلك تم تسجيل الأيجادات والمستأصلات الجراحية المرافقة.وتم تحليل البيانات من خلال تطبيق البرنامج الأحصائي لتحليل المعلومات. لتحليل chi squareوباستعمال SPSS version 19

النتائج: تم مراجعة ٢٠٥٢ تقرير زرعي نسجي، وكانت نسبة الذكور ٤٧,١٢% والباقي (٥٢,٨٨%) اناث.وقد كان ٦١,٩ % من المجموع الكلي للحالات موجبة نسبة لوجود الأتهابات الحادة وكالأتي: ٣٢,٩% التهاب الزائدة الدودية الحاد، ٢٦,١% التهاب الزائدة القيحي و ٤,٥% الغانغارينا. بينما كان ٣٨,١% من المجموع الكلي للحالات سالب نسبة لوجود الألتهابات وكما يلي: ٢٨,٥% من العينات مشخصة كتضخم العقيدات اللمفاوية لجدار الزائدة الدودية ، ٦,٢%طبيعية و٠,٢% تحوي ورم الكارسينويد. وقد كانت الحالات السالبة للألتهاب الحاد أكثر حدوثا في الأناث مثل التهاب ماحول الزائدة ، تضخم العقيدات اللمفاوية والورم الكارسينويد أما الألتهاب المزمن للزائدة الدودية فهو مثار للنقاش. من مجموع ٢٠ حالة استأصال للزائدة الدودية تحتوي على الدودة الدبوسية وجد ان ٩٥% سببت تضخم العقيدات اللمفاوية ولم توجد علاقة بين وجود الديدان الدبوسية والتهاب الزائدة الحاد.

التوصيات: أوصي اطباء الزرع النسجي بالتقيد بالصفات المجهرية في تشخيص كل مجموعة مرضية.

Abstract:

Objective: To review and see the pattern of histopathological diagnoses of one year appendectomy specimens.

Methodology: This retrospective study was carried in Sulaimani Teaching Hospital over the period of one year (from 1st of January to 31st of December 2009). All pathological reports were reviewed retrospectively for patient's age, sex, histopathological diagnosis and operative findings (if present). Histopathological diagnoses then were classified into either positive or negative for acute inflammation. Any associated findings or any surgical specimen removed with the appendix was recorded. The obtained data were analyzed by using the statistical package social sciences (*SPSS)* version 19; with Chi square to test for significance between data.

Results: Hospital pathological reports of 2052 appendectomy cases were reviewed, (47.12%) were males and (52.88%) were females. 61.9% of all appendectomy cases were positive for acute inflammation (32.9% had acute appendicitis; 26.1 % had acute suppurative appendicitis , and 4.5% had gangrenous appendicitis), while 38.1% were negative (28.5 % had reactive follicular hyperplasia, 6.2% were normal, and 0.2% had carcinoid tumors). Negative for acute inflammation cases were generally significantly more common in females e.g. periappendicitis, Reactive Follicular Hyperplesia and carcinoid tumor but eosinophilic appendicitis cases like acute appendicitis were more common in males. Normal appendixes versus Reactive Follicular Hyperplesia (without associated appendicitis) are two entities that intermingle. Chronic appendicitis is controversial entity. Out of 20 cases with *Entrobius vermicularis* (95%) cases were associated with reactive follicular hyperplasia and it shows non significant association with acute appendicitis.

Recommendation: We recommend that the pathologists must be strict to histological criteria for each pathological entity before the diagnosis.

Keywords: appendectomy, Entrobius vermicularis, carcinoid tumor.

Introduction:

Histologically a distinguishing feature of the appendix is the extremely rich lymphoid tissue of the mucosa and submucosa, which in young individuals forms an entire layer of germinal follicles and lymphoid pulp. Muscularis mucosa and submucosa may be inconspicuous; muscularis propria contains complete longitudinal and circular layers and prominent ganglion cells [(1)].

The appendix of the newborn is almost devoid of lymphoid tissue. This lymphoid tissue reaches its height of development in late childhood or adolescence [(2)]. In the elderly some histological changes occur: the lymphoid tissue undergoes progressive atrophy during life to the point of complete disappearance in advanced age, the appendix, particularly the distal portion, sometimes undergoes fibrous obliteration with presence of plasma cells and eosinophils infilteration [(1)].

Acute appendicitis is the most common general surgical emergency [(3)].

The incidence of acute appendicitis roughly parallels to that of lymphoid development, with the peak incidence in late teens and twenties. Obstruction of the lumen is the dominant factor for acute appendicitis. Although fecoliths and lymphoid hyperplasia are the usual factors of obstruction, some unusual factors could also be the reason e.g. intestinal worms, malignant or benign tumors, foreign body, parasite or anatomic variance [(4)].

Despite the advances in surgery over the past century, the diagnosis of acute appendicitis continues to present clinicians with problems, especially in young females[(5)]. The gold-standard for diagnosis of acute appendicitis is histopathology [(6)]. There are no definite guidelines as to whether all appendices should be sent for histopathology as a routine; however many of appendiceal tumors are diagnosed on appendectomy specimens [(7)].

Methodology:

This retrospective study was carried in Sulaimani Teaching Hospital, over the period of one year (from 1st of January to 31st of December 2009).

All pathological reports of patients who underwent appendectomy were reviewed retrospectively for patient's age, sex, histopathological diagnosis and operative findings (if present).

Histopathological diagnoses then classifyed into either positive or negative for acute inflammation. The positive cases (neutrophils infiltration) were sub classified into 3 subgroups:

1. Acute appendicitis.
2. Acute suppurative appendicitis (figure-6).
3. Gangrenous appendicitis.

While negative cases (no neutrophils infiltration) include these 7 categories:

1. Normal.
2. Reactive follicular hyperplasia (figure-7).
3. Eosinophilic appendicitis (figure-8).
4. Chronic appendicitis.
5. Periappendicitis.
6. Granulomatus appendicitis.
7. Carcinoid tumor (figure-9).

Any associated findings like Entrobius Vermicularis (figure-10), ovarian cyst, Meckel's diverticulum, tubal pregnancy and other operative findings or surgical specimens were recorded.

Results:

Table 1. Age Groups of 2052 Patients, the Ages Range from 4months-98 Years with A mean Value of 23.43, Median 22.00 and Standard Deviation 11.857.

Age of patients in years	Frequency	Percent
≤ 10	218	10.6
11 - 20	725	35.3
21 - 30	704	34.3
31 - 40	259	12.6
41 - 50	89	4.3
51 - 60	34	1.7
61 - 70	13	0.6
71 - 80	6	0.3
81 - 90	2	0.1
91+	2	0.1
Total	2052	100.0

≤=equal and less, +=and more.

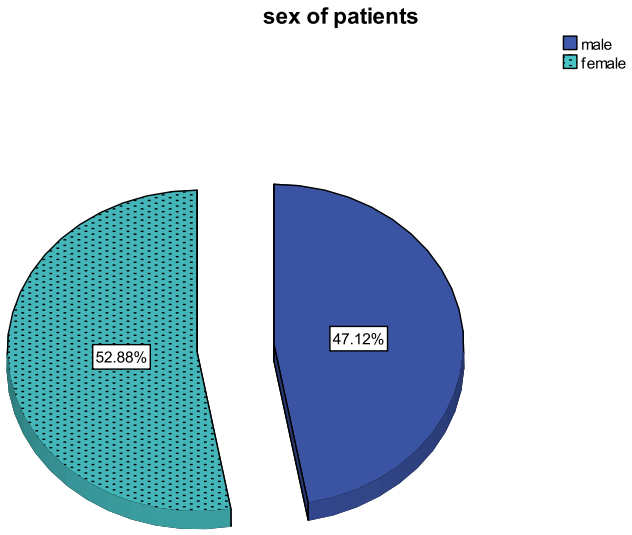

Figure 1 . Sex Distribution in 2052 Patients with Appendectomy.

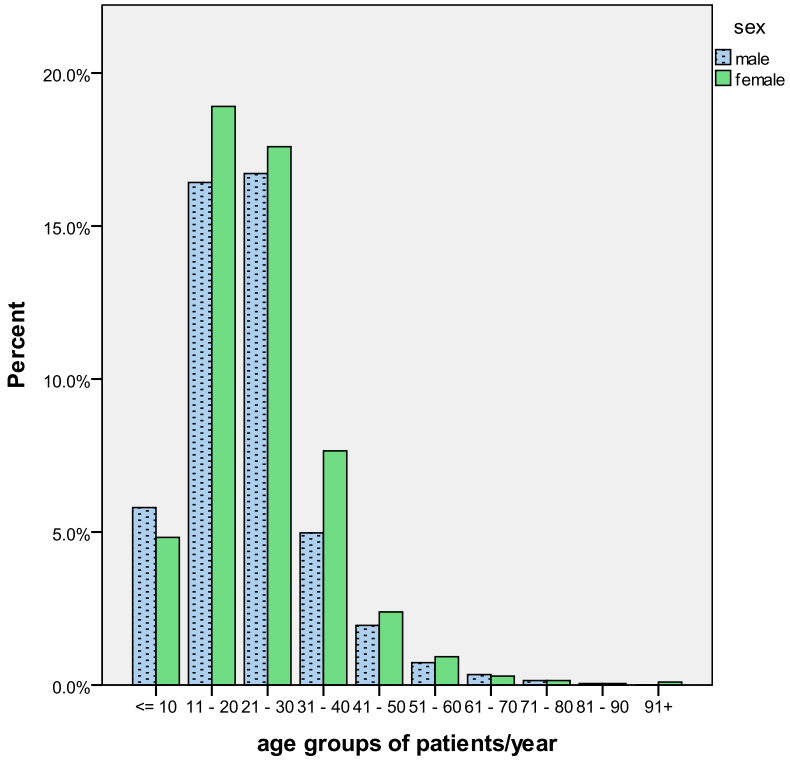

Figure 2. Age and Sex Distribution in 2052 Patients with Appendectomy

Table 2. Frequency of Positive and Negative Cases for Acute Inflammation

Presence of inflammation	Frequency	Percent
negative for acute inflammation	**781**	**38.07**
positive for acute inflammation	**1271**	**61.93**
Total	**2052**	**100.0**

Table 3. Sex Distribution in Different Diagnosis, this Table Shows that From the Positive for Acute Inflammation Cases, Males were more Significantly Affected (715 cases) than Females (556) Cases with P value =0.0001

	Diagnosis	Sex No. (Percent)		Total	Percent from total
		male	female		
Positive for acute inflammation	acute appendicitis	341 (50.5)	334 (49.5)	675	32.9
	acute suppurative appendicitis	313 (62.3)	190 (37.7)	503	24.5
	gangrenous appendicitis	61 (65.6)	32 (34.4)	93	04.5
	RFH	195 (33.3)	390 (66.7)	585	28.5
Negative for acute inflammation	normal	30 (23.5)	98 (76.5)	128	6.2
	periappendicitis	12 (42.9)	16 (57.1)	28	1.4
	chronic app	3 (17.7)	14 (82.3)	17	0.8
	eosinophilic app	12 (66.7)	6 (33.3)	18	0.9
	granulomatous app	0 0	1 (100)	1	0.0
	carcinoid tumor	1 (25)	3 (75)	4	0.2

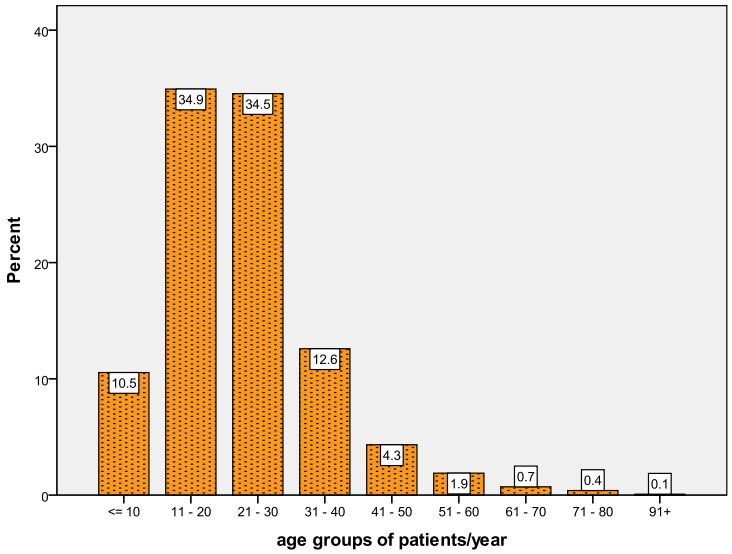

Figure 3. The Age Groups Distribution in 1271 Positive for Acute Inflammation Cases

Table 4. Relationship between Age groups and sex in 585 Cases of RFH, in this Table Female Patients (66.7%) were Significantly Highly Affected more than Males (33.3%) with P value =0.0001.

		Sex			
Age groups of patients/year		male	female	Total	percent
	≤ 10	34	40	74	12.6
	11 - 20	66	159	225	38.5
	21 - 30	75	122	197	33.7
	31 - 40	15	44	59	10.1
	41 - 50	4	15	19	3.2
	51 - 60	1	6	7	1.2
	61 - 70	0	3	3	0.5
	71 - 80	0	0	0	0
	81 - 90	0	0	0	0
	91+	0	1	1	0.2
Total		195	390	585	100.0
percent		33.3	66.7	100.0	

Table 5. Age and Sex Groups of Patients with Carcinoid Tumor

Age groups / years					
11 - 20		21 - 30		31 - 40	
male	female	male	female	male	female
0	1	1	1	0	1
1		2		1	

Table 6. Presence of *E.vermicularis* in Different Sex Group

	Frequency	Percent	p. value
male	5	25.0	
female	15	75.0	0.046
Total	20	100.0	

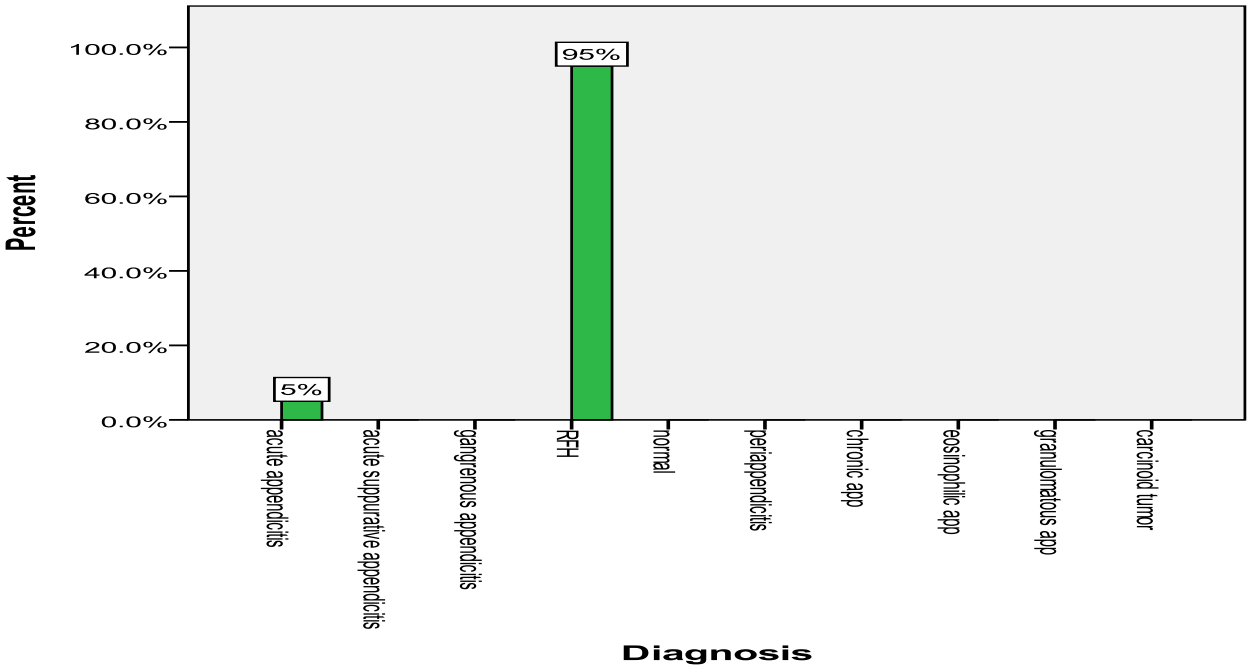

Figure 4. Presence of E. vermicularis in Different Diagnosis

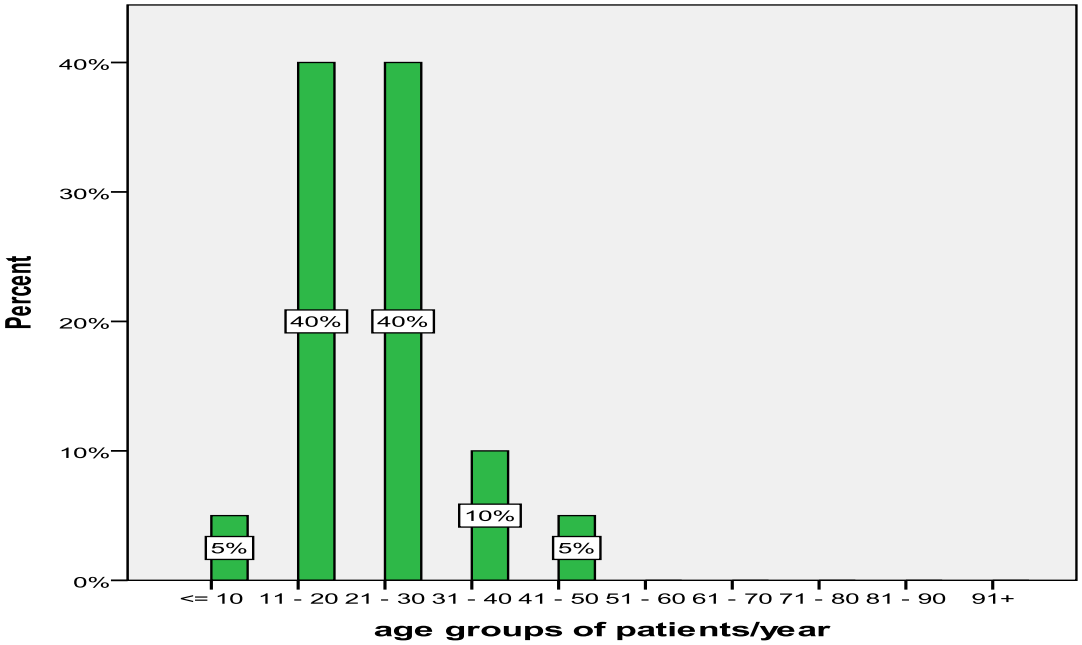

Figure 5. Presence of E. vermiculris in Different Age Group Patients

Table7. Relation between Associated Findings and Diagnosis

Associated findings		Diagnosis				
		acute appendicitis	RFH	normal	per appendicitis	Total
	ovarian cystectomy	1	23	30	3	57
	Meckeles diverticulum	0	4	1	0	5
	tubal pregnancy	0	1	1	0	2
	cholecystectomy	0	0	1	0	1
	mesenteric lymphadenitis	0	1	0	0	1
	orchiectomy	0	0	0	1	1
	small intestine gangrene	0	1	2	0	3
	cecal lesion	0	0	1	0	1
	perforated sigmoid	1	0	0	1	2
Total		2	30	36	5	73

RFH= Reactive Follicular Hyperplasia

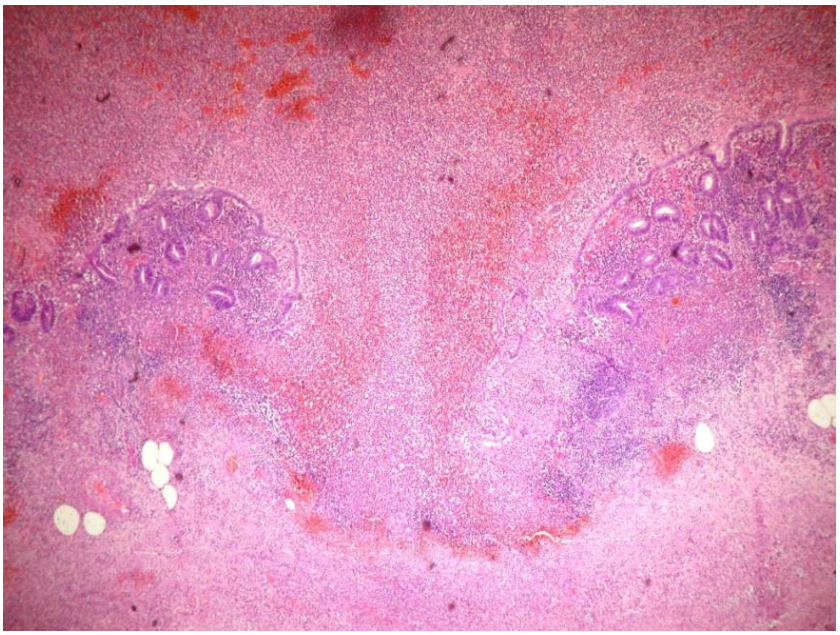

Figure 6. Acute Suppurative Appendicitis HEMATOXYLIN AND EOSINx40

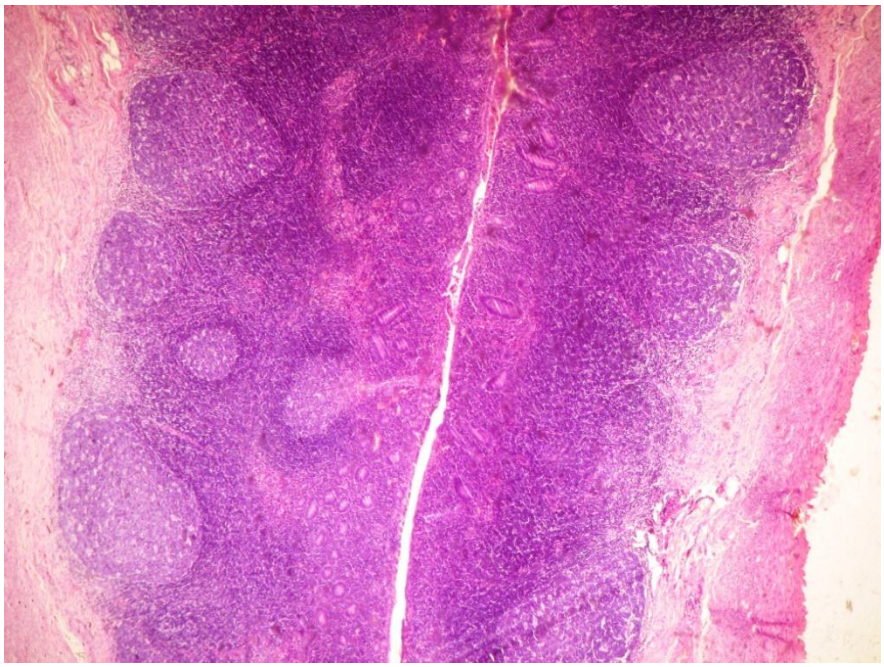

Figure 7. Reactive Follicular Hyperplasia in Appendix HEMATOXYLIN AND EOSINx40

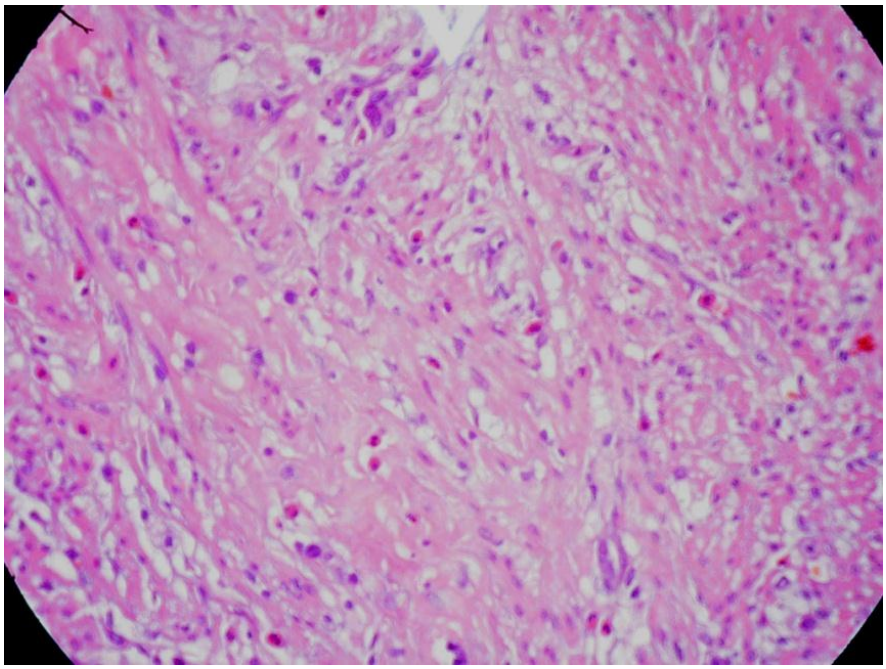

Figure 8. Eosinophilic Appendicitis HEMATOXYLIN AND EOSINx100

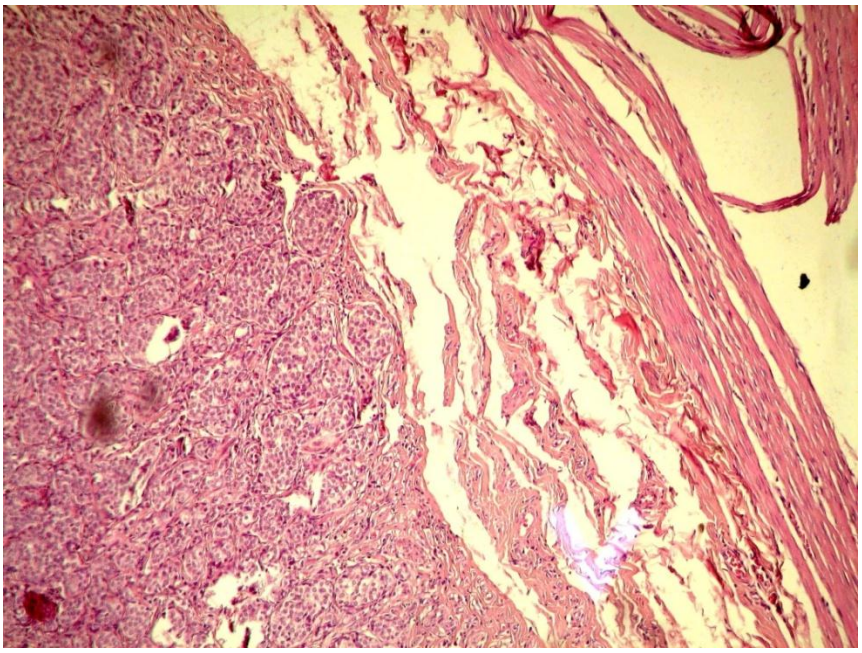

Figure 9. Carcinoid Tumor in Appendix HEMATOXYLIN AND EOSINx40

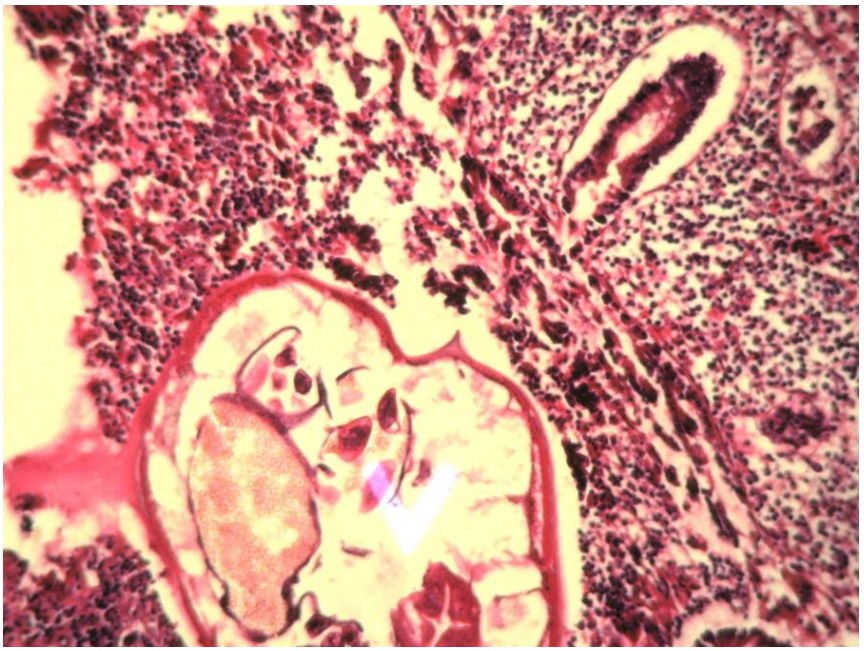

Figure 10. *E. vermicularis* in the Lumen of the Appendix HEMATOXYLIN AND EOSINx400

Discussion:

The histopathological examination of the appendix serves two purposes, first it allows the diagnosis of acute appendicitis to be confirmed. Second histopathological examination may disclose additional pathologies that may not be evident intraoperatively which may impact patient management [8].

Age This study shows that the highest occurrence (69.4%) of acute inflammation is in 2nd and 3rd

decade. This is the same finding as observed by Zulfikar I et al who did 2 years review of 323 cases [9] and Ojo et al in their study from Nigeria [10]. But Ngodngamthaweesuk et al who did a 5-year review of 449 patients found that young children (<10 years old) were statistically more significantly affected [11]. In this study 3 cases were ‹6 months while in many other studies on appendectomy in children the least age was one-half year [12].

Sex: is the other important clinical feature in appendicitis. In this study males positive for acute inflammation were significantly more (56.3%) affected than females, this is highly consistent with Ngodngamthaweesuk N, et al who found that male patients operated upon for lower abdominal pain had histological feature of acute appendicitis significantly more than females [11].

In this study **normal** appendix was observed in 6.2% of total 2052 cases which is less than that observed by other studies; 10.8% [9], and 10% [12].

Hyperplasia of the lymphoid tissue is a common normal feature in those younger than 20 years. Duzgun AP et al in Ankara reviewed 2458 cases in six years and divided the patients with lymphoid hyperplasia into two groups: younger and older than 20 years. Those below 20 years 5.3% were accepted as normal, whereas in those older 20 years the lymphoid hyperplasia was considered as important cause in the pathogenesis of acute appendicitis [8]. In the present study 585 (28.5%) of total cases showed **RFH**, 299 cases were ≤ 20 years if this number is added to 128 normal appendectomies then the percent of normal appendices rises to 20.8% (427 cases) which is higher than that observed by other studies [9, 12].

Other studies on appendicial lymphoid hyperplasia in children did not regard RFH as normal since it causes severe abdominal pain indistinguishable from AA. The increase and swelling of the lymphoid elements, together with the inelasticity of the peritoneal sheath of the appendix, is the most likely explanation of this pain [13]. Furthermore, as the majority of these cases conform to a recognizable syndrome, lymphoid hyperplasia should be considered as a clinical entity among diseases of the appendix [2].

The ability of the lymphatic system and its ready response to a wide variety of stimuli, especially infection, is well known. Some studies considered that abdominal symptoms suggestive of and frequently indistinguishable from acute appendicitis occur in association with upper respiratory infections. Varicella, oxyuriasis and perhaps a high fat diet may evoke a lymphoid response in the appendix [2].

It is believed that **chronic appendicitis** is rare; about 1.5 to 10% of all appendix inflammations ([14, 15]. Its existence is disputed clinically and pathologically. Falk et al report fibrosis, chronic inflammatory infiltrates, and neural cell proliferation is the most specific pathologic features in chronic appendicitis [16]. Lai DH et al in 2006 reviewed 16 cases having appendicitis with symptoms over few weeks. Histopathology revealed that all 16 patients proved to have acute inflammation of appendix. No chronic inflammation was found. They suggest that it is better to use the name of "recurrent appendicitis" but not "chronic appendicitis" [17]. This study showed 0.8% patients had chronic appendicitis and only one case (0.05%) had granulomatous appendicitis. But in Zulfikar I et al study 10% patients had chronic granulomatous changes consistent with tuberculosis [9].

Periappendicitis referred to inflammation of the appendiceal serosa, with no inflammation in the mucosa. It means spread of inflammation from nearby organs. It could be acute or chronic. But it should be remembered that surgical manipulation may induce neutrophilic infiltration of the periappendix [1]. In this study periappendicitis is a much less finding, it is found in 28 cases only and the majority (57.1%) were

found in females. Five cases had other associations; 3 cases were associated with ovarian cyst, 1 case with orchiectomy and one case with perforated sigmoid..

In eosinophilic appendicits there should be no neutrophils. Eosinophils are the only inflammatory cells, between muscle fibers with odema separating muscle fibers (the Eosinophil - Edema lesion) or (E-E lesion) [18].

It may be associated with helminthes infection like schistosomaiasis, strangyloides or enterobius. It is possible that the disease is triggered by Type I Hypersensitivity [19]. It could be part of eosinophilic gastroenteritis which is a rare and heterogeneous condition characterized by patchy or diffuse eosinophilic infiltration of gastrointestinal (GI) tissue, first described by Kaijser in 1937. Peripheral blood eosinophilia and elevated serum IgE are usual but not universal [20]. In this study 18 cases (0.9%) had esinophilic appendicitis. As in other types of acute appendicitis esinophilic appendicitis were found more common in males (2/3). KP Aravindan et al in 2010 in India studied 8 cases of eosinophilic appendicitis also found that the male/female resembled classical acute appendicitis (75%), with a mean age 24.3 years [18].

Carcinoid tumors are the most common appendiceal tumor; make up 51% of all malignant tumors of the appendix. The reported incidence of appendiceal carcinoids in several studies ranges from 0.02 to 1.5% of surgically removed appendices. A large female preponderance is reported in all series (2-3:1). Incidence peaks at ages 20-39 years [21-23]. This study showed 0.2% of specimens had carcinoid, 75% of cases were females, similar to other series [24]. Three were of solid pattern, & 1 adenocarcinoid. Duzgun AP, et al. found carcinoid tumor in 3 cases out of 2458 cases (0.1%) and all of them were females [8]. Zulfikar I et al found 0.6% specimens with carcinoids [9].

Meckel's diverticulitis can mimic acute appendicitis in clinical history, physical findings and operative findings. It is always important to consider this as possible cause of acute abdomen [25], in this study 5 cases (0.24%) had Meckel's diverticulitis and none of them associated with AA, Zulfikar I et al found 1.2% of cases presented as acute appendicitis and had Meckel's diverticulitis as coexisting pathology [9].

Entrobius vermicularis (Oxyuriasis) is associated with:

- normal appendix,
- esinophilic infilteration,
- RFH
- Granuloma formation [26].

The association of *E. vermicularis* infection and acute appendicitis is controversial. It has also been noted that parasites may be incidental findings in cases where inflammation is already present [27].

In the present study *E. vermicularis* was found in 20 cases, and 95% of them associated with RFH and only 1case associated with AA. Duzgun AP, et al. found 4 (0.4%) cases had E. Vermiclaris and none of them had acute appendicitis on histology [8] which is in correlation with the literature [28]. In a similar study in Hamadan province, western Iran, the reactive follicular hyperplasia and acute suppurative appendicitis were the most observed pathologic findings associated with E. Vermiclaris [29].

Gh Mowlavi et al., in their study mentioned that E. vermicularis causes reactive follicular hyperplasia in most cases; and could not necessarily be claimed as the causative agent of acute appendicitis, they showed that *E.vermicularis* was likely to be involved partly in the etiology of appendicitis in young children [26]. H Kazemzadeh et al concluded that, parasitic infestation rarely causes acute appendicitis [30].

Recommendations:

1. We recommend that the pathologists must be strict to histological criteria for each pathological entity before the diagnosis.
2. The researchers should review the microscopical pictures to avoid misdiagnosed cases.
3. The surgeons have to read the results of this review to avoid unnecessary operations.

References:

1. PathologyOutlines.com, **Last revised 10 December 2010**.
2. Alfred a. Nathans, hyman merenstein, Samuel s. Brown.L**ymphoid hyperplasia of the appendix : Clinical Study** *Pediatrics* 1953;12;516,Downloaded from pediatrics .aappublications.org at iraq:aap sponsored on February 19, 2012
3. Marudanayagam R, Williams GT, Rees BI. **Review of pathological results of 2660 appendicectomy specimens**. J Gastro 2006; 41: 745-9.
4. Kozar RA and Roslyn JJ. The appendix. In: Schwartz SI, editor. **Principles of Surgery**, 7th Ed. NY, USA: McGraw-Hll 1999; 1383-95.
5. Rao PM, Rhea JT, Novelline RA, Mostafavi AA, McCabe CJ. **Effect of computed tomography of the appendix on treatment of patients and use of hospital resources**. N Engl J Med 1998; 338(3): 141-146.
6. Jones AE, Phillips AW, Jarvis JR, Sargen K. **The value of routine histopathological examination of appendicectomy specimens.** BMC Surg. 2007; 7:17.
7. Cusherie A, Giles GR, Mossa AR. **The small intestine and Vermiform appendix. Essential Surgical Practice.** 4th ed. London: Butterworth Heine-mann's; 2002: p. 563-7.
8. Duzgun AP, Moran M, Uzun S, Ozmen M, Ozer VM, Seckin S, et al. **Unusual findings in appendicectomy specimens**. Indian J Surg. 2004: 66 Issue 4 (August): 221-6.
9. Zulfikar i., khanzada t. W., sushel c. Et al. **Review of the pathologic diagnoses of appendectomy specimens**, annals vol. 15. No. 4 oct. - dec. 2009, 168-170.
10. Ojo OS, Udeh SC, odesanmi WO. **Review of the histo-pathological findings in appendices removed for acute appendicitis in Nigerians**. J R Coll Surg Edinb 1991; 36: 245
11. Nampet Ngodngamthaweesuk, Anucha Tunthangtham, Dusadee Sakonya,et al. **Acute Appendicitis : A 5-year Review of Histopathology and Clinical Presentation.** Thai J Surg Jul. - Sept. 2003; Vol. 24 No. 3, 81-84.
12. Law D, Law R, Eisman B. **The continuing challenge of acute and perforated appendic-itis**. Am J Surg 1976; 131: 533-5.
13. Thomas A. Smith, **Lymphoid hyperplasia of the appendix in children its relation to recurrent appendicitis Annals of surgery.** 07/1924; 79(6):871-8.
14. Mattei P, Sola JE, Yeo CJ. **Chronic and recurrent appendicitis are uncommon entities often misdiagnosed**. J Am Coll Surg 1994; 178: 385-9
15. Savrin RA, Clausen K, Martine EW, Cooperma M. **Chronic and recurrent appendicitis**. Am J Surg 1979; 137: 355-7.
16. Falk S, Schutze U, Guth H, Stutte HJ. **Chronic recurrent appendicitis**. A clinicopathologic study of 47 cases. Eur J Pediatr Surg 1991; 1: 277-81.
17. LAI, DH, CHUANG, CH, YU, JC et al. **Chronic or recurrent appendicitis?**. Rev. esp. enferm. dig., 2007, vol.99, no.10, p.613-615. ISSN 1130-0108.
18. KP Aravindan, Deepthy Vijayaraghavan, Marie Therese Manipadam. **significance of eosinophil - Edema lesion**. Indian J Pathol Microbiol [serial online] 2010 [cited 2012 Feb 11];53:258-61.
19. Aravindan KP. **Eosinophils in acute appendicitis: Possible significance**. Indian J Pathol Microbiol 1997; 40:491-8.

20. **Eosinophilic gastroenteritis From Wikipedia**, the free encyclopedia.
21. Cortina R, McCormick J, Kolm P, Perry RR. **Management and prognosis of adenocarcinoma of the appendix.** Dis Colon Rectum 1995; 38: 848-52.
22. Pelizzo G, La Riccia A, Bovier R, Chappius JP. **Carcinoid tumours of appendix in children**. Pediatric Surg Int; 17: 399-402.
23. Moertel CL, Weiland LH, Telander RL. **Carcinoid tumor of the appendix: Treatment and prognosis**. N Eng J Med 1987;317:1699-701.
24. Bast RC, Kufe DW, Pollock RE, editors. **Neoplasms of alimentary tract. In: Cancer Medicine** (5th ed). Section 29. BC Decker Inc Canada 2000.
25. Loh DL, Munro FD, Wilson Storey D, Orr JD. **Early Appendicitis – a safe diagnosis?** Ann Acad Med Singa-pore 2006 July; 33: 530-1.
26. Mowlavi GH, Massoud J, Mobedi I, et al. **Enterobius vermicularis: A controversial cause of appendicitis.** Iranian J Publ Health. 2004;33:27-31.
27. Budd JS, Armstrong C. **Role of Enterobiusvermicularis in the etiology of appendicitis**. Br J Surg. 1987; 74:748-9.
28. Blair NP, Bugis SP, Turner LJ, MacLeod MM. **Review of the pathologic diagnoses of 2,216 appendectomy specimens**. Am J Surg 1993;165:618-20.
29. Syavashi MR (1997). **A survey on the prevalence of histopathological findings of parasitic appendicitis of parasitic origin.** The second national congress on Parasitology. Tehran, Iran.
30. H Kazemzadeh , N Afshar-Moghadam, AR Meamar, HR Rahimi, **EB Kia 1Enterobious vermicularis and the Appendix Iranian J Parasitol**: Vol. 3, No. 3, 2008, pp. 54-55.