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ORIGINAL STUDY

Yersinia infection in acute appendicitis in children in Shebin Elkom Teaching Hospital

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Abstract

Background: *Yersinia enterocolitica* is being recognized as an important bacterial cause of acute gastrointestinal infection. The association of *Yersinia enterocolitica* infections with acute appendicitis has been suggested (Tae Joon Son et al, 2009). The aim to ascertain whether *Yersinia enterocolitica* is a possible infectious agent in appendicitis in Shebin Elkom. We try to support or to deny this suggestion.

Methods: A prospective randomized study was done to 48 patients admitted to surgical department from outpatient clinic of Shebin Elkom Teaching Hospital over 14 months from January 2020 to March 2021. The purpose and nature of the study were explained to all participants and written voluntary consents were obtained before their participation. Approval was taken from the research committee of the General Organization of Teaching Hospitals and Institutions (GOTHI) with approval number HSH00039. Our patient ages ranged from 2.5 years to 15 years old (mean 7.04 ± 1.93). 26 were males and 22 were females. All of them were diagnosed clinically as having acute appendicitis. The study included two groups classified as follows: Group I: 39 patients (positive histopathology of appendicitis) and group II: 9 patients (negative histopathology of appendicitis). Appendectomy was done for all patients, followed by histopathological examination and appendix culture on *Yersinia* selective media *Yersinia* Selective Agar Base.

Results: The results showed that from the 48 patients, 39 were positive histopathology of appendicitis (the specimens were inflamed appendices) group (1). The rest of patients were negative histopathology of appendicitis (normal appendices) group (2). In group (1): 10 patients of the 39 were +ve for *Yersinia* with 25.6% and 29 patients were -ve 74.4%. In group (2): all the nine patients were -ve for *Yersinia* infection with 100%. We compared between the two groups using the test of significance (chi square test). It was 2.92. The p value was 0.17, it was statistically non-significant.

Conclusion: We were unable to implicate *Y. enterocolitica* as one of the causative pathogens in acute appendicitis. However, we thought there to be more need for investigation for association of *Y. enterocolitica* with acute appendicitis. Physicians should keep recent *Y. enterocolitica* infection in mind in patients with symptoms resembling appendicitis.

Keywords: *Yersinia enterocolitica*, Diarrhea, Acute appendicitis and appendix culture

1. Introduction

Yersinia enterocolitica is recognized as a significant bacterial agent responsible for acute gastrointestinal infections. The potential link between *Y. enterocolitica* infections and acute appendicitis was proposed by Son et al. [1].

Y. enterocolitica is classified as a gram-negative bacillus and is the causative agent of yersiniosis, a zoonotic disease. This infection manifests as acute diarrhea, terminal ileitis, mesenteric adenitis, and can sometimes mimic appendicitis. In rare instances, it may even lead to sepsis, as noted by Delibato et al. [2].

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Within the genus *Yersinia*, there are 11 species, with three of them posing significant threats to humans: *Yersinia pestis*, *Y. enterocolitica*, and *Yersinia pseudotuberculosis*. *Yersinia* is a gram-negative bacillus that gives rise to acute bacterial enteric diseases. *Y. enterocolitica* infections typically result in symptoms such as fever, abdominal pain, diarrhea, and occasionally vomiting, which may resemble appendicitis, as reported by [3].

In ~25 % of cases, bloody diarrhea has been documented. The incubation period ranges from 3 to 7 days, and *Y. enterocolitica* is typically transmitted via the fecal-oral route. Nosocomial transmission has also been documented, as well as transmission through transfusion of blood from symptomatic donors. Diagnosis of *Yersinia* infections can be achieved through stool culture, but it can also be cultured from vomitus or standard blood media. Additionally, the culture of *Y. enterocolitica* can be conducted on tissue samples, such as portions of inflamed appendices, as highlighted by [1,3].

Acute yersiniosis often presents with symptoms resembling appendicitis, including fever, right lower quadrant abdominal pain, an elevated white blood cell count, vomiting, and diarrhea. Surgical exploration of patients with these symptoms may reveal a normal appendix but with inflammation of the terminal ileum and mesenteric lymph nodes. This condition, referred to as pseudo appendicitis, is frequently observed in young children and often leads to unnecessary appendectomies, as documented by [4] and Bettina M et al. in 2013 [5].

The association between *Y. enterocolitica* infection and acute appendicitis has been reported in ~6 % of cases in European countries [6].

2. Patients and methods

A prospective randomized study was conducted on a cohort of 48 patients who were admitted to the surgical department at Shebin Elkom Teaching Hospital. The study spanned a duration of 14 months, from January 2020 to March 2021. Before their participation, all patients received a detailed explanation about the purpose and nature of the study, and written informed consent was obtained from each participant. Ethical approval for the study was granted by the research committee of the General Organization of Teaching Hospitals and Institutions (GOTHI), with approval number HSH00039.

The age range of our patient cohort was between 2.5 and 15 years, with a mean age of 7.04 years (± 1.93). Out of the 48 patients, 26 were male, and 22 were female.

All patients were clinically diagnosed with acute appendicitis. Before undergoing appendectomy, each patient underwent a comprehensive assessment, which included a complete medical history and physical examination. Key clinical indicators, such as vomiting, anorexia, migration of pain, tenderness, rebound pain, and fever, were evaluated. Additionally, abdominal ultrasound examinations were performed. Routine laboratory investigations were carried out, encompassing total and differential leukocyte counts, as well as C-reactive protein levels, using Roche diagnostic kits with the Cobas Integra 400 plus instrument.

The study population was divided into two groups: group I comprised 39 patients with a confirmed histopathological diagnosis of appendicitis, while group II consisted of 9 patients with a negative histopathological diagnosis of appendicitis.

For all patients, an appendectomy was performed, followed by a thorough histopathological examination of the removed appendix. Additionally, appendix cultures were conducted on *Yersinia* selective media, specifically *Yersinia* Selective Agar Base. This medium, supplied by LIOFILCHEM, Roseto degli Abruzzi (TE)–ITALY, serves as both a differential and selective medium for the isolation of *Y. enterocolitica*. The specimens were directly inoculated onto the medium and incubated aerobically at 30 ± 1 °C for 18–24 h. *Y. enterocolitica*, capable of fermenting mannitol, induces a localized pH reduction, resulting in colonies with a distinctive appearance, characterized by a red center surrounded by a transparent border, often referred to as a ‘bull’s-eye’ colony. Nonfermenting organisms typically form colorless, translucent colonies. *Yersinia*’s growth leads to colonies featuring a dark red center and a transparent periphery. The size, edge width, and surface structure of these colonies may vary depending on the serotype. The study’s findings were systematically collected and subjected to rigorous analysis.

2.1. Statistical analysis of the data

The collected data underwent rigorous analysis using IBM SPSS software package version 20.0 (IBM Corp, Armonk, NY). Categorical data were presented in the form of numbers and corresponding percentages. To compare between the two groups, the χ^2 test was employed. In cases where more than 20 % of the cells exhibited expected counts of less than 5, the Fisher Exact correction test was applied as an alternative method.

For continuous data, an assessment of normality was conducted using the Shapiro–Wilk test. Quantitative data were expressed with reference to the

range (minimum and maximum values), mean, standard deviation, and median. To compare two groups concerning normally distributed quantitative variables, the Student *t*-test was utilized. Conversely, for quantitative variables that did not exhibit a normal distribution, the Mann–Whitney test was employed. Significance levels for the obtained results were set at the 5 % threshold (Tables 1–3).

The results showed that from the 48 patients, 39 were positive histopathology of appendicitis (the specimens were inflamed appendices) group (1) (Table 4).

The rest of patients were negative histopathology of appendicitis (normal appendices) group (2) (Table 4).

In group (1), 10 (25.6 %) patients of the 39 were +ve for Yersinia and 29 (74.4 %) patients were –ve for Yersinia.

In group (2), all the nine (100 %) patients were –ve for Yersinia infection.

We compared between the two groups using the test of significance (χ^2 test). It was 2.92. The *P* value was 0.17, it was statistically nonsignificant (Figs. 1–3).

Table 1. Comparison between negative and positive of appendix culture according to demographic data.

	Total (n = 48)	Appendix culture		Test of Significance	P
		Negative p (n = 36)	Positive (n = 12)		
Sex				$\chi^2 = 0.250$	0.617
Male	25 (52.1 %)	18 (50 %)	7 (58.3 %)		
Female	23 (47.9 %)	18 (50 %)	5 (41.7 %)		
Age (y)				t = 0.166	0.869
Mean ± SD	7.04 ± 1.93	7.07 ± 1.92	6.96 ± 2.07		
Median (Minimum–maximum)	7 (4–12)	7 (4–12)	6.5 (5–11)		

SD, Standard deviation; t, Student t-test; χ^2 , Chi square test.

p: *P* value for comparing between negative and positive of appendix culture.

Table 2. Comparison between negative and positive of appendix culture according to symptoms and signs.

Symptoms and signs	Total (n = 48)	Appendix culture		Test of Significance	P
		Negative p (n = 36)	Positive (n = 12)		
Vomiting	33 (68.8 %)	25 (69.4 %)	8 (66.7 %)	0.032	FE _p = 1.000
Anorexia	44 (91.7 %)	32 (88.9 %)	12 (100 %)	1.455	FE _p = 0.560
Migration	33 (68.8 %)	23 (63.9 %)	10 (83.3 %)	1.584	FE _p = 0.292
Tenderness	48 (100 %)	36 (100 %)	12 (100 %)		
Rebound pain	31 (64.6 %)	21 (58.3 %)	10 (83.3 %)	2.459	FE _p = 0.169
Fever	35 (72.9 %)	26 (72.2 %)	9 (75.0 %)	0.035	FE _p = 1.000

FE, Fisher Exact; χ^2 , Chi square test.

p: *P* value for comparing between negative and positive of appendix culture.

*Statistically significant at *P* less than or equal to 0.05.

Table 3. Comparison between negative and positive of appendix culture according to laboratory findings.

	Total (n = 48)	Appendix culture		Test of Significance	P
		Negative p (n = 36)	Positive (n = 12)		
CRP				U = 174.0	0.316
Mean ± SD	25.20 ± 19.12	23.74 ± 19.59	29.58 ± 17.71		
Median (Minimum–maximum)	18 (2.5–64)	15 (2.5–64)	25 (9–56)		
TLC (× 10 ³)				t = 2.571*	0.014*
Mean ± SD	12.74 ± 3.90	12.18 ± 4.28	14.40 ± 1.67		
Median (Minimum–maximum)	13.2 (5.4–20.3)	13.10 (5.4–20.3)	14.25 (12.0–16.5)		
Absolute neutrophil × 10 ³				t = 2.195*	0.034*
Mean ± SD.	8.82 ± 3.71	8.36 ± 4.09	10.19 ± 1.66		
Median (Minimum–maximum)	9.51 (0.85–15.25)	8.81 (0.85–15.25)	9.52 (7.50–12.16)		
Histopathology	29 (60.4 %)	19 (52.8 %)	10 (83.3 %)	$\chi^2 = 3.514$	FE _p = 0.091
Sift to left	36 (75 %)	24 (66.7 %)	12 (100 %)	$\chi^2 = 5.333^*$	FE _p = 0.023*

FE, Fisher Exact; SD, Standard deviation; t, Student t-test; TLC, total leucocytes count; U, Mann Whitney test; χ^2 , Chi square test; CRP, C-reactive protein.

p: *P* value for comparing between negative and positive of appendix culture.

*Statistically significant at *P* less than or equal to 0.05.

Table 4. Comparison between the studied groups regarding the presence of *Yersinia* infection.

	The studied groups		Test of significance Chi square test	P value
	+ve histopathology (inflamed appendix) No = 39 No (%)	-ve histopathology (normal appendix) No = 9 No (%)		
Yersinia				
Present	12 (30.7)	0	2.92	0.17 NS
Absent	27 (69.3)	9 (100)		

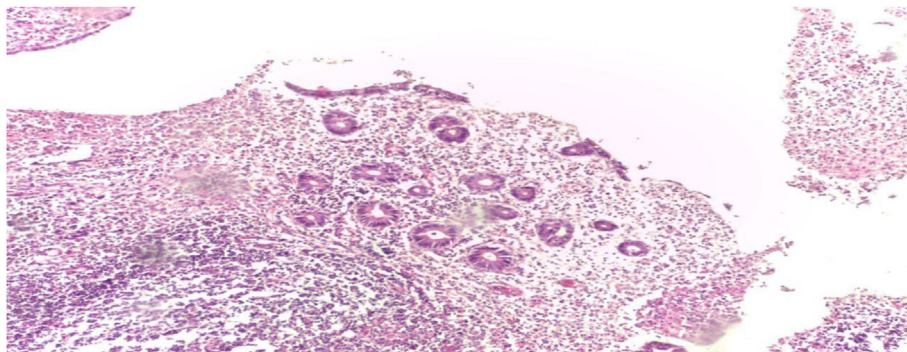
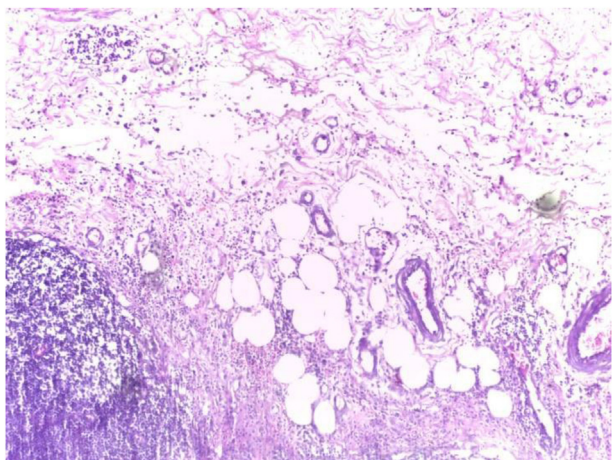


Fig. 1. Surface ulceration with acute appendicitis (X4).

Fig. 2. Acute appendicitis by low power showing inflammatory infiltrate by Polymorphonuclear leukocytes extending to fat ($\times 4$).

3. Discussion

The observed connection between acute appendicitis and *Y. enterocolitica* infection has drawn considerable attention in the medical community. Acute *Y. enterocolitica* infections typically exhibit symptoms persisting for ~10 days, with over a quarter of patients requiring hospitalization. Strikingly, the clinical presentation of acute yersiniosis can mimic that of appendicitis, characterized by fever, right lower quadrant abdominal pain, elevated white blood cell counts, vomiting, and diarrhea [7]. Surgical exploration often reveals a perplexing scenario: a normal appendix alongside

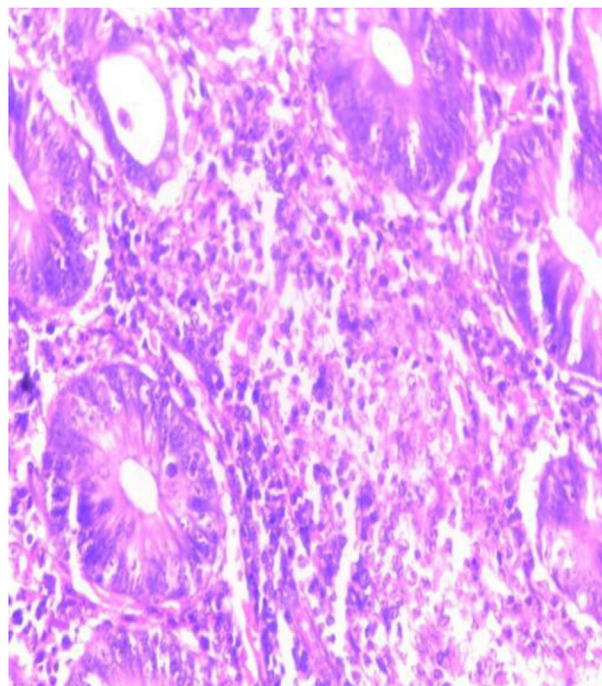


Fig. 3. Microscopic picture of acute appendicitis showing infiltration by inflammatory cells mainly Polymorphonuclear leukocytes (X20).

inflammation of the terminal ileum and mesenteric lymph nodes, leading to the coined term 'pseudo appendicitis'. Notably, this phenomenon appears to be more prevalent among young children, resulting in frequent appendectomies. In their study, Son et al. [1] reported a higher frequency of

appendectomies in yersiniosis patients compared with a reference group, suggesting a potential link between these surgical interventions and *Y. enterocolitica* infections.

The attribution of *Y. enterocolitica* as a possible causative pathogen for appendicitis has been proposed by some authors, such as Bennion et al. [6]. Their work indicates that *Y. enterocolitica* may play a substantial role in the development of acute appendicitis. However, it is worth noting that other researchers have not definitively implicated *Y. enterocolitica* as a primary causative organism in acute appendicitis. These conflicting findings underscore the need for further investigations, conducted over a broader geographical area and throughout various seasons, to elucidate the potential association between *Y. enterocolitica* and acute appendicitis [1].

3.1. Conclusion

Our study did not establish *Y. enterocolitica* as one of the definitive causative pathogens in acute appendicitis. Nonetheless, our findings underscore the importance of continued investigation into the potential association between *Y. enterocolitica* and acute appendicitis.

It remains essential for physicians to maintain vigilance regarding recent *Y. enterocolitica* infections when assessing patients with symptoms resembling appendicitis. While our study did not definitively confirm a causal link, the overlap in clinical presentation between *Y. enterocolitica* infections and appendicitis warrants ongoing consideration.

Further research, conducted on a broader scale and across various seasons, is warranted to elucidate the complex relationship between these two medical entities and to guide clinical practice.

Funds

No Fund.

Conflict of interest

Yes there is conflict of interests.

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