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Research Article

Correlation between the Clinical and Pathological Diagnosis of Acute Appendicitis Where Pre-Operative Radiological Diagnosis is Unreliable: Our Experience at General Hospital Potiskum, Yobe State, Nigeria

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Abstract: ***Background***: Harold Ellis in 1989 said, "the treatment of acute appendicitis is appendectomy – and the sooner it is done, the better." Delayed diagnosis is associated with increased risk of having a complicated appendicitis, often, a perforated appendix. The desire to make an accurate and prompt diagnosis of acute appendicitis, reduce negative appendicectomy rate and improve the operative morbidity associated with surgery for appendicitis; has remained aflame in surgeons. This desire is almost unmet, especially, in the early stages of appendicitis, in females of reproductive age and in children. In this cohort of patients, making accurate preoperative diagnosis is difficult, because of atypical presentation and the presence of swathes of differentials with similar clinical symptoms and the occasional failure of simple radiological tools like Ultra Sound Scan(USS), to clinch the diagnosis. It is therefore imperative to probe the reliability of clinical assessment in making an accurate diagnosis, especially, in areas where the reliability of the results of USS is not strong and there is dearth of high resolution radiological tools of assessment, such as; Computed Tomography (CT) and Magnetic Resonance Imaging(MRI). ***Objectives***: We aim to correlate the clinical and histopathological diagnoses of acute appendicitis and determine the reliability of clinical assessment in achieving an accurate diagnosis of acute appendicitis and reduce the negative appendicectomy rate. ***Patients And Methods****:* This is a prospective cross-sectional study of one hundred and twelve (112) cases of clinically diagnosed acute appendicitis seen over a year period (1st January, 2020-31st December, 2020), at the General Surgery Unit of General Hospital Potiskum, Yobe State-Nigeria. The clinical profile of the patients, such as the bio-data, clinical symptoms, duration of nausea, vomiting and right lower quadrant pain and physical examination findings were outlined. Preoperative laboratory and radiological investigations when used and pre-hospital treatment deployed were also analysed. All the patients had open appendicectomy or exploratory laparotomy done and the diagnosis of acute appendicitis was confirmed by histopathological examination. The presence of extra-vascular Neutrophils in the Muscularis propria is considered diagnostic. Informed consent was obtained from all patients according to the Helsinki guidelines and Ethical clearance was granted by the hospital management. All data were analysed with SPSS 20.0 software for correlation of outcomes. ***Results****:* The study population were 112 patients aged 16 years and above, 44.6% were males and 55.4% were females, giving a male-female ratio of 1:1.25. The mean age is 30.5(+_2.35), with an age range of 16-69 years. Right Iliac fossa pain is the most common presenting complaint, seen in 94.6% of the patients, followed by anorexia at 66.1% and nausea (53.6%). The least common symptoms are diarrhoea (17.0%) and urinary frequency (24.1%). The most consistent clinical signs are tenderness at the Mc Burney's point (92.9%), fever (67.9%) and rebound tenderness (59.8%). The least signs elicited are, right iliac fossa mass (16.1%), copes' obturator (25.0%) and copes' psoas (43.8%) signs. About 54.5% of the patients had Leucocytosis with evidence of left shift. Up to 76.8% of the patients took some treatment before presentation and oral/parenteral antibiotics are the most frequently utilised (26%). Only 63.4% of the patients had a diagnostic abdominal USS, 8.9% did an erect plain abdominal radiograph, 27.7% could not afford to pay for any radiological investigation and none (100%) did an abdominal Computed Tomography Scan. Almost all the patients had open appendicectomy, 94.6% was via a Lanz's incision, only 5.4% had laparotomy via a midline incision. The most common intra-operative finding is that of a turgid, grossly swollen, non-perforated appendix (44.6%) and the least common is an appendicular mass (2.7%). About 3.6% of patients had a tumour of the of the appendix. The most common histopathological diagnosis was that of appendicitis, seen in 75.9% of patients; evidenced by the presence of polymorpho-nuclear Neutrophils in the muscularis propria. The Negative result was 14.3% and 8.0% had a diagnosis of 'peri-appendicitis', due to presence of

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Neutrophils in the sub-serosa only; all were females with adnexal inflammation. Thus, the total 'Negative appendicectomy rate was 22.3%. Two patients (1.8%) had an unusual diagnosis of adenocarcinoma of the appendix. The most common operative complication is Nausea and Vomiting, occurring in 28.6% of the patients, and the least common is entero-cutaneous fistula, seen in only one patient (0.9%). ***Conclusion****:* The diagnosis of acute appendicitis can be reliably established from clinical details with a 75.9% accuracy and a hard to get radiological confirmation may not be needed in a poor resource setting. ***Limitations:*** Only adult patients were recruited, living out a large chunk of data from the paediatric patients.

Keywords: Acute Appendicitis, Clinical and Pathological Diagnoses, Unreliable Radiological Assessment.

INTRODUCTION

The pathological entity of Acute Appendicitis (AA) is thought to be as old as mankind. It was historically reported that an autopsy on an Egyptian Mummy that lived during the Byzantine era revealed a right lower quadrant (RLQ) adhesion suggestive of a repeated Acute Appendicitis [1-3]. In modern history, Reginald Fitz is recognised as the first to report a detailed description of the pathological entity [4]. Since its description, it has remained the most common cause of acute surgical abdomen globally [5], and appendicectomy is one of the most frequently performed procedures worldwide; accounting for up to one-third of all emergency surgeries performed in both developing and developed countries [6]. Many reports from Nigeria placed the incidence of AA at 22.1-49.8 new cases per 100,000, per annum 7], and this reflects a rising pattern of incidence over a decade [8, 9]. Reports from other parts of the African continent is similar. Naaeder [10] from Ghana, Asefa [11] from Ethiopia and Awori [12] from Nairobi, all indicated similar trend.

Despite the ubiquitous nature of acute appendicitis, making an accurate diagnosis is not a given, because of the presence of atypical presentation and the availability of array of differentials in women of reproductive age group and in children [13, 14]. The typical clinical symptoms and complimentary laboratory abnormalities may not be found in up to 20% to 33% of patients at presentation, especially in the early phases of AA [15]. Complimentary Imaging studies have proved useful in getting an accurate diagnosis in such situation [16]. Even in the best of centres, achieving a high rate of accuracy in identifying cases of AA will depend on combining a detailed history, physical examination and an imaging study [2, 3]. The predictive power of clinical examination in making a diagnosis of AA has been reported to be between 71% to 97% and the precision improves with the experience of the examiner [17]. The diagnosis of AA has been shown to be largely clinical [18] and the final arbiter is the result of histopathological analysis [19].

If the initial diagnosis of AA is missed at presentation, the consequence may be dire. A delayed diagnosis often results in a complicated appendicitis [20]. The most common complications seen are perforation and gangrene [21]. In developed countries, the proportion of complicated forms of AA is about 20% at presentation [11]. In Africa, this constitute up to 40-50% [22]. This emphasize the need for identifying a simple and effective diagnostic tool. However, the need for early and prompt diagnosis of AA to evade complications should be weighed against overzealous performance of appendicectomy, increasing the 'negative appendicectomy rate' and associated operative morbidity; especially in women of reproductive age group. The global negative appendicectomy rate is reported to be between 20-30% [23, 24]. The negative appendicectomy rate is however disproportionately low in the developed nations of the West, because of an improved diagnostic accuracy through the use of computer-aided diagnosis, imaging by ultrasonography, laparoscopy, and even radioactive isotope imaging [25-28]

As Harold Ellis noted, surgical removal of the inflammed appendix is the most effective treatment of AA [29]. Open appendectomy (OA) has been considered as the gold standard surgical treatment of AA and associated operative outcome is considered satisfactory [30]. After the huge success and popularity of Laparoscopic Cholecystectomy in the Western countries, laparoscopic Appendicectomy (LA) began to be used with varying success rates [31]. It was noted to have the dual diagnostic and therapeutic advantages, with the possibility of reducing negative appendicectomy rates [32, 33]. Kramer reported a negative appendicectomy rate of 22% following LA. He however, noted a sharp decrease in the rate to 3% if the Laparoscopic procedure is actively used to identify an obviously inflammed appendix before the LA is done [34]. Surgical Site Infection (SSI) of varying grades is the most reported postoperative morbidity and is mostly associated with perforated appendicitis [35]. Improvement in management strategy through the use of broad spectrum antibiotics has significantly reduced the overall mortality and morbidity [36]. The case

fatality rate for appendicitis is diametrically different between the developed and developing nations of the world. In Sweden in the 1990s, it was 2.4/1000 [37], which is just less than 0.2%. The reported case fatality rate for Africa ranges from 0.9 to 4%. This is unacceptably high, even with the documented higher perforation rates [22]. Since developing complicated AA, its attendant high morbidity and mortality are related to delayed diagnosis [22], it is imperative for the African surgeon to devise a way of getting the accurate diagnosis promptly and easily.

Although there is a large volume of data from Africa that assessed the incidence, morbidity and case related fatality of AA, not much has been about the establishment of accurate diagnosis relying on the strength of clinical details only. Many of the patients presenting at rural hospitals are poor, barely capable of affording the surgery, post-operative care, and often; the cost of radiological and laboratory investigations [6].

We therefore, designed this study to probe the effectiveness of a detailed clinical history and physical examination in making an accurate diagnosis of AA, to allow for early surgical intervention without the need for costly Imaging studies and reduce the unnecessary high morbidity and mortality associated with complicated AA in Africa.

PATIENTS AND METHODS

This is a prospective cross-sectional study of one hundred and twelve (112) cases of clinically diagnosed acute appendicitis seen over a year period (1st January, 2020-31st December, 2020), at the General Surgery Unit of General Hospital Potiskum, Yobe State-Nigeria. It is a secondary tier health care facility that has a single radiographer and no trained Radiologist. The radiology unit uses a 3MHz, grey scale, curved probe for USS. The patients were admitted for emergency or elective appendicectomy. All the patients are aged 16 years and above, 15 years being the upper limit for the paediatric age group in the hospital. The exclusion criteria were patients admitted with generalised peritonitis due to hollow viscus perforation and those with clinically identifiable causes of RLQ pain, such as right pyelonephritis, renal colic, right salphingitis, twisted right ovarian cyst, right ectopic pregnancy or Mittelschmertz pain. Patients that declined surgery or were unfit for surgery were also excluded. A detailed history was taken, concentrating on clinical symptoms and the duration of nausea, vomiting and right lower quadrant pain. All females were asked of their last menstrual period. History was obtained of pre-hospital treatment taken. The details of physical examination findings were outlined, especially, RLQ tenderness, rebound tenderness, rovsing, copes obturator and psoas signs. Preoperative complete blood count, plasma glucose level and serum electrolytes were analysed in those who can afford. All females had blood-based pregnancy test, as test strips were donated by the hospital. Abdominal USS was requested for all the patients, erect or lateral decubitus abdominal radiograph for those with rebound tenderness. But, not all the patients had the pre-operative imaging done. The presence of a non-compressible, blind-ended tubular structure in the RLQ with a maximum luminal diameter >7mm was considered diagnostic by the radiographer. Informed consent was obtained according to the Helsinki guidelines and Ethical clearance was given by the hospital management. Either open appendicectomy for uncomplicated or exploratory laparotomy for complicated cases was done, with intra-operative assessment of the gross appearance of the appendix. A grossly swollen appendix with hyperaemic serosa and peri-appendiceal oedema or fluid was considered uncomplicated. The presence of gangrene, perforation, appendicular mass, localised or generalised abscess collection was considered complicated AA. Rare finding of tumours were also noted. The diagnosis of acute appendicitis was confirmed by histopathological examination. The presence of extra-vascular Neutrophils in the Muscularis propria is considered diagnostic. All resected appendices without the histopathological marker for AA, evidence of neoplasia or ova of parasite are considered 'negative appendicectomy'. Presence of Neutrophils in the sub-serosa only is considered 'peri-appendicitis' and were considered as part of negative appendicectomy. All patients were followed-up for up to 30 days after the surgery for post-operative complications. All data obtained was assessed using the Statistical Package for Social Sciences, version 20.0 (IBM, Armonk, NY, USA). Continuous variables were presented as mean ± Standard Deviation. Categorical variables were expressed as frequencies and percentages. The Pearson's chi square test was used to determine the relationship between two categorical variables. A confidence interval of 95% and a $P<0.05$ were considered statistically significant.

RESULTS

The study population were 112 patients, 44.6% were males and 55.4% were females, giving a male-female ratio of 1:1.25. All are adults. The mean age is 30.5(+_2.35), with an age range of 16-69 years. Right Iliac fossa pain is the most common presenting complaint, seen in 94.6% of the patients, followed by anorexia (66.1%) and nausea (53.6%). Only 28.6% of the patients presented with the classical Murphy's sequence of an initial non-specific, peri-umbilical pain that later settled in the RLQ (Table-1). The most consistent clinical signs are tenderness at the Mc Burney's point (92.9%), fever (67.9%) and rebound tenderness (59.8%). The least signs elicited are: right iliac fossa mass (16.1%), copes obturator (25.0%) and copes psoas (43.8%) signs. About 62.5% of the patients presented at the hospital more than 24 hours after the

onset of RLQ pain (Table-2). A total of 76.8% of the patients took some form of treatment before presenting at the hospital and almost half of these patients took either an Antibiotic or an Analgesic (Figure-2). Up to 92% of the patients did not have any comorbidity that may obscure the diagnosis of AA (Table-3).

Only 63.4% of the patients had a diagnostic abdominal USS done and all were performed by the radiographer. About 8.9% of the patients had an erect or lateral decubitus abdominal radiograph on suspicion of a perforated appendix, 27.7% could not afford to pay for any radiological investigation and none (100%) of the patients had a diagnostic abdominal CT Scan. Only 54.5% of the patients showed leucocytosis on complete blood count (Figure-3). All showed evidence of immature bands.

A total of 94.6% had open appendicectomy via a Lanz's incision and 5.4% had laparotomy via a midline incision, for complicated appendicitis. A total of 44.6% of the patients had grossly inflammed appendix and 25.9% had an apparently normal looking appendix, making a total of 70.5% of uncomplicated AA. A total of 26.0% of the patients had complicated AA, distributed as follows: gangrene (8.9%), perforation (5.4%), appendicular mass (2.7%), localised abscess (5.4%) and generalised abscess (3.6%). Gangrene (8.9%) and Perforation (5.6%) are most common types of complicated AA found (Table-4). There was the rare finding of appendix tumour in 3.5% of the patients (Table-4).

In this study, up to 48.3% of those with complicated AA are aged 50 years and above (Table-5, X2= 0.000. P= 0.005). A total of 75.9% of those with complicated AA presented at hospital more than 24 hours after the onset of RLQ pain (TABLE 6, X2= 0.101, P= 0.005). A total of 89.7% of those with complicated AA also had a positive rebound tenderness on physical examination (Table-7, X2= 0.003, P= 0.005). Up to 65.5% of patients with complicated AA also had a positive Rovsing sign on abdominal examination (Table-10, X2= 0.002, P= 0.005). Almost half (48.3%) of those who vomited twice or more had complicated AA (Table-8, X2= 0.000, P= 0.005). Only 9.1% of those who took oral or parenteral antibiotics before presentation developed a complicated AA and none had a localised or generalised abscess collection (Table-9, X2= 0.002, P= 0.005).

Histopathologic analysis showed that, 75.9% of the resected appendices showed evidence of AA and the negative appendicectomy rate is 22.3% (Table-11). The rare find of an adenocarcinoma of the appendix was in 1.8% of the specimens analysed. There was no finding of a carcinoid tumour of the appendix (Table-11). Up to 84.0% of those with Negative appendicectomy were females (Table-2, X2= 0.002, P= 0.005). A total of 72.4% of normal looking appendices intra-operatively turned out to be negative appendectomies and 27.6% of those apparently looking normal appendices showed evidence of AA (Table-13, X2= 0.000, P= 0.005). A total of 13.4% and 0.9% developed SSI and Faecal Fistula post-operatively, while, majority did not develop any significant morbidity (Table-14). All (100%) of those who developed SSI had a complicated AA (Table-15, X2= 0.000, P= 0.005). There was no recorded mortality.

Table-1: Showing the Distribution of the Presenting Symptoms

ANOREXIA	66.1%
PERIUMBLICALPAIN	28.6%
RLQPAIN	94.6%
NAUSEA/VOMITING	66.1%
DIARRHOEA	17.0%
URINARY_FREQUENCY	24.1%

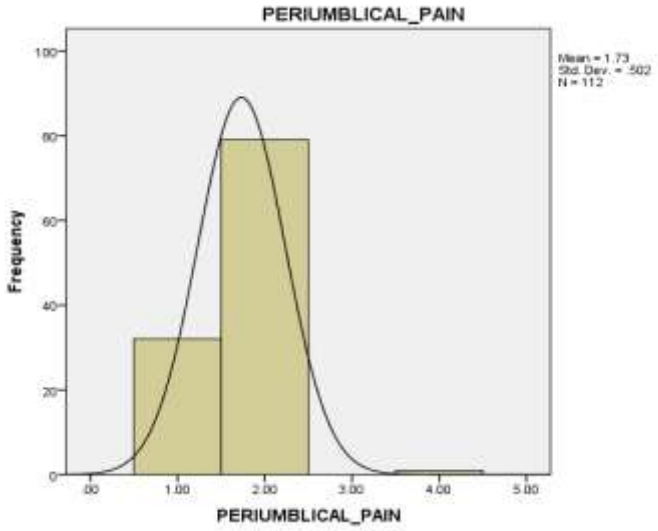

Fig-1: Showing the Frequency of Peri-Umbilical Pain

Table-2: Showing the Time Interval between Symptoms Onset and Presentation

DURATION	Frequency	Percent
24 hours	31	27.7
24-48 hours	45	40.2
more than 48 hours	25	22.3
none	11	9.8
Total	112	100.0

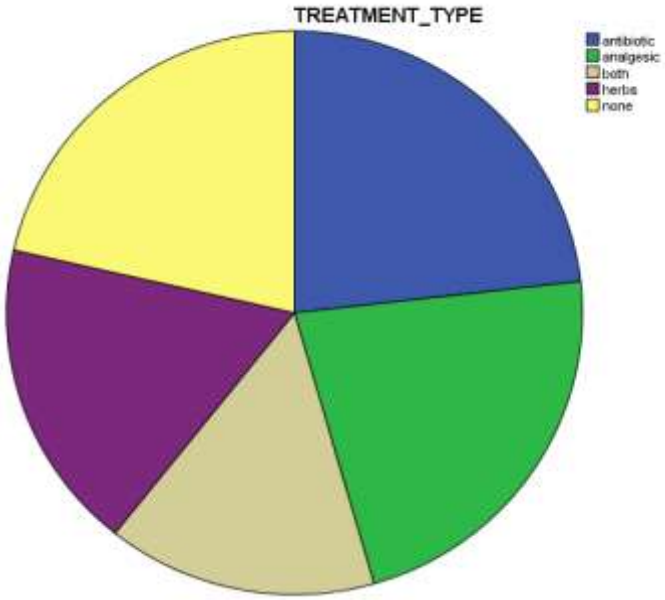

Fig-2: Showing the Distribution of Pre-Hospital Treatment Taken

Table-3: Showing the Distribution of Comorbidities

COMORBIDITY	Frequency	Percent
none	103	92.0
sickle cell disease	2	1.8
right tube ectopic gestation	4	3.6
herpes zoster	1	0.9
chest infection	2	1.8
Total	112	100.0

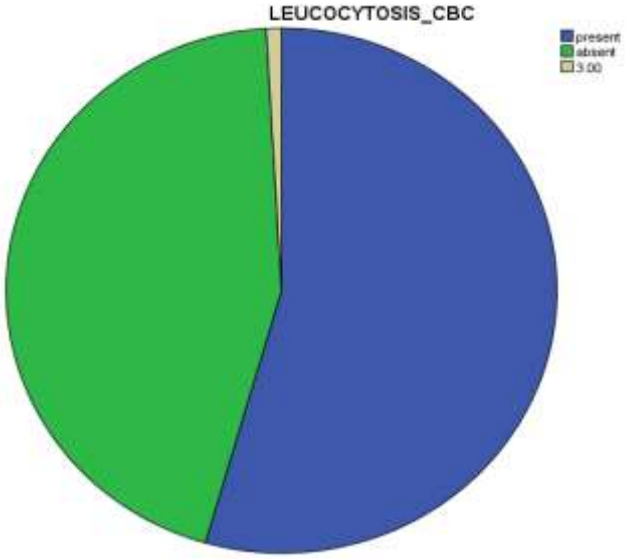

Fig-3: Showing the Distribution of Leucocytosis on CBC

Table-4: Showing the Distribution of Intra-Operative Findings

INTRA-OP FINDING	Frequency	Percent
normal appendix	29	25.9
grossly inflammed	50	44.6
gangrenous	10	8.9
ruptured	6	5.4
appendicular mass	3	2.7
localised abscess	6	5.4
generalised abscess	4	3.6
appendicular tumour	4	3.6
Total	112	100.0

Table-5: Showing Correlation between Age and Severity Of AA

AGE	INTRAOP_FINDING								Total
	normal appendix	grossly inflammed	gangrene	ruptured	appendicular mass	localised abscess	generalised abscess	appendicular tumour	
16-25	8	20	2	1	0	1	0	0	32
26-35	17	17	4	0	1	1	1	0	41
36-45	4	10	1	2	0	0	1	2	20
46-55	0	3	2	2	0	3	1	0	11
5.00	0	0	1	1	1	0	0	1	4
56-65	0	0	0	0	1	1	0	1	3
65 and above	0	0	0	0	0	0	1	0	1
Total	29	50	10	6	3	6	4	4	112

X^2= 0.000, P= 0.005, statistically significant.

Table-6: Showing Correlation between Interval of RLQ Pain Onset and Complicated AA

DURATION OF RLQ PAIN	INTRAOP_FINDING								Total
	normal appendix	grossly inflammed	gangrene	ruptured	appendicular mass	localised abscess	generalised abscess	appendicular tumour	
24 hours	5	19	3	1	1	1	1	0	31
24-48 hours	12	23	5	1	0	1	1	2	45
more than 48 hours	7	6	2	4	1	2	2	1	25
none	5	2	0	0	1	2	0	1	11
Total	29	50	10	6	3	6	4	4	112

X^2= 0.101, P= 0.005, not statistically significant

Table-7: Showing Correlation between Rebound Tenderness and Complicated AA

REBOUND TENDERNESS	INTRAOP_FINDING								Total
	normal appendix	inflammed	gangrene	ruptured	appendicular mass	localised abscess	generalised abscess	appendicular tumour	
present	10	30	9	5	3	6	3	1	67
absent	19	20	1	1	0	0	1	3	45
Total	29	50	10	6	3	6	4	4	112

X^2= 0.003, P= 0.005, statistically significant)

Table-8: Showing the Correlation between Vomiting Frequency and Complicated AA

VOMITING FREQUENCY	INTRAOP_FINDING								Total
	normal appendix	grossly inflammed	gangrene	ruptured	appendicular mass	localised abscess	generalised abscess	appendicular tumour	
once	6	21	2	2	0	1	1	0	33
twice	7	2	2	1	0	3	1	1	17
multiple	0	1	2	3	2	0	1	1	10
none	16	26	4	0	1	2	1	2	52
Total	29	50	10	6	3	6	4	4	112

(X^2=0.000, P= 0.005, statistically significant)

Table-9: Showing Correlation between Pre-Hospital Antibiotic Intake and Complicated AA

PRE-HOSPITAL TREATMENT	INTRAOP_FINDING								Total
	normal appendix	grossly inflammed	gangrene	ruptured	appendicular mass	localised abscess	generalised abscess	appendicular tumour	
antibiotic	5	17	2	1	0	0	0	1	26
analgesic	8	15	1	0	1	0	0	0	25
both	5	4	0	1	1	4	2	0	17
herbs	3	3	5	3	0	2	2	2	20
none	8	11	2	1	1	0	0	1	24
Total	29	50	10	6	3	6	4	4	112

X^2=0.002, P= 0,005, statistically significant

Table-10: Showing Correlation between a Positive Rovsing Sign and Complicated AA

ROVSING SIGN	INTRAOP_FINDING								Total
	normal appendix	grossly inflammed	gangrene	ruptured	appendicular mass	localised abscess	generalised abscess	appendicular tumour	
present	6	31	7	4	2	5	1	0	56
absent	23	19	3	2	1	1	3	4	56
Total	29	50	10	6	3	6	4	4	112

X^2= 0.002, P= 0.005, statistically significant

Table-11: Showing the Distribution of the Histopathology Result

HISTOPATHOLOGY	Frequency	Percent
appendicitis	85	75.9
negative	16	14.3
Peri-appendicitis	9	8.0
adenocarcinoma	2	1.8
Total	112	100.0

Table-12: Showing Correlation between Gender and Negative Appendicectomy

GENDER	HISTOPATHOLOGY_RESULT				Total
	appendicitis	negative	Peri-appendicitis	adenocarcinoma	
male	46	4	0	0	50
female	39	12	9	2	62
Total	85	16	9	2	112

X^2=0.002, P=0.005, statistically significant

Table-13: Showing the Correlation between Intra-Operative Finding and Histopathology

INTRA-OP FINDING	HISTOPATHOLOGY_RESULT				Total
	appendicitis	negative	Peri-appendicitis	adenocarcinoma	
normal appendix	8	15	6	0	29
grossly inflammed	47	1	2	0	50
gangrenous	9	0	1	0	10
ruptured	6	0	0	0	6
appendicular mass	3	0	0	0	3
localised abscess	6	0	0	0	6
generalised abscess	4	0	0	0	4
appendicular tumour	2	0	0	2	4
Total	85	16	9	2	112

X^2=0.000, P= 0.005, statistically significant.

Table-14: Showing the Distribution of Post-Operative Morbidity

MORBIDITY	Frequency	Percent
nausea and vomiting	32	28.6
paralytic ileus	18	16.1
wound infection	15	13.4
faecal fistula	1	.9
none	46	41.1
Total	112	100.0

Table-15: Showing the Correlation between Intra-Op Finding and Post-Op Morbidity

INTRA-OP FINDING	COMPLICATIONS					Total
	nausea and vomiting	paralytic ileus	wound infection	faecal fistula	none	
normal appendix	8	0	0	1	20	29
grossly inflammed	19	8	2	0	21	50
gangrenous	1	4	4	0	1	10
ruptured	1	2	3	0	0	6
appendicular mass	1	0	0	0	2	3
localised abscess	0	2	4	0	0	6
generalised abscess	0	2	2	0	0	4
appendicular tumour	2	0	0	0	2	4
Total	32	18	15	1	46	112

X^2=0.000, P= 0.005, statistically significant

DISCUSSION

The initial report is that of the rarity of AA in the African population due to a predominantly fibre rich diet [2]. Many reports have indicated a rising trend in incidence of AA in Nigeria and the whole of West Africa [5]. The rise in incidence similar to that in western societies has been attributed to the nutritional transition from the fibre rich African meals to a high calorie, low residue western diets [8]. Out of the 112 patients studied, 44.6% were males and 55.4% were females, with a male-female ratio of 1:1.25. This is similar to reports from other parts of the world that estimated the lifetime risk for developing AA to be 7% for all, 12% for men and 25% for women [40]. Many other reports however, indicated a male preponderance [41, 42]. The increased presence of negative appendicectomy in the females due the presence of multiple differentials of AA is attributed to numerous reports of higher incidence [14]. This is evident in this study, as all those with the histopathological diagnosis of peri-appendicitis were females (Table-12, X2= 0.002, P= 0.005). The Pearson's chi square is less than the P- value and this makes the correlation statistically significant. The mean age in this study is 30.5(+_2.35), with an age range of 16-69 years. Although, AA can affect people of all age groups, it is known to be the disease of the young and the adolescent in the developed nations [43, 44]. There is a similar report from the South-Eastern Nigeria that documented a mean age of 19.9 years SD 9.12 [45]. However, many reports from within and outside Africa have noticed increased presentation beyond the adolescent years. Njeze [45] from the South-Eastern Nigeria, Ojo [9] from South-Western Nigeria and Zulfikar *et al*., [46] from Pakistan, all reported that AA commonly present in the second and third decades of life. Even more surprising is a report from Kano, North-Western Nigeria. They reported that about 90% of their patients were aged 40 years and below, but, the incidence after 40years decreased to 9.1% [47]. The Baker's hygiene hypothesis has been postulated to explain the increased incidence beyond adolescence. The hypothesis alleges that improvements in sewage disposal and provision of safe drinking water minimised exposure of infants and children to enteric organisms and potentially modifies the host response of the adolescent child to bacterial and viral infections [48].

The diagnosis of AA has been reported to be predominantly clinical through establishment of evidence of peritoneal irritation in the RLQ, with the aid of a thorough history and physical examination [49]. In our study, right Iliac fossa pain is the most common presenting complaint, seen in 94.6% of the patients, followed by anorexia (66.1%) and nausea (53.6%). Other reports from the developed and developing nations also highlighted the prominence of RLQ pain and Anorexia in making the diagnosis of AA [47, 50, 51]. Presence of Anorexia is said to be universal and is related to stomach produced hunger Hormone-Ghrelin. There are studies that indicated a sharp decrease in the serum levels of Ghrelin in patients with AA [52] and pre-operative assay of its serum level has been used as a diagnostic indicator of AA, especially, in its early stages [53]. Only 28.6% of the patients presented with the classical Murphy's sequence of an initial non-specific, peri-umbilical pain that later settled in the RLQ (Table-1). There are variable reports concerning this classical presentation, explained by the pathological processes in AA. The initial visceral peritoneal and the final parietal peritoneal irritations result in the sequence. Jain *et al*., in India reported the shifting pain in 58.7% of their studied subjects [14]. The most consistent clinical signs noted in this study are tenderness at the Mc Burney's point (92.9%), fever (67.9%) and rebound tenderness (59.8%). The least signs elicited are: right iliac fossa mass (16.1%), copes obturator (25.0%) and copes psoas (43.8%) signs. This is similar to report by Jain *et al*., They found tenderness at RLQ in 100%, rebound tenderness in 55.3% and low grade fever in 72.7% of their patients [14]. Alfredo Alvarado in his famous study reported almost similar finding [54]. Reliance on clinical evidence of peritoneal irritation alone in making the diagnosis of AA has been reported to be associated with a negative appendicectomy rate of 15% to 30% [55], and the risk of missing a perforated appendix may reach 3.4%, due to the overlap of clinical features of AA with right sided urological and gynaecological conditions [56]. Combining both clinical and Laboratory evidences of peritoneal inflammation improve the odd of making an

accurate and early diagnosis of AA [53]. We included Leucocytosis with differential Neutrophil count in our study as a marker of diagnosis of AA. Only 54.5% of our patients showed leucocytosis on complete blood count (Figure-3) and all showed evidence of immature bands. It is unfortunate that not all of our patients could afford to pay for the CBC. Anderson did a meta-analysis of diagnostic studies of AA and reported that individual clinical and laboratory variables had weak discriminatory power but, showed strong predictive power when combined together [57]. The most predictive among the two variables were laboratory tests of inflammation, which include leucocytosis on CBC, the raised percentage of neutrophils and C reactive protein levels [57]. He showed that the most important clinical indicators are history of migratory peri-umbilical pain and evidence of peritoneal irritation such as, RLQ tenderness and rebound tenderness [57]. In an effort to improve diagnostic accuracy, several clinical practice tests were devised with scores that can lead to an accurate diagnosis of AA [58]. The various clinical tests were risk stratification tests that classified those assessed in to low, medium and high-risk patients for AA [59]. Among these clinical practice tests, the Alvarado score was deliberately designed to reduce the need for imaging studies in making the diagnosis of AA [60]. This is very relevant in places were such imaging facilities are lacking or the results obtained are unreliable. The Alvarado score utilised 8 clinical and laboratory variables to indicate the risk of appendicitis [61]. Scores less than 5/10 indicate a decreased risk of appendicitis and high scores over 8/10 an increased risk [62]. No significant edge in predictive power has been conclusively shown after comparing the Alvarado score with clinical diagnosis alone [62]. Because of this, and the fact that, not all of our patients can afford to pay for laboratory tests such as CBC (Figure-3), we did not include the Alvarado or any other clinical scoring system in our study.

Only 63.4% of the patients had a diagnostic abdominal USS done and all were performed by the radiographer. USS result although is operator dependent, it is thought to be an excellent diagnostic aid in cases of AA [63, 64]. It has a sensitivity of 55-96% and specificity of 85-98% [65-68]. Although, less accurate than a CT Scan (sensitivity of 92-97% and specificity of 85-94%), it is more widely available and there is no exposure to harmful ionising radiations [69, 70]. Many workers questioned the rationale of mandatory use of Imaging tools in making diagnosis of AA in those with high clinical scores or index of suspicion [71, 72]. They advised that Imaging study should be reserved for those with equivocal clinical findings, especially, women of reproductive age group [73], here; a diagnostic abdominal USS and Laparoscopy are known to mitigate the high negative appendicectomy rates [74]. About 8.9% of the patients had an erect or lateral decubitus abdominal radiograph on suspicion of a perforated appendix, and air under the right diaphragm was seen in cases of perforated appendix. About 27.7% of the patients could not afford to pay for any radiological investigation and none (100%) of the patients had a diagnostic abdominal CT Scan. In this study, a total of 44.6% of the patients had grossly inflammed appendix and 25.9% had an apparently normal looking appendix, making a total of 70.5% of uncomplicated AA. A total of 26.0% of the patients had complicated AA, distributed as follows: gangrene (8.9%), perforation (5.4%), appendicular mass (2.7%), localised abscess (5.4%) and generalised abscess (3.6%). Gangrene (8.9%) and Perforation (5.6%) are most common types of complicated AA found (Table-4). The major causes of morbidity reported by Edino *et al*., were also perforation and gangrene [47]. Reports from other parts of Nigeria however, indicated a higher perforation rate of 19.0% [38] and 13.9% [31]. The most important contributors to increased perforation rate in our study are: delayed presentation (Table-6, X2= 0.101, P= 0.005) and advanced age (Table-5, X2= 0.000. P= 0.005). The correlation with advanced age above 50 years is statistically significant. Yang *et al.*, [75] in South Africa and Edino *et al*., [47] in Nigeria reported the same relationship. The perforation rate from large databases in developed western nations was estimated to be around 20% [11]. Acute Appendicitis in the extreme of ages has been associated with perforation rate as high as 80% [76, 77].

The negative appendicectomy rate in this study is 22.3% and a positive histopathological diagnosis of AA was made in 75.9% of the patients (Table-11). Other tertiary health centres in Nigeria have reported almost similar rates of 29.5% (78) and 32.2% [79] respectively. With universal use of preoperative diagnostic imaging study, many centres in Nigeria have reported a lower negative appendicectomy rate of about 14.1% [8, 21, 47, 80]. A great majority of those with negative appendicectomy were females of reproductive age group (Table-12, X2= 0.002, P= 0.005), and the correlation is statistically significant. These women often have right sided gynaecological inflammatory or non-inflammatory conditions with a potent mimicry for AA [47]. In these cohort of patients, the use of diagnostic laparoscopy, CT scan or USS, is said to improve the negative rate [78, 79]. Flum *et al*., in a large sample size study has noticed no significant decrease in the global negative appendicectomy rate of 15-20% over 15-year period; despite the use of pre-operative imaging and diagnostic laparoscopy [81]. The rare finding was that of an adenocarcinoma of the appendix in 1.8% of the specimens. Although a rarity, the world-wide incidence of appendiceal tumors is placed between 0.4%-1.7% for all appendices removed for AA [82-85]. A study from Nigeria reported the prevalence of tumour-related AA as 2.2% of overall cases [86].

Carcinoid tumour, rather than a primary adenocarcinoma of the appendix is the most prevalent malignancy of the appendix; occurring in 0.4-1.0% of appendicectomy specimens [87]. It is estimated to make up to two-thirds of all appendiceal tumours [88, 89]. The primary adenocarcinoma of the appendix encountered in our study is very rare. It is seen in 0.08-0.2% of all appendices removed for AA and makes up a total of 4-6% of primary malignant tumours of the appendix [90]. It has been reported that up to 28-29% of specimens removed during interval appendicectomy for appendicular mass may also have either of the two malignancies [91]. No Ova, Parasite or Tuberculous granuloma was seen.

Post-operative wound infection is the most common morbidity after Appendicectomy (13.4%) and the least common complication is Entero-Cutaneous fistula (0.9%). Majority did not develop any significant morbidity (Table-14). All (100%) of those who developed post-operative wound infection had a complicated AA (Table-15, X2= 0.000, P= 0.005), and this correlation is statistically significant. The post-operative wound infection rate is by far less than that of Edino *et al*., in North-Western Nigeria (26.8%) and Okobia in Southern Nigeria [79]. But, more than the reported rate in Europe and USA [92]. The proportion of the study population that were operated as emergency appendicectomy and those with complicated AA may increase the wound infection rate. There was no recorded mortality. This is similar to global trend, where overall mortality following emergency appendicectomy is <1% [93].

CONCLUSION

The diagnosis of AA can be made with high degree of accuracy by using a detailed history and thorough physical examination, especially, in the adult male patient. The incorporation of laboratory and imaging studies although helpful, is not mandatory. Delay in presentation at the hospital and the advanced age of a patient increase the risk of developing a complicated AA. Performing a histopathological analysis of all appendicectomy specimens is essential in determining the negative appendicectomy rate. Where clinical feature is equivocal, an adjunct Imaging study or a diagnostic laparoscopy will help to make an accurate diagnosis.

Conflict of Interest: None Declared

Limitations: Only adult patients were recruited and a significant number of participants could not do the requested laboratory test for inflammation.

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