International Surgery Journal
Roushan CP et al. Int Surg J. 2021 Dec;8(12):3511-3515
http://www.ijsurgery.com
pISSN 2349-3305 | eISSN 2349-2902

DOI: https://dx.doi.org/10.18203/2349-2902.isj20214739

Original Research Article

Factors predictive of complicated appendicitis in children

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Received: 30 September 2021
Accepted: 28 October 2021

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ABSTRACT

Background: Clinical features of acute appendicitis are often overlapping with other abdominal pathology in children. This increases the risk of complicated appendicitis (CA). It is still difficult to identify CA preoperatively. The study aims to identify pre operative risk factors in children for CA.
Methods: A prospective study was conducted in pediatric surgery unit of department of general surgery of a university hospital of Kathmandu, Nepal. All children up to 16 years diagnosed and operated for appendicitis were included in the study. Based on intraoperative findings and histopathological examination (HPE), patients were grouped in simple appendicitis (SA) and CA. Pre-operative clinical and laboratory variables of between simple and CA were compared. P≤0.05 was considered as significant.
Results: A total of 73 children were included out of which 61 (83.6%) had SA and 12 (16.4%) had CA. Mean age of participants was 12.8±2.9 years. More than half (64.4%) of the participants were male. The median duration of symptoms was 2 days. In bivariate analysis, gender, serum Na, duration of symptoms and rebound tenderness were significantly associated with severity of appendicitis. In multivariate analysis, rebound tenderness (OR-15.36) and duration of symptoms (OR-9.96) were found to be associated with CA.
Conclusions: Male patients, rebound tenderness, longer duration of symptoms and hyponatremia can be used to predict CA. Duration of symptoms and rebound tenderness are independent risk factors for CA.

Keywords: Children, CA, Predictive factors

INTRODUCTION

Acute appendicitis (AA) is the most common cause of acute abdomen in surgical practice. The lifetime risk of developing appendicitis is 8.6% for males and 6.7% for females.[1] Clinical features of AA in children are often overlapped with other common abdominal condition in children. This may delay in diagnosis and often results in CA. Appendicitis is defined as complicated when there is evidence of gangrenous appendix, peri appendicular abscess, perforation or peritonitis secondary to infection of the appendix.[2] This often results in a longer length of hospital stay and greater rate of morbidity and mortality.

Longer duration of symptoms, high WBC count, hyponatremia, age<5 years, CRP>10 mg/dl, co-morbid conditions are often associated with CA.[3,4] The ability to identify children at risk for CA is important, as it demands early intervention and dictates decisions regarding further workup and management. Clinical diagnosis of acute appendicitis has overall sensitivity of 45-81% and specificity of 36-53%.[5] Leukocytosis, neutrophilia is universally raised in infectious condition. They aid to diagnose AA but cannot be used as predictor. Sensitivity and specificity of ultrasound in diagnosing AA in children have ranged from 44-94% and 47-95% respectively.[6,7] So, diagnosis of acute appendicitis itself require combination of clinical judgment, lab findings

and radiological imaging. Definitive diagnosis of CA can be made intra-op/at HPE of specimen.

It has been over 100 years since Fitz presented his classical paper describing clinical feature of appendicitis and recommended early surgical removal of inflamed appendix.[8] In recent literatures, simple AA can be managed with antibiotics alone while CA always requires surgical intervention.[9] So it is utmost important to diagnose CA preoperatively. This study was conducted to find factors that could predict CA preoperatively.

METHODS

This is a prospective observational study conducted in pediatric surgery unit of department of general surgery, Tribhuvan university teaching hospital between October 2019 to September 2020. Informed consent to conduct this study was obtained from the child's parents or guardians. This study was approved by 'institutional review committee' of institute of medicine, Tribhuvan university with reference no. 1531(6-11)/E2/076/077.

All children up to 16 years who were diagnosed and operated for appendicitis were included in the study. Those participants who had normal appendix on histopathology were excluded from the study. The diagnosis of acute appendicitis was established by clinical examination, leukocytosis, neutrophilia and positive ultrasonographic finding.

Data was collected from patient pertaining to age, sex, referral, duration of symptoms, fever, anorexia, rebound tenderness and other laboratory parameters including serum Na level, serum K, WBC count, platelets, neutrophil, PT/INR. ultrasonography (USG) was performed to aid to diagnosis but not included in the study. The decision to operate was based on combined clinical judgment, lab findings and USG. Per-op findings were noted during surgery and final diagnosis of AA/ gangrenous appendicitis was made on HPE of specimen. HPE was performed to diagnose presence/ absence of appendicitis and evidences of gangrenous appendicitis.

Patients were grouped in 'SA' and 'CA' based on intraoperative findings or gangrenous appendix on HPE. Variables between SA and CA were compared. For the purpose of analysis, the data was entered into the MS excel 2007 and final analysis was done by SPSS version 22.0. The categorical data were analyzed as count and percent, continuous data as mean and standard deviation. Differences were evaluated by the student's t test for continuous parametric data, the Wilcoxon test for the continuous nonparametric data and Pearson's chi-squared test for noncontinuous data. Logistic regression was performed to identify independent risk factors. A $p<0.05$ was considered statistically significant.

RESULTS

During the study period, 78 children were diagnosed and operated for appendicitis. However, 5 were excluded because 4 were normal on HPE report and 1 had alternative diagnosis. Total of 73 children were included in the study. Majority of the participants 61 (83.56%) had SA and remaining 12 (16.44%) had CA.

The mean age of participants was 12.8±2.9 years. Majority of patients 59 (81%) participants were more than 10 years of age with only one participant being below 5 years. More than half 47 (64.4%) of the participants were male and 26 (35.6%) were female. More than three quarters 57 (78.1%) of patients directly came in our hospital while other had first visited other hospital and referred.

Out of 73 participants 14 (19.2%) had fever, 25 (34.2%) anorexia and 44 (60.3%) had rebound tenderness. The median duration of symptoms was 2 days. The average values of serum sodium and potassium were 136±3 and 4±0.6 mmol/L respectively. Also, the mean WBC, platelet and neutrophil percent counts were 13915±4993, 256432±85302 and 79±11 respectively.

Bivariate analysis

In bivariate analysis, gender, serum Na, duration of symptoms and rebound tenderness were significantly associated with CA. However, there was no significant association found between severity of appendicitis and other explanatory variables as shown in Table 1.

Multivariate analysis

To assess the predictors of CA, first bivariate analysis was done (Table 1). The variables that showed significant association with CA in bivariate analysis ($p<0.2$) were further analyzed with binary logistic regression model (Table 2). A significance level was set at $p<0.05$. Rebound tenderness [OR-15.36, 95% CI (1.13-208.26)] and duration of symptoms [OR- 9.96, 95% of CI (2.00-49.58)] were found to be predictors of CA in multivariate analysis. Sensitivity and specificity for duration of symptoms was 91.7-81.3% and for rebound tenderness it was 33.3-34.3% respectively.

Table 1: Association of different variables with severity of appendicitis.

Characteristics	Categories	Severity of appendicitis (%)		P value
		Complicated	Not complicated	
Age (years)	Mean ± SD	11.75±3.79	13.05±2.66	0.15a
Gender	Male	11 (91.6)	36 (59.01)	0.04b*
	Female	1 (8.4)	25 (40.99)	

Continued.

Characteristics	Categories	Severity of appendicitis (%)		P value
		Complicated	Not complicated	
Referral	Yes	5 (41.6)	11 (18.03)	0.12b
	No	7 (58.4)	50 (81.97)	
Temperature	Febrile	2 (16.6)	12 (19.7)	1.00b
	Afebrile	10 (83.3)	49 (80.3)	
Anorexia	Present	5 (41.7)	20 (32.8)	0.74b
	Absent	7 (58.3)	41 (67.2)	
Rebound tenderness	Present	4 (33.3)	40 (65.6)	0.05b
	Absent	8 (66.7)	21 (34.4)	
Duration of symptoms (days)	Median (IQR)	4 (5-3)	2 (2-1)	0.00c*
Serum K (mEq/L)	Mean ± SD	4.21±0.47	4.048±0.57	0.34a
Serum Na (mEq/L)	Mean ± SD	133.83±3.15	136.98±3.27	0.003a*
WBC count (mm3)	Mean ± SD	13652.50±4979.48	13967.05±4725.39	0.83a
Platelets (mm3)	Mean ± SD	257083.33±84347.18	256304.92±81343.78	0.97a
Neutrophil (%)	Mean ± SD	78.75±10.02	79.25±10.63	0.88a

[a]Independent t-test, [*]Significant at p<0.05, [b]Fisher's exact test, [c]Mann-Whitney U test.

Table 2: Logistic regression for independent predictors of CA.

Characteristics	Categories	OR (95% CI)	P value
Age (Years)		0.87 (0.60-1.27)	0.488
Gender	Male	3.31 (0.246-44.44)	0.366
Rebound tenderness	No	15.36 (1.13-208.26)	0.040*
Duration of symptoms		9.96 (2.00-49.58)	0.005*
Serum Na		7.05 (0.41-120)	0.245
Referral	No	7.05 (0.41-120.36)	0.177

*Significant at p<0.05.

DISCUSSION

Diagnosis of AA in young children is frequently difficult because of similar sign and symptoms with other common abdominal pathology, age related communication difficulties and a large proportion with atypical and nonspecific clinical presentations. These overlapping features in children often delay the diagnosis and the disease may progress to complicated one.[10] It also results in longer length of hospital stay, greater rates of morbidity and mortality and has a great impact on the child and family. Predicting the risk of CA preoperatively help the surgeons to anticipate course of disease, plan management and predict the outcomes.

The proportion of CA in a clinical setting varies in literature. In a large series by Omling et al that included 38,939 children showed that CA was present in 18.8% of patients.[11] Feng W showed as high as 63.9% of CA in children.[12] In our study, overall CA were 12 (16.44%) from which 9 were perforated while 3 were gangrenous.

Various risk factors associated with increased incidence of perforation include extremes of age, male sex, rural locality, delays in presentation or diagnosis, lack of insurance or financial coverage status, hospital volume, presence of appendicolith, elevated neutrophils and raised CRP.[13-16]

Many authors have reported appendicitis to be more common in males, however the cause behind this is not known. Hwang and Krumbhaar et al found that the proportion of lymphoid tissue was higher in male appendices than in female, and that this difference persisted at all ages.[17] the difference if incidences are universal in developing as well as developed countries. Oquntola and Ayoade found higher incidence of acute appendicitis in male in a South-western region of Nigeria.[18] This study showed CA has male preponderance but failed to show significance in multivariate analysis.

Rebound tenderness is one the most common presenting sign of acute appendicitis and has a valuable place in Alvarado score in diagnosing acute appendicitis. Golledge et al found that rebound tenderness had sensitivity of 0.82, specificity of 0.89 and accuracy of 86%.[19] This study showed that rebound tenderness is 15 times (OR-15.36) more important in diagnosing CA that SA. However, it was less sensitive (sensitivity 33.3%) and less specific (specificity 34.3%).

Prolonged duration of symptoms is associated with increased intra luminal edema within appendix. Increased intraluminal tension compromise vascular supply to appendix and eventually leads to perforation.[20] Average duration of symptoms with CA was more than 4 days in our study. Multivariate analysis also showed that longer

duration of symptoms is almost 10 times (OR-9.96) more predictive of CA than SA.

Our findings were consistent with study done by Pham XB in 2016 which included 392 patients undergoing appendectomy, demonstrated that patient with CA had longer duration of symptoms (≥24 hours).[21] The study showed that delaying appendectomy is not a predictor of CA as once the antibiotics are started, it halts the inflammatory process.[21] Another study by Temple showed that >60% patients presented with CA when the duration of pain was >72 hours.[22]

A study done by Brender that included 150 patients showed that a treatment delay of more than 36 hours was associated with a 65% or greater incidence of perforation. Mean delay for the group with perforation of the appendix was 66.7 hours compared with 35.8 hours for the group having appendicitis without perforation ($p<0.01$).[23] Our study demonstrated that hyponatremia could be a predictor of CA. Serum sodium level has not been explored with respect to CA in children. Prior data have established strong association between hyponatremia and infectious disease process.[21] Thus, an electrolyte panel my help to diagnose CA in children.

For ease of diagnosing CA Avanesov et al used 3 clinical parameter and 4 CT parameter to develop Appendicitis severity Index (APSI) score.[24] A score of ≥4 points predicted CA. We do not perform CT scan routinely for appendicitis and analyze APSI score to predict CA. By analyzing the clinical components of APSI score, our result showed duration of symptoms predicts CA. other clinical components were age and fever.

CONCLUSION

Male patients, rebound tenderness, longer duration of symptoms and hyponatremia can be used to predict CA. Duration of symptoms and rebound tenderness are independent risk factors. This information will guide surgeons to counsel the parents regarding anticipated course of disease, plan management and predict the outcomes.

ACKNOWLEDGEMENTS

Author would like to thank Dr. Vivek Karn, Dr. Vibhav Lal for their constant support in analyzing data and helping us to find the related articles. We would also like to express our sincere gratitude to department of pediatric surgery for guiding us throughout out study.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Roushan CP, Sah GK, Mandal P, Koirala DP, Dahal GR. Factors predictive of complicated appendicitis in children. Int Surg J 2021;8:3511-5.