ORIGINAL ARTICLE

Comparative analysis of epidemiological and clinical characteristics of appendicitis among children and adults

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ABSTRACT

BACKGROUND: This study aimed to investigate whether there are some differences between pediatric and adult patients with appendicitis.

METHODS: We retrospectively reviewed the records of 279 pediatric and 275 adult patients with respect to demographics, past medical history, duration of symptoms, laboratory and radiological findings, operation notes, pathological reports, length of hospital stay and post-operative outcomes.

RESULTS: No significant differences were found with respect to gender, rates of perforation and negative appendectomy, laboratory findings, and overall outcomes between children and adults. However, our study suggests that the diagnosis is more difficult in children, the most preferred radiologic diagnostic methods are abdominal ultrasound and plain X-ray in children vs. computed tomography in adults, air-fluid levels and right-sided scoliosis are more commonly detected on X-ray in children, appendiceal perforation is more common at both extreme of ages, the appendix is perforated earlier and length of hospital stay is longer in children, and misdiagnosis at first admission in children and advanced age in adults were the risk factors associated with the complications.

CONCLUSION: The present study found some important differences between childhood and adulthood appendicitis. If these differences are considered when evaluating the patients, more desired outcomes can be achieved for both clinicians and patients.

Keywords: Abdominal pain; adult; appendicitis; child.

INTRODUCTION

Acute abdominal pain is a common reason for admission to the emergency department (ED).[1] Although numerous conditions cause acute abdominal pain, appendicitis is considered in the differential diagnosis of mostly every patient.[2,3] Although appendicitis is one of the most studied surgical conditions in the literature, pediatric and adult patients have been examined separately in almost all publications. Children are not little adults; therefore, it is inevitable that there are some differences in cases with appendicitis between children and adults. Thus, a retrospective clinical study was conducted to evaluate whether there are some differences between pediatric and adult patients with appendicitis.

MATERIALS AND METHODS

Ethical Approval

Permission from the institutional review board was obtained

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before the study (IRB number: 2019–199). Informed consent was obtained from the patients.

Study Design

All patients who presented to the ED with acute abdominal pain and underwent appendectomy for suspected appendicitis at a tertiary care teaching hospital between 2015 and 2018 were included in the study. The medical records of the patients were retrospectively reviewed with respect to demographics, medical history, duration of symptoms, laboratory and radiological findings, operation notes, pathological reports, length of hospital stay, and post-operative outcomes. The patients who had incomplete medical records, incidental appendectomy as a part of another procedure and concomitant conditions such as ovarian pathology and pregnancy were excluded.

Patients were divided into two main groups: pediatric group (<18 years) and adult group (≥18 years). Additionally, we categorized our patients into 6 age categories: under 6 years, 6-11 years, 12–17 years, 18–30 years, 31–60 years, and over 60 years. Patients were also divided into three subgroups as follows: acute appendicitis (AA), perforated appendicitis (PA), and negative appendectomy (NA). PA was defined by surgical observation of a visualized hole in the appendix and/or intra-abdominal abscess formation, and/or a free fecalith in the abdominal cavity. NA was determined by pathological report of the normal appendix or lymphoid follicular hyperplasia. Duration of symptoms was the interval between symptoms onset and surgery. All of the abdominal plain X-rays (AXRs) were assessed for the presence of fecalith, air-fluid levels, right-sided scoliosis, and pneumoperitoneum. Abdominal ultrasound (USG) and computed tomography (CT) reports were also examined for diagnostic accuracy, the presence of fecalith, and the diameter of appendix.

Statistical Analysis

Data were analyzed using SPSS 20.0 (IBM Inc., Chicago, IL, USA). The descriptive statistics were presented as mean ± standard deviation or median with the minimum-maximum range in the parentheses for continuous variables, frequency (percentage) for categorical variables. Student t-test was used for independent two samples, and One-way ANOVA was used for comparing several groups. The Chi-square test was preferred to determine the relationships between categorical variables. Multivariate logistic regression model was established to analyze the risk factors associated with complications, and the results were expressed as odds ratio (OR) and 95% confidence interval (CI). The optimal cut-off values were calculated by using ROC analysis, in which the area under the curve (AUC) reflected diagnostic accuracy. Comparisons were usually given in the parentheses and expressed as (pediatric group% vs. adult group%, p-value). In all analyses, $p<0.05$ was considered as statistically significant.

RESULTS

The results of the study are summarized comparatively in Table 1.

Patient Demographics

The study included a total of 554 patients, of whom 279 were children and 275 were adults. The appendicitis group consisted of 253 children (90.7%) and 261 adults (94.9%). Males were affected more than females in all age groups ($p>0.05$), except for the patients over 60 years of age. The median age of the children with appendicitis was 11 years (2–17) compared to 29 years (18–82) in adults ($p<0.001$). The peak incidence belonged to the patients aged between 12 and 17 years in children and those aged between 18 and 30 years in adults (Fig. 1). In cases with NA, the median age was 9.5 years (4–17) in children and 25 years (18–64) in adults ($p<0.001$). Unlike children, the NA group consisted mostly of female patients in adults (46.2% vs. 71.4%, $p=0.020$).

Pathological Groups

The pathological characteristics of the patients are given in Table 2. AA was significantly more common in adults ($p=0.019$). Although pediatric group had higher perforation (22.2% vs. 16.4%) and NA rates (9.3% vs. 5.1%), these were not statistically significant ($p>0.05$). The perforation rate was significantly higher in patients under 6 years of age (64.9%) and over 60 years of age (60.9%) ($p<0.001$). Retrocecal appendicitis was observed in 9.1% of children and 12.5% of adults ($p=0.198$), but not associated with a higher rate of perforation in both age groups ($p>0.05$). Appendiceal neoplasms were identified as neuroendocrine tumors (NET) in four children (1.4%) and low-grade mucinous neoplasm in an adult (0.4%), and all cases were presented as AA. Lymphoid hyperplasia was more common in the pediatric group (6.1% vs. 1.5%, $p=0.008$).

Duration of Symptoms

Patients with PA had significantly longer duration of symptoms (median=48 h) than those with AA (median=24 h) in both age groups ($p<0.001$). The duration of symptoms was also found to be longer at both extremes of ages (<6 year and >60 years). The incidence of PA in pediatric and adult groups was 4.6% versus 7.2% within the first 24 h after the onset

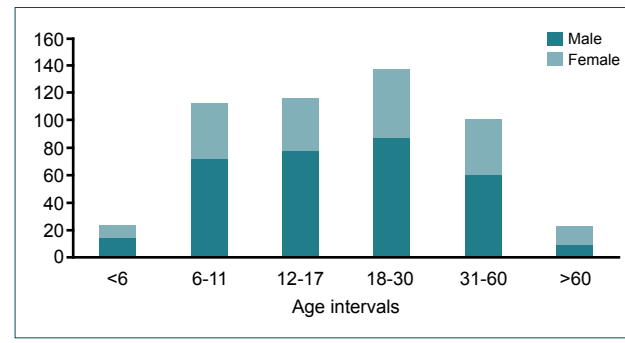

Figure 1. Incidence of appendicitis according to age intervals.

Table 1. Comparison of children and adults according to pathological groups*

Patient characteristics	Acute appendicitis			Perforated appendicitis			Negative appendectomy		
	Children (n=187)	Adults (n=187)	p	Children (n=62)	Adults (n=45)	p	Children (n=26)	Adults (n=14)	p
Epidemiological and clinical									
Age, years, Md	12 (2–17)	27 (18–75)	<0.001	8.5 (2–17)	47 (18–82)	<0.001	9.5 (4–17)	25 (18–64)	<0.001
Male to female ratio	2.1	1.6	0.210	1.4	1.1	0.628	1.2	0.4	0.020
Duration of symptoms, hours, Md	24 (2–144)	24 (2–360)	0.620	48 (12–288)	48 (5–240)	0.781	24 (6–48)	36 (12–120)	0.243
Missed appendicitis, %	8.4	1.9	<0.001	45.2	–	<0.001	NA	NA	NA
Antibiotic history, %	2.1	9.3	<0.001	25.8	8.9	<0.001	–	21.4	0.015
Retrocecal position, %	9.1	12.4	0.268	9.7	13,6	0.528	3.8	–	0.480
Complications, %	1.1	2.8	0.157	30.6	31.1	0.874	–	7.1	0.173
Hospital stay, days, Md	3 (1–6)	1 (1–12)	<0.001	9 (3–22)	6 (2–22)	<0.001	3 (1–6)	2 (1–10)	0.003
Laboratory									
WBC ($\times 10^3/\mu L$), M	15.86±4.40	14.51±3.83	0.064	16.58±5.68	15.88±6.18	0.344	11.21±3.92	11.51±3.13	0.510
CRP (mg/L), M	26.01±35.08	28.30±36.52	0.314	127.43±67.16	130.34±72.00	0.773	26.73±27.72	32.73±27.62	0.294
Radiological									
AXR performed, %	98.9	65.1	<0.001	96.8	57.8	<0.001	96.2	35.7	<0.001
USG performed, %	97.9	22.3	<0.001	90.3	24.4	<0.001	96.2	64.3	<0.001
CT performed, %	6.4	85.1	<0.001	29.0	82.2	<0.001	3.8	85.7	<0.001
Fecalith on CT/USG, %	12.9	20.3	0.044	25.0	29.3	0.601	12.0	–	0.199
Appendix diameter, mm, M	8.83±2.24	10.36±2.51	0.004	9.96±3.18	12.08±3.53	<0.001	6.74±1.74	6.97±1.81	0.601

*Appendiceal neoplasms not included, Md: Data are given as median (range); M: Data are given as mean±SD; CRP: C-reactive protein; WBC: White blood cell; AXR: Abdominal plain X-ray; USG: Ultrasound; CT: Computed tomography.

Table 2. Comparison of pathological characteristics between children and adults

Pathological groups	Children, n (%)	Adults, n (%)	p
1. Acute appendicitis	187 (67.1)	215 (78.1)	0.019
2. Perforated appendicitis	62 (22.2)	45 (16.4)	0.457
3. Negative appendectomy	26 (9.3)	14 (5.1)	0.637
Normal appendix	9 (3.2)	10 (3.6)	0.961
Lymphoid hyperplasia	17 (6.1)	4 (1.5)	0.008
4. Appendiceal neoplasms	4 (1.4)	1 (0.4)	0.701

of symptoms, 18.6% versus 8.1% if symptoms were present for between 24 and 48 h, and 60.9% versus 46.2% if symptoms were present for more than 48 h, respectively. The risk of perforation increased significantly after 24 h in children (p<0.001), while after 48 h in adults (p<0.001).

Missed Appendicitis

The rate of readmission due to misdiagnosis at initial presentation was significantly higher in children when compared to adults (17.4% vs. 1.5%, p<0.001). All of the perforated cases were diagnosed on their first admission in adults. In contrast, the rate of misdiagnosis was as high as 45.2% in children with PA at initial admission. The rate of perforated cases who initially received antibiotics due to misdiagnosis was also significantly higher in the pediatric group (25.8% vs. 8.9%, p<0.001).

Laboratory Findings

Normal C-reactive protein (CRP) level (<6 mg/L) and white blood cell (WBC) count (<10.000 /μL) were observed in 26.1% and 8.3% of pediatric patients, and 23.0% and 11.1% of adults, respectively. The mean CRP levels of the groups did not differ significantly between the NA and AA groups (p>0.05), but there was a significant increase in PA groups compared to the AA (p<0.05). Conversely, the mean WBC values of the groups significantly increased in appendicitis group compared to the NA group (p<0.05), but there was no significant difference between AA and PA groups (p>0.05) (Fig. 2). Therefore, we could not find a significant cut-off value of WBC for PA. The optimal cut-off value of CRP for PA was 64 mg/L (AUC=0.911, p<0.001) in children and 84 mg/L (AUC=0.887, p<0.001) in adults.

Imaging Studies

AXR was performed in 98.2% of pediatric patients and 62.2% of adults (p<0.001). Overall, non-specific findings were detected significantly higher in pediatric group (44% vs. 29%, p=0.002). Of these, air-fluid levels (15.0% vs. 8.2%, p=0.035) and right-sided scoliosis (28.6% vs. 17.1%, p=0.006) were detected significantly higher in pediatric group. All AXR with air-fluid levels belonged to perforated cases in both age groups. The incidence of fecalith on AXR were similar in both age groups (7.7% vs. 8.2%, p=0.842). Pneumoperitoneum was observed only in 2 children with PA (0.7%), but not in adults (p=0.349).

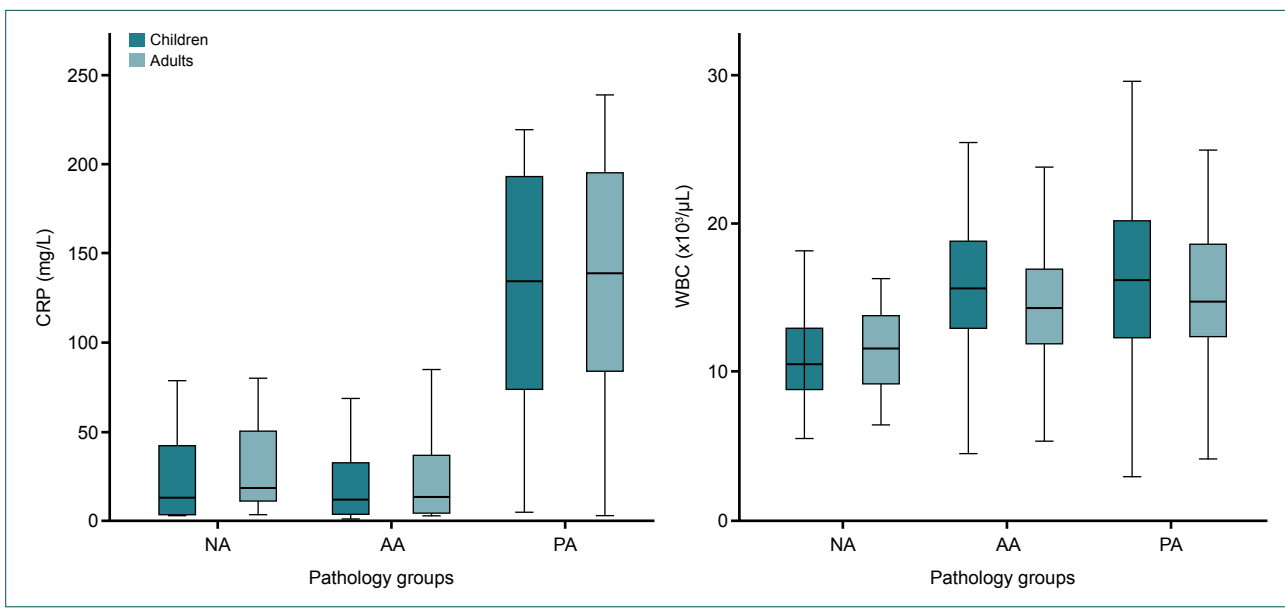

Figure 2. Box plots showing mean C-reactive protein and white blood cell values between the groups.

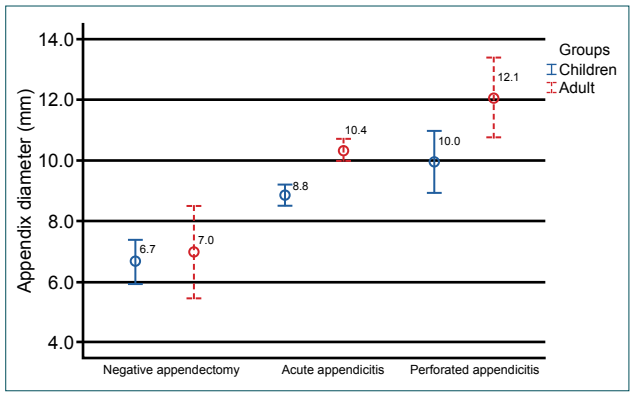

Figure 3. The mean diameter of appendix between the groups.

Abdominal USG was more frequently preferred in children (96.1% vs. 23.3%, p<0.001), and demonstrated a sensitivity and specificity of 87.2% and 52.0% in children versus 81.4% and 60.0% in adults, respectively. In contrast, abdominal CT was the most frequently used imaging modality in adults (11.5% vs. 84.7%, p<0.001), and demonstrated a sensitivity and specificity of 96.8% and NA (specificity not calculated since true negative examples were not available) in children versus 99.1% and 75.0% in adults, respectively. Unlike the adult group, CT was mostly preferred for perforated cases in children (p<0.001).

The mean appendix diameter was significantly larger in adult patients with appendicitis compared to the children (p<0.05) (Fig. 3). The optimal threshold diameter of appendix for the diagnosis was 7 mm (AUC=0.831, p<0.001) in children, and 8 mm (AUC=0.881, p<0.001) in adults. Patients with PA had the largest appendix diameter with a cut-off value of 10 mm in children (AUC=0.597, p=0.043) and 12.5 mm in adults (AUC=0.667, p=0.003). Overall, the incidence of fecalith on CT or USG was 15.2% in children and 20.6% in adults (p=0.104). There was no significant relationship between the presence of a fecalith and PA in both age groups (p>0.05). The rate of patients without USG or CT was as low as 1.4% in both age groups, and the absence of imaging methods did not significantly affect NA and PA rates (p>0.05).

Complications

No mortality was observed in all groups. The rate of complications in the groups is given in Table 3. There were no complications in the NA group, except for an adult patient complicated with wound infection. As we compared to the overall complications rates, there was no significant difference between the groups (7.4% vs. 7.7%, p=0.620). PA was significantly associated with complications compared to AA in both age groups (p<0.001). Misdiagnosis at first admission in children (OR=3.63, CI=1.36–9.70), and advanced age in adults (OR=1.049, CI=1.020–1.080) were found to be the risk factors significantly associated with the complications.

Table 3. The rate of complications in the groups

Complications	Children %	Adults %	p
Wound infection	3.9	3.3	0.656
Intra-abdominal abscess	0.7	3.3	0.004
Postoperative ileus	1.4	0.4	0.366
Pleural effusion	1.4	–	0.057
Incisional hernia	–	0.7	0.816
Total	7.4	7.7	0.620

Length of Hospital Stay

The length of hospital stay was significantly longer in patients with PA in both age groups (p<0.001). Adult patients had significantly shorter hospital stay compared to pediatric patients (p<0.001).

DISCUSSION

Appendicitis is one of the most prominent diseases in the differential diagnosis of acute abdominal pain. Although appendicitis is a disease of all age groups, children and adults were handled separately in almost all previous studies. To our knowledge, only one previous study has sought the answer to whether there is a difference between adults and children in terms of appendicitis.[4] However, this study found no significant differences between children and adults except for a few issues; moreover, some issues have not been fully clarified. In this respect, the present study compared the two age groups from a new perspective in terms of both previously known and controversial issues.

The demographics of appendicitis is well-known topic that has been investigated already in several studies.[5] The present study obtained similar results that the peak incidence was highest among adolescents and young adults, but was substantially low at both extreme ages, and there was a male predominance in both children and adults.

The term "time is money" is also applies to appendicitis, because the increased duration of symptoms is associated with increased risk of perforation.[6,7] Duration of symptoms longer than 36 h significantly increases the risk of perforation in adults.[8] On the other hand, there is no general consensus on when the risk of perforation is significantly higher in children, but the general opinion is that this period is shorter than adults.[7,9] We found that the risk of perforation increased significantly after 24 h in children and 48 h in adults. The present study also showed that adult patients were easily diagnosed on their first presentation, while initial misdiagnosis and associated antibiotic treatment rate were significantly higher in children with PA. These findings suggest that clinicians still have more diagnostic difficulties in children during the early period of appendicitis.

Early and accurate diagnosis with prompt intervention remains the cornerstone of the treatment. Several laboratory tests and imaging methods have been used to diagnose appendicitis.[10] Of these, inflammatory markers have long been routinely used, in which WBC and CRP are the most well-known parameters.[11] The present study did not find a significant difference in inflammatory markers between children and adults and supported the results of previous studies that WBC is more sensitive than CRP in the initial phase of AA, but has not a prognostic value indicating the disease progression, on the other hand, CRP is not an ideal diagnostic tool for ruling out or determination of AA, and has more diagnostic accuracy in detecting PA.[12,13] However, patients with appendicitis may have WBC count and CRP level within normal limits,[14] as occurred in our patients. These results indicate that inflammatory markers alone lack of accuracy to diagnose or exclude appendicitis in neither children nor adults.

Today, various imaging modalities are used in the diagnostic workup. Of these, AXR has been used especially in children as an initial imaging workup in our study. However, AXR has a limited role in the diagnosis when compared to USG and CT.[15] Some radiographic signs have been historically described for appendicitis.[16] We detected these signs in 44% of children and 29% of adults. The most specific sign is the presence of a fecalith. As classical knowledge, it can be visualized on 10%–20% of plain films.[16,17] The present study found the incidence of fecalith as 7.7% in children and 8.2% in adults. Right-sided scoliosis and air-fluid levels were the other non-specific signs that we observed more frequently in children. Pneumoperitoneum is rarely encountered as a radiographic finding in association with PA, and several authors have speculated on its incidence ranging from 0 to 7.1% in adults,[18] but data are missing in the pediatric literature. As a novel finding, we found its incidence to be 0.7% in children.

USG and CT are the most favored imaging modalities especially in patients with atypical symptoms. Nowadays, CT represents an excellent diagnostic option for all ages, with a sensitivity and specificity of >90%.[19] So, it has become almost routine in the diagnosis of appendicitis in adults. On the other hand, although USG has a lower sensitivity and specificity, it remains a preferred diagnostic tool for children due to the lack of ionizing radiation.[20] CT was performed in 84.7% of adult patients in our study, in contrast, this rate was as low as 11.5% in the pediatric group in whom USG was the preferred imaging modality. Another issue we investigated was that what should be the threshold diameter of the appendix for the diagnosis. Because the diameter of the appendix increases with the disease progression as we found in our study. A traditional threshold value of 6–7 mm is most commonly considered positive for AA, our study suggested a threshold value 7 mm for children and 8 mm for adults for more accurate diagnosis.

Despite developments in clinical understanding and technological advances, PA continues to be a substantial problem facing clinicians today. Perforation rates in children and adults vary from 22% to 62% and 17% to 32%, respectively.[21,22] Unlike a general belief that pediatric patients have a higher perforation rate than adults, the present study found a higher but not statistically significant perforation rate of 22.2% in children compared to 16.3% in adults. Previous studies have suggested some possible predictors factors for PA.[6,7] In our study, these factors in children included patients younger than 6 years of age, duration of symptoms longer than 24 h, CRP ≥64 mg/dL, appendix diameter of 10.25 mm or more. On the other hand, those in adults included patients older than 60 years of age, duration of symptoms longer than 48 h, CRP ≥84 mg/dL, appendix diameter of 12.50 mm or more. However, some studies proposed that retrocecal position of the appendix and the presence of fecalith increase the risk of perforation,[6,23,24] but our results did not support these arguments. We also showed that air-fluid levels and pneumoperitoneum detected on AXR were non-specific findings of PA.

Historically, acceptable NA rates ranged from 15% to 25%,[25,26] but the reported rates have decreased to 1–12% due to widespread use of imaging studies.[23,27,28] Currently, lymphoid hyperplasia is also considered as NA, and most commonly identified in pediatric patients.[29] The present study found similar NA rates of 9.3% in children and 5.1% in adults, and a significantly higher lymphoid hyperplasia rate in the pediatric group. This result could be a reflection of the lack of CT scans in children. Recent studies proposed some predictive factors for NA, which include female gender, younger age, no preoperative imaging and a CRP ≤6 mg/L and WBC ≤10.000 /μL.[30] However, our study found that only female gender and younger age have meaningful impact on NA rate in adults. Another controversial issue is that whether NA is associated with morbidity. Although some studies say yes to this question,[31] only one adult patient complicated with wound infection in our study.

Appendiceal neoplasms are identified in approximately 1% of appendectomy specimens.[32] Of these, NETs are the most common one, and generally occur in young patients.[33] In our study, appendiceal NETs were only identified in the pediatric group with an incidence of 1.4%. On the other hand, only one patient presented with low-grade mucinous neoplasm in the adult group.

The presence of perforation plays an important role in patient morbidity. In our study, the complications were significantly associated with PA in both groups. The present study indicated that the misdiagnosis at first admission in children, and advanced age in adults were the risk factors for the development of complications. The patients with PA had also prolonged length of hospital stay. But this period was significantly higher in children compared to adults.

There are some limitations of our study. First, this study is retrospectively designed based on the data obtained in a sin-

gle center. Second, the duration of symptoms were also unable to reliably examine due to often reported in days instead of hours. Further prospective studies are needed for more sensitive results.

Conclusion

We found no significant differences with respect to gender, rates of perforation and NA, laboratory findings, and overall outcomes between children and adults. On the other hand, the results of the study suggest that the diagnosis is more difficult in children, the most preferred diagnostic methods are USG and AXR in children versus CT in adults, there are some significant differences in terms of radiological findings, PA is more common at both extreme of ages, the appendix is perforated earlier in children, and length of hospital stay is longer in children, and misdiagnosis at first admission in children and advanced age in adults are the risk factors significantly associated with the complications. If these differences are considered, more promising outcomes can be achieved for both clinicians and patients.

Ethics Committee Approval: This study was approved by the Suleyman Demirel University Clinical Research Ethics Committee (Date: 25.06.2019, Decision No: 2019–199).

Peer-review: Internally peer-reviewed.

Authorship Contributions: Concept: H.H.A., L.D., Ö.C.; Design: H.H.A., L.D., Ö.C.; Supervision: L.D., M.Ç.S.; Resource: H.H.A., L.D., E.B., A.Y.H.; Materials: H.H.A., L.D., E.B., A.Y.H.; Data: H.H.A., L.D., E.B., A.Y.H.; Analysis: L.D., AK; Literature search: L.D., E.B.; Writing: H.H.A., L.D., M.Ç.S.; Critical revision: L.D., M.Ç.S.

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ORİJİNAL ÇALIŞMA - *ÖZET*

Çocuklar ve yetişkinler arasında apandisitin epidemiyolojik ve klinik özelliklerinin karşılaştırmalı analizi

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AMAÇ: Bu çalışmanın amacı, apandisitli pediatrik ve yetişkin hastalar arasında bazı farklılıklar olup olmadığını araştırmaktır.
GEREÇ VE YÖNTEM: İki yüz yetmiş dokuz pediatrik ve 275 erişkin hastanın kayıtları demografik özellikler, geçmiş tıbbi öykü, semptomların süresi, laboratuvar ve radyolojik bulgular, ameliyat notları, patolojik raporlar, hastanede kalış süresi ve ameliyat sonrası sonuçlar açısından geriye dönük olarak incelendi.
BULGULAR: Çocuklar ile yetişkinler arasında cinsiyet, perforasyon ve negatif apendektomi oranları, laboratuvar bulguları ve komplikasyonlar açısından anlamlı bir fark bulunmadı. Bununla birlikte, çalışmamız çocuklara tanı koymanın daha zor olduğunu, en çok tercih edilen radyolojik yöntemlerin çocuklarda karın grafisi ve ultrasonografi, erişkinlerde ise bilgisayarlı tomografi olduğunu, hava-sıvı seviyelerinin ve sağ taraflı skolyozun çocuklardaki grafilerde daha çok tespit edildiğini, apendiks perforasyonunun her iki uç yaş grubunda daha sık görüldüğünü, çocuklarda apendiks perforasyonunun daha erken geliştiğini ve hastanede kalış süresinin daha uzun olduğunu, çocuklarda ilk başvuru esnasında tanı konulamamasının ve erişkinlerde ise ileri yaşın komplikasyonlarla ilişkili risk faktörleri olduğunu ortaya koydu.
TARTIŞMA: Bu çalışma erişkinlerde ve çocukluk çağında görülen apandisitler arasında bazı önemli farklılıklar olduğunu gösterdi. Hastalar değerlendirilirken bu farklılıklar göz önüne alınırsa hem klinisyenler hem de hastalar için arzu edilen sonuçlar elde edilebilir.
Anahtar sözcükler: Apandisit; çocuk; erişkin; karın ağrısı.

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