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LOWER GASTROINTESTINAL SURGERY

Identification of deficits in appendicitis diagnostic variables in females in South Africa – a descriptive study

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Background: Acute appendicitis (AA) is a common surgical emergency and misdiagnosis in females is common given the potential broad differential diagnosis. There is a paucity of data on AA misdiagnosis in developing countries. Therefore, this study aims to describe the routine workup of females with suspected AA at a South African government hospital and identify factors associated with AA misdiagnosis.
Methods: This was a retrospective review of the medical records of all females older than 12 years operated on by general surgeons with a suspected diagnosis of AA over a two-year period. Demographic and clinical data, including examinations and investigations were extracted and analysed using descriptive and inferential statistics.
Results: A total of 180 females were included, and 48 (26.7%) of them were misdiagnosed with AA. Of the misdiagnosed, 22 (46%) had pelvic inflammatory disease, 15 (31%) had a normal appendix, 10 (21%) had ovarian cysts, and one (2%) had endometriosis. Gynaecologic bimanual examination was performed in 123 (68.3%) patients. Twelve (6.7%) patients had a computed tomography scan, and 16 (8.9%) had an abdominal ultrasound. The absence of nausea, vomiting, and anorexia (OR = 2.43; $p = 0.023$), the presence of cervical excitation tenderness (OR = 4.32; $p = 0.009$), and adnexal tenderness (OR = 3.06; $p = 0.021$) were independent predictors of misdiagnosed AA.
Conclusion: One in four of our participants was misdiagnosed. We recommend the routine use of clinical parameters and diagnostic imaging to improve the diagnostic accuracy of AA. In resource-limited settings, point-of-care ultrasound should also be considered.
Keywords: appendicitis, misdiagnosis, South Africa, appendectomy

Introduction

Acute appendicitis (AA) is the most common emergency surgical condition worldwide and affects one in seven persons.[1] AA treatments include appendectomy (surgical removal) or non-operative treatment with antibiotic therapy for early cases.[2,3] However, non-operative treatment is characterised by 27% failure rates, and many cases present late and with complications, making surgery the mainstay of treatment.[4-6] The risk of surgery must be balanced with its benefits. Perioperative mortality in Africa is twice as high as in other settings[7] and unnecessary surgery results in increased costs to the healthcare system and adds to patient morbidity.[8,9] Limiting misdiagnosis and unnecessary surgical exploration must be balanced against the risk of missing an AA diagnosis and failing to provide early definitive treatment.

Diagnosing AA remains a challenge universally. The misdiagnosis rate is 20–40% in high-income countries (HICs)[10] despite routine imaging with abdominal computed tomography (CT) scanning that has a 87–100% sensitivity and 83–98% specificity for AA.[11] Abdominal ultrasound (aUS) is another imaging modality used in AA with a high specificity (81%), although its sensitivity (67%) is too low to be diagnostic on its own.[12] The clinical diagnosis of AA is most challenging among females.[1] In Zimbabwe and Iran, the misdiagnosis of females with appendicitis is 24%[13] and 28%, respectively.[14] Clinical features such as lower abdominal pain, elevated temperature, and leukocytosis are common in both AA and pelvic inflammatory disease (PID), which contributes to appendicitis misdiagnosis.[15] PID is a common condition in low- to middle- income countries (LMICs) where early treatment is just as important to prevent complications such as infertility and increased risk of ectopic pregnancy.[16] It is therefore prudent that an accurate diagnosis of lower abdominal pain in females is promptly made so that appropriate care can be provided expeditiously. Data on AA misdiagnosis in LMICs are limited. Therefore, this study aimed to describe the routine workup of females

with suspected AA at a South African state hospital and to determine factors associated with AA misdiagnosis.

Methods

Study design and setting

This was a retrospective analysis of females who underwent surgical exploration from 1 October 2015 to 30 September 2017 by the general surgery service for suspected AA at New Somerset Hospital (NSH). NSH is a regional-level state hospital located in Cape Town, South Africa, which serves a population of 500 000 people[17] and receives referrals from two district hospitals and 15 community health centres (CHCs).

Data collection

Patients eligible for inclusion were identified from the electronic database maintained at NSH by the general surgery service. Gender was determined through medical records, and only those recorded as "female" were included in the study. Clinical and demographic information was obtained from medical records. Variables included age, gender, history and physical findings, laboratory and radiological results, and pre- and postoperative diagnoses. Paediatric populations, males, and those who were treated non-operatively for AA were excluded from the analysis.

History findings included anorexia, nausea and vomiting, and being sexually active (yes/no). Physical findings included vital signs, the presence of right iliac fossa (RIF) tenderness, and vaginal examination findings such as a non-physiological vaginal discharge, cervical excitation tenderness (CET), and adnexal tenderness. A non-physiological vaginal discharge was defined as a discharge that was described as greenish and/or malodorous. CET was defined as pain on manipulation of the cervix during vaginal examination, while adnexal tenderness was defined as lateral pelvic pain during vaginal examination. Laboratory tests included white cell count/mm^3 and urinalysis. The presence of leucocytes or a combination of leucocytes and blood in the urine was considered abnormal. Radiologic imaging included abdominal x-rays, transvaginal and aUS, and abdominal CT scans. All radiology was performed by the radiology service except for transvaginal ultrasound, which was performed by the gynaecology service. All study participants were first evaluated by a member of the general surgery team, usually a medical officer or a surgery registrar. The gynaecology team were consulted *ad hoc* for suspected gynaecology pathology. The primary outcome was misdiagnosis, defined as a preoperative diagnosis of AA but a different intraoperative finding. Those who had a different intraoperative diagnosis were classified as the misdiagnosed group, and those with intraoperative findings of AA were classified as the correct diagnosis group.

Data analysis

Data were extracted from the operative database and patient medical records onto a standardised data collection form and then imported into STATA 15 (College Park, TX, USA) for analyses. All variables, including the outcome, were summarised using descriptive statistics. Data were expressed as counts and proportions (%) for categorical variables, while continuous variables were summarised using mean (± standard deviation) and median (interquartile range). Chi-squared test was used to compare the categorical proportions, and continuous variables were compared using the t-test. Univariate and multivariable logistic regression was used to determine the risk factors for misdiagnosis of appendicitis. Age was included *a priori,* and other factors with p-value < 0.1 on univariate analyses were included in the multivariate model. A p-value of < 0.05 was considered statistically significant.

Results

One hundred and eighty females were included in the study. The median age was 27 years (interquartile range 21–38). All 180 (100%) patients had an abdominal examination; 123 (68.3%) had a gynaecologic bimanual exam; 172 (95.6%) had a urine pregnancy test; and 178 (98.8%) had a urine analysis. Fifty (27.7%) patients had a formal consultation with the gynaecology service. Twelve (6.7%) patients underwent CT scanning, and 16 (8.9%) were investigated by aUS.

Table I: Clinical characteristics and investigations performed in female patients with suspected appendicitis

Diagnostic variables	Suspected appendicitis			
	Total, *n* (%)	Correct diagnosis	Misdiagnosis	*p*-value
General findings and investigations	180 (100)	132 (73.3)	48 (26.7)	
Heart rate (beats/minute)[a]	98.8 (18.1)	98.7 (18.5)	99 (17.2)	0.903
Temperature (°C)[a]	37.2 (1)	37.2 (1.0)	37.3(0.8)	0.685
WBC (x 10^9/L)[b]	14 (10–19)	13 (10–18)	15 (9–22)	0.984
Normal urinalysis	162 (91)	120 (92.3)	42 (87.5)	0.320
Gastrointestinal examination findings				
RIF tenderness	140 (77.8)	108 (81.8)	32 (66.7)	0.104
Nausea/vomiting/anorexia	120 (66.7)	95 (80)	25 (52.1)	**0.012**
Radiological examination performed				
Abdominal ultrasound	16 (8.9)	11 (8.3)	5 (10.4)	0.664
Transvaginal ultrasound	43 (23.9)	24 (18.2)	19 (39.6)	**0.003**
CT scan	12 (6.7)	10 (7.6)	2 (4.2)	0.417
Gynaecological examination performed	123 (68.3)	87 (65.9)	36 (75)	0.326

WBC –, white blood cell count, RIF – right iliac fossa, CT – computed tomography
[a] mean (standard deviation); [b] median (interquartile range)

Table II: Gynaecologic findings on history and examination in female patients with suspected acute appendicitis

	Postoperative diagnosis			
	Correct Diagnosis	Misdiagnosis	Total	*p*-value
Sexually active	42 (31.8)	29 (60.4)	71 (39.4)	**0.001**
Bimanual pelvic examination	**87**	**36**	**123**	
Adnexal tenderness	20 (22.9)	20 (55.6)	40 (32.5)	**0.001**
Cervical excitation tenderness	8 (9.2)	15 (41.7)	23 (18.7)	**< 0.001**
Non-physiologic vaginal discharge	10 (11.5)	6 (16.7)	16 (13.0)	0.272

Table III: Univariate and multivariate analysis of variables associated with the misdiagnosis of appendicitis in female patients

Variable	Univariate			Multivariate		
	OR	95% CI	*p*-value	OR	95% CI	*p*-value
Age (years)	0.99	0.97–1.02	0.432	0.99	0.97–1.02	0.730
Heart rate (beats/minute)	1.00	0.98–1.02	0.902			
Temperature (°C)	1.07	0.76–1.51	0.683			
Abnormal urinalysis	1.71	0.59–5.00	0.324			
White blood cell count (10^9/L)	1.01	0.96–1.06	0.675			
No nausea/vomiting/anorexia	2.36	1.19–4.67	**0.013**	2.48	1.16–5.28	**0.019**
No RLQ tenderness	2.38	1.11–4.97	**0.026**	1.63	0.70–3.82	0.382
Adnexal tenderness	4.40	1.83–9.56	**0.001**	3.29	1.31–8.25	**0.010**
Vaginal discharge	1.57	0.52–4.72	0.419			
Cervical excitation tenderness	7.05	2.59–19.31	**< 0.001**	4.77	1.61–14.10	**0.005**

RLQ – right lower quadrant

Forty-eight (26.7%) patients were misdiagnosed with AA. In the misdiagnosed group, the most common diagnosis was PID (n = 22, 46%), followed by normal intraoperative findings (n = 15, 31%), ovarian cyst (n = 10, 21%), and endometriosis (n = 1, 2%). Clinical characteristics such as heart rate, temperature, white cell count, and normal urinalysis were statistically similar in both the AA and the misdiagnosed groups. The proportion of patients with RIF tenderness in each group was also not significantly different. The lack of gastrointestinal symptoms was significantly associated with the misdiagnosed group ($p = 0.012$). Clinical characteristics are shown in Table I.

Adnexal tenderness and CET were significantly associated with AA misdiagnosis. Over half (55.6%) of those who were misdiagnosed had adnexal tenderness compared to 22.9% in those with correct diagnosis ($p = 0.001$). Similarly, 41.7% of those who were misdiagnosed had CET compared to 9.2% among those with the correct diagnosis ($p < 0.001$) (Table II).

In the univariate analysis, the absence of nausea, vomiting, or anorexia (OR = 2.36; $p = 0.013$), absence of RIF tenderness (OR = 2.38; $p < 0.026$), presence of CET (OR = 7.06; $p < 0.001$), adnexal tenderness (OR = 4.40; $p = 0.001$) and undergoing a transvaginal ultrasound (OR = 2.94; $p = 0.004$) were significantly associated with a misdiagnosis (Table II).

In the multivariate analysis, only the absence of nausea, vomiting, and anorexia (OR = 2.43; $p = 0.023$), presence of CET (OR = 4.32; $p = 0.009$), and adnexal tenderness (OR = 3.06; $p = 0.021$) were significantly associated with a misdiagnosis (Table III).

Discussion

AA can cause significant morbidity and mortality, if left untreated.[18] In LMICs, persons with AA present late,[6] and surgical care is the mainstay of treatment. Our study shows that the preoperative diagnosis of AA was incorrect in one out of four females. Other LMICs studies have reported similar findings (16–28%),[13,14] which are comparable to those reported in HICs (20–40%).[10]

In our study, certain clinical findings, such as tachycardia, fever, and leukocytosis, were not useful in distinguishing AA from other conditions in females. Clinical prediction rules (CPRs), such as the appendicitis inflammatory response (AIR) score[19] and the adult appendicitis score (AAS),[20] were created to rely on the history, physical and laboratory values, and theoretically could play a role in diagnosing AA in resource-limited settings. The Alvarado score is one of the most common CPRs and is considered 68–96% sensitive and 58–89% specific in certain settings.[21] It is reported to be well-calibrated in men, inconsistent in children, and with a tendency to overpredict AA probability in females.[22] A previous study in South Africa reported that the score might not be as useful in the Black African population and that severity of disease presentation may be a confounding factor.[23] In addition, CPRs use laboratory tests such as neutrophil count or C-reactive protein that are not routinely ordered in our setting due to cost constraints.

PID, resulting from infection of the fallopian tubes, was the most common differential diagnosis for suspected AA in our study.[24] While imaging can improve diagnostic accuracy, these tests are prohibitively costly or unavailable in many resource-limited settings,[25-27] including in South African government hospitals. In this study, less than 10% of female patients underwent aUS, and less than 10% had abdominal/pelvic CT scanning.

Given the existing limitations in accessing more reliable diagnostic tools, such as the CT scan in South Africa and other LMICs, reliance on clinical history and examination is critical in diagnosing AA in these settings. However, in our study, only two-thirds of females with suspected AA had a

gynaecologic bimanual exam despite the presence of adnexal and CET being associated with a misdiagnosis. A standard workup that includes gynaecologic examinations should be implemented, including a gynaecology consultation if any positive findings are noted. To improve the accuracy of the clinical examination, we recommend the routine use of a neutrophil count and C-reactive protein to validate use of CPRs, such as the AIR[19] and AAS[20] scores. Finally, a formal aUS might not be available after hours at many state hospitals, but the use of point-of-care ultrasound by general surgeons could improve the diagnostic accuracy of AA when used in conjunction with clinical parameters.[28]

Limitations

This study has certain limitations. Firstly, females who were initially diagnosed with a gynaecologic condition, such as PID, who ultimately had a surgical exploration and were found to have AA, were not included in this study. Also, we could not use C-reactive protein as a potential predictor for AA since the required laboratory parameters were unavailable. We could also not calculate the sensitivity and specificity of imaging tests for AA since fewer than 10% had either. Another limitation is that we could have underestimated early appendicitis in grossly normal specimens since we did not send all specimens for routine histology. Lastly, the findings of this single-centre study may not be generalisable to other settings.

Conclusion

One in four of our participants was misdiagnosed. We recommend the routine use of clinical parameters and diagnostic imaging to improve the diagnostic accuracy of AA. In resource-limited settings, point-of-care ultrasound should be considered.

Conflict of interest

None.

Funding source

None.

Ethical approval

This study was approved by the University of Cape Town Research Ethics Committee (HREC R052/2016). Informed consent was waived for the study as there was no form of participant contact. Data were de-identified before statistical analysis.

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