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## Research Article

### ABDOMINAL SURGICAL EMERGENCY IN SOUTH EASTERN NIGERIA

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#### ABSTRACT

**Objective:** Abdominal surgical emergencies constitute significant disease burden world-wide. An emerging trend due to changing demographics and westernization has been observed in many regions of the developing economy. We present the spectrum, management and outcome measures of emergency abdominal operations in Abakaliki, Southeast Nigeria.

**Methods:** This is a descriptive prospective study of all consecutive teenage and adult patients operated for abdominal emergencies between January 2009 and December 2013 at Federal Teaching Hospital Abakaliki(FETHA). The data were analyzed using Statistical Package for Social Sciences (SPSS) version 22.0.

**Result:** A total of 684 patients operated for abdominal emergencies were enrolled, 398(58.2%) males and 286 (41.8%) females. The ages of the patients ranged from 16-85 years with a mean of 38.89 +/- SD 17.58. The most common diagnoses were appendicitis (264, 38.6%), adhesive bands (77,11.3%) and trauma(66, 9.6%). Nearly a third (85, 32.2%) of the patients with appendicitis had complicated disease pre-operatively and 22.7% of the excised appendices were histopathologically normal. Majority (96.1%) of the 77 patients managed for adhesive bands had previous abdominal surgeries. Approximately three-quarter (50, 75.8%) of abdominal traumas were due to road traffic accidents (RTA). Indeed 80.0% and 48.4% of blunt and penetrating injuries respectively resulted from RTA. Post-operative morbidity and mortality rates were 34.1% and 4.8% respectively. At a median follow up of 10 months, 16 (2.3%) incisional hernias developed and 48.0% of patients with colonic cancer developed extensive intra-peritoneal metastasis.

**Conclusion** Appendicitis, adhesive bands and trauma have taken over from strangulated external hernias as major causes of abdominal emergencies in our environment. Late presentation and advancing age are associated with poor outcomes.

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## INTRODUCTION

Surgery has a neglected profile in the global health priority despite an estimated 11-15% of the global burden of disease (predominantly in low and medium income nations) amenable to surgical treatment [1, 2]. An estimated 234 million major operations are performed annually world-wide, but only 3.5% of procedures are done in the developing world [1, 2]. Indeed, estimates suggest that the burden of unmet needs is vast in sub-saharan Africa [1,2,3]. It has been reported that 80-90% of surgeons in West Africa work in urban areas, although 85% of the population live in rural areas and in 2003, Nigeria had one paediatric surgeon per 2.2 million children [2].The impact of surgical disease through "Disability Adjusted Life Years (DALYs) is considerably higher in Africans(38 DALYs) compared to Americans with DALYs of 21%[2]. The double burden of poor access to surgical services and high risk of

adverse outcomes has rekindled interest on this topic globally, manifested by recent decision of World Health Organization (WHO) to include a resolution on access to safe surgery and anaesthesia on the agenda of the 2015 World Health Assembly [1, 2].

In resource-limited setting like ours, global disease burden has continued to shift from communicable to non-communicable diseases and injuries [3, 4]. World-wide, appendicitis, bowel obstructions, abdominal injuries, strangulated hernias, volvulus and acute biliary pathology remain the most common causes of abdominal surgical emergencies in adults [1,3,5,6]. Abdominal surgical emergencies are common and often present diagnostic and treatment challenges particularly in resource-limited settings like ours [5, 7]. Overall, abdominal pain is the commonest cause of emergency department visits, accounting for 7.0% (8 million) of the 119 million visits in USA in 2006[8].

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The indications for emergency abdominal operations vary from region to region and even within the same region, cultural and socio-demographic factors may alter the pattern [5,9,10,11]. In many series in the developing world, changing demographics, delayed presentation and high morbidity and mortality for abdominal surgical emergency have been described [4,5,7,12]. World-wide, appendicitis is the commonest indication for emergency abdominal operation [5,13,14].

In South Africa, a recent multicenter study involving six indigenous hospitals showed that, though trauma was the overall commonest diagnosis, appendicitis and gynecological cases were the leading causes in hospitals 6 and 4 respectively while hospital 5 had the highest rates of morbidity and mortality [11]. Perhaps, this prompted the authors [11] to conclude that emergency abdominal operations are likely to be subject to performance variation with hospital location playing important roles in disease spectrum and outcome measures.

In our practice in Abakaliki, Nigeria, emergency abdominal operations constitute significant proportion of a surgeon's workload, yet there is paucity of data on this condition in our environment. The aim of this study is to document the clinical spectrum, presentations and outcome measures of emergency abdominal operations in Abakaliki, southeast Nigeria.

## PATIENTS AND METHODS

**Design and setting:** This is a descriptive prospective study of patients operated for abdominal surgical emergencies at Federal Teaching Hospital, Abakaliki (FETHA) between January 2009 and December 2013. Federal Teaching Hospital Abakaliki is a teaching health institution in the southeast geopolitical zone of Nigeria.

**Subjects:** All consecutive 684 patients who presented with abdominal emergency and subsequently underwent operations were included. Patients who refused to give consent and those below the age of 16 years were excluded. Recruitment of patients to participate in the study commenced with records of socio-demographic data in a standard pro-forma. Comprehensive clinical assessment by either a consultant general surgeon or a senior registrar in surgery was done routinely. Basic blood and urine investigations were carried out. Ultrasound and x-ray facilities were available only during day time hours. Only two patients had abdominal computed tomography examination pre-operatively, but none of the operated patients underwent laparoscopy as a means of diagnosis or treatment in the course of their management. Patients were routinely resuscitated with appropriate intravenous fluids, electrolytes, blood and oxygen when indicated. Interventional surgical procedures were carried out as merited by each case and the post-operative outcome measures entered into the pro-forma.

**Statistical data analysis:** Statistical data analysis was done using statistical package for social sciences (SPSS) software version 22.0 (IBM, USA 2015). Mean, median and standard deviation were used to summarize continuous variables. Categorical variables were reported as percentages. Chi-square test was used to determine the P-values for categorical variables with a p-value of less than 0.05 considered to constitute a statistically significant difference.

**Ethical consideration:** The protocol for this study was approved by the "Research and Ethical Committee" of the Federal Teaching Hospital, Abakaliki before commencement of the study.

## RESULTS

In the current report, 2,243 patients with abdominal emergencies were seen, accounting for 27.6% of all emergency cases. Of the patients in the abdominal emergency group, 684 (30.5%) were managed operatively. This population of patients who received surgical treatment formed our study cohorts. There were 398 (58.2%) males and 286 (41.8%) females, giving male to female ratio of 1.4: 1. Their ages ranged from 16 - 85 years with a mean of 38. 89 +/-SD 17.58. In the current study, the indications for emergency abdominal operations recorded against the corresponding years are shown in table 1 below.

**Table 1** Indications for emergency abdominal operations

Year	Appen-dicitis	Intest. Bands	Trauma	Typh perf	Ext. Hernia	Perf. Pud	Colon Cancer	Intussu-sception	others
2009	40	6	6	8	18	12	3	4	18
2010	41	10	9	10	14	10	4	2	10
2011	43	12	11	12	12	6	4	1	20
2012	60	18	14	14	10	4	6	4	11
2013	80	31	23	18	6	4	8	4	20
Total	264	77	66	62	60	36	25	15	79
%	<b>38.6</b>	<b>11.3</b>	<b>9.6</b>	<b>9.1</b>	<b>8.8</b>	<b>5.3</b>	<b>3.6</b>	<b>2.2</b>	<b>11.5</b>

Intest=intestinal; Typh=Typhoid; perf=perforation; Ext=External; pud=peptic ulcer disease.

The peak age range incidence was 16-25 years where appendicitis, abdominal trauma and external hernias occurred at frequencies of 1 in 3, 1 in 4 and 1 in 10 patients respectively. Approximately one third (34.1% , 90 cases) of the operations for appendicitis (complicated and uncomplicated) was performed in the 16-25 years age range.

The duration of acute symptoms prior to presentation ranged from 30 minutes to 7 days with a median of 3 days, though approximately one-quarter (25.3%, 173cases) of the patients had recurrent symptoms ranging from one month to 12 years. Furthermore, over two-third (69.4%, 475 cases) of the patients presented within four days of onset of index illness, but less than one-third (28.1% , 192 cases) did so within the first 48 hours of symptoms. There is a statistically significant relation between presentation after 48 hours of symptoms (late presentation) and prior visit to alternative medicine homes and other patent medicine dealers (p<0.05). Only 103 (15.1%) of the patients had their operations performed within six hours of admission, the rest (581,84.9%) waited for a period ranging from 6 hours to 5days mainly due to financial constraints (60.2%), followed by hospital logistics (34.4%) and resuscitation time (5.4%). Post-operative morbidity and mortality were higher in patients with delayed operation compared to those with early surgery (p<0.05). Nearly one quarter(23.4%, 160 cases) of the patients harbored one or more co-morbid conditions ranging from hypertension, diabetes, chronic obstructive pulmonary diseases, tuberculosis, renal diseases, cardiac abnormalities to malignancy. Mortality rate was also higher in this group compared to those without co-morbidities (p<0.05).

Surgery for suspected appendicitis was the commonest emergency abdominal operation carried out during the study period, accounting for 38.6% (264 patients, 140 males, 124 females) of the total operations performed. Among the patients with appendicitis, 30.3% (80 patients) had complicated disease at the time of admission. Indeed, appendicitis was the commonest cause of peritonitis in this study, accounting for 40.0% of all peritonitis encountered. Histology report showed that 77.3% (204 cases) of the appendix biopsies were truly inflamed while 22.7% (60 cases; 56 females and 4 males) showed normal histopathology, giving negative appendectomy rates of 40.0% in females and 2.9% in males. The distribution of patients with appendicitis according to their age groups and frequencies of complicated disease prior to admission is shown in figure 1 below.

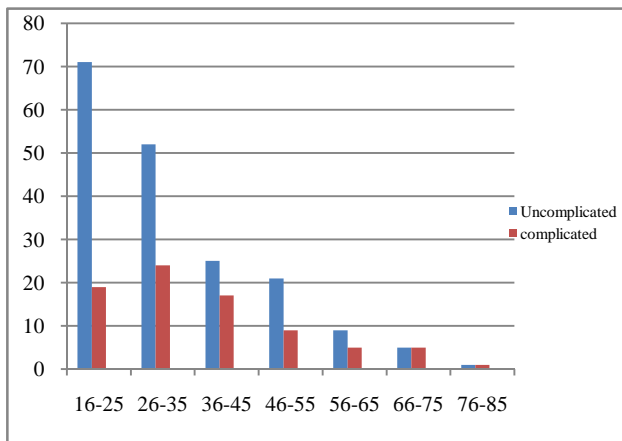


Figure 1 Age distribution of patients with appendicitis

Adhesive intestinal obstruction was the second (11.3%, 77 cases) most frequent abdominal surgical emergency encountered in this study. Nearly three-quarter (74.0%, 57 cases) of patients with intestinal bands presented after 48 hours of onset of illness. During operation for adhesive bands, 93.5% (72 patients) had multiple adhesions, 28.6% (22 cases) had gangrenous bowel segments while 1.3% (1 case) was congenital in origin. The predisposing (preceding) operative procedures or conditions implicated in the development of adhesive bands identified during clinical assessment of patients in the index study are shown in figure 2 below.

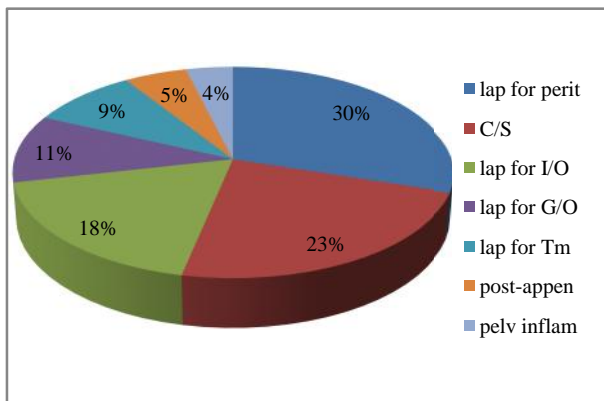


Figure 2 Percentage of previous laparotomies/conditions in patients with abdominal emergency

Lap=laparotomy;Perit=peritonitis;C/S=Caesarean section; I/O=intestinal obstruction; G/O=gynecologicaloperations;Tm=Trauma;post-appen=post-appendectomy ;pelv=pelvic; inflam=inflammation

Trauma, the third commonest indication for emergency abdominal operation in this study showed the most dramatic and complex presenting pattern with nearly a quarter (24.2%, 16 patients) presenting with hypovolemic shock at outset. Over one-third (39.4%, 26cases) of the trauma patients required blood transfusion prior to exploratory laparotomy. More than half (53.0%, 35 cases) were due to blunt trauma. Road traffic accident (RTA) accounted for the greater majority (80.0, 28 patients) of the blunt abdominal traumas while fall from height, industrial accidents and domestic violence represented 11.4 % (4 patients ), 5.7% (2 patients) and 2.9% (1 patient) of patients with blunt traumas respectively. Of the 31 trauma patients with penetrating injuries , RTA accounted for 48.4%(15 patients) while 41.9%(13 cases), 6.5% (2 cases ) and 3.2% (1case) were due to civilian violence (gunshots, assaults with knives , cutlasses and sharp metallic objects), industrial accidents and falling astride sharp objects respectively.

Of the 88 abdominal visceral injuries (20 patients sustained multiple intra-abdominal injuries), the spleen (30.7%, 27 cases) was the most frequently injured organ, followed by small intestine (20.5%, 18 cases), then liver (18.2%,16 cases) and kidney (10.2%, 9 cases). Other injured organs were urinary bladder (8.0%, 7cases), large intestine (4.5%, 4 cases) stomach (3.4%, 3 cases), diaphragm (2.3%,2 cases), gall bladder(1.1%,1 cases) and urethra (1.1%,1case).

Strangulated external hernias constitute the fifth most common indication for emergency abdominal operations and the second commonest cause of intestinal obstruction in this study. The various types of strangulated abdominal wall hernias encountered are shown in table 2 below.

Table 2 Correlation of hernia sites and distribution of bowel obstruction.

Types of hernia	Obstruction	Strangulated	Total	%
Inguinal	17	30	47	78.3
Femoral	1	5	6	10.0
Umbilical	1	1	2	3.3
Spigellian	1	0	1	1.7
Epigastric	1	0	1	1.7
Para-umbilical	2	0	2	3.3
Incisional	1	0	1	1.7
<b>Total</b>	<b>24</b>	<b>36</b>	<b>60</b>	<b>100.00</b>

Small bowel resection was carried out in 70 patients, 30 (42.9%) of whom had strangulated external abdominal wall hernias, 22(31.4%) had intestinal bands and 8(11.4%) had trauma. Additional small bowel resections were performed in 4(5.7%) individuals with typhoid perforations, 3(4.3%) patients with intussusception, 2(2.9%) with entero-cutaneous fistula and 1(1.4%) patient with septic abortion.

Emergency colonic resections with or without colostomies were performed in 49 patients. Of these, 25(51.0%) were due to malignant obstruction, 10 (20.4%) for intussusception and 5(10.2%) for large bowel volvulus. Further 6(12.2%), 2(4.1%) and 1(2.0%) colonic resections were done on account of external hernias, trauma and abdominal tuberculosis respectively.

The duration of hospital stay ranged from 3 days to 47days with a mean of 9.94 +/- SD 6.15. Surgical site infection (SSI) occurred at the rates of 10.8% in patients with uncomplicated appendicitis, 16.5% in trauma patients and 38.3% in patients

with secondary peritonitis. Post-operative anastomotic leaks occurred in 12(11.8%) of 102 intestinal resections with primary anastomoses done in this study. The leaks were higher in patients with multiple perforations, gross peritoneal contamination, multiple associated intra-abdominal injuries and shock. Other post-operative outcome measures are shown in table 3 below.

**Table 3** Post-operative outcome measures after emergency abdominal operations.

Complications	Frequency	Percentage (%)
Wound Infection	108	15.8
Peritonitis	44	6.4
Anastomotic Leak	12	1.8
Atelectasis	6	0.9
Prolonged Ileus	36	5.3
Entero-cutaneous Fistula	4	0.6
Acute Renal Failure	7	1.0
Others	16	2.3
Mortality	33	4.8
<b>Total</b>	<b>266</b>	<b>38.9</b>

Out of the 684 operated patients, 486(71.1%), 330(48.2%), 141(20.6%) and 89(13.0%) were available for follow up at 1month, 3months, one year and beyond one year respectively. The duration of follow up ranged from one to 24 months with a median of 10 months. Thirty three patients died post-operatively giving a mortality rate of 4.8%. Mortality rates were higher in patients with delayed presentation, advanced age, co-morbidities, intra-abdominal malignancy and peritonitis.

Beyond thirty post-operative days, 16 (2.3%), 36 (5.3%) and 6 (0.9%) of the follow up patients developed incisional hernia, partial intestinal obstruction from adhesions and intestinal hurry respectively. Nearly half (12, 48.%) of the patients with large bowel tumours showed features of advanced intra-peritoneal metastasis after 18 months of surveillance. All the follow-up patients with partial intestinal obstruction from bands were successfully managed conservatively. The major findings in our study compared to previous similar studies are shown in table 4 below.

**Table 4** Comparison of major findings in the index and previous similar studies.

Major Findings	Index Study (%)	Ile-Ife [7] (%)	Ghana [14] (%)	Zaria [5] (%)	Sudan [15] (%)
Appendicitis	38.6	65.3	22.4	50.5	63.0
Typhoid perforation	5.3	2.3	16.2	9.4	1.0
Trauma	9.6	10.0	8.3	9.2	11.6
External hernias	8.8	7.0	-	14.6	11.0
Neoplasm	3.7	1.7	-	1.5	1.0
Intestinal bands	11.3	2.0	-	3.3	1.4
Mortality	4.8	1.1	7.3	4.5	8.5
Design	Prosp	Prosp	Prosp	Prosp	Prosp

Prosp=Prospective;

## DISCUSSION

World-wide, abdominal surgical emergencies constitute significant proportion of emergency admissions, accounting for 7.0 – 29.5% of all emergency department visits [4,5,8,10]. The above data agree with the figure of 27.6% recorded in the index study. It has been cited that the pattern of these conditions is changing rapidly in the developing world, perhaps due to

westernization of life styles and increased laparotomy rates [3,4,5,7,15]

In the past, intestinal obstruction predominantly from strangulated external hernias was the leading cause of abdominal surgical emergency in many African series [5,16]. Currently, available data show that appendicitis has taken over from intestinal obstruction as the commonest cause of surgical abdomen in the West African sub-region [5,7,13]. Furthermore, this epidemiological shift indicates that adhesive intestinal bands are now more prevalent than strangulated external hernias in the sub-region akin to the pattern in temperate lands [6,13,17]. Our findings support the above transition as we determined that appendicitis is the leading cause of abdominal surgical emergency in our setting followed by adhesive bands and trauma in that order.

Across the globe, appendicitis remains the most common indication for emergency abdominal operation [7,13,18,19] followed by intestinal obstruction in some studies [10,15,20] and in other series by trauma [5,6]. In the current report, appendicitis represents over one-third (38.6%) of all cases, comparable to figures of 30.4% in Ilorin [10], Nigeria and 28.0% in Ethiopia [4]. Our figure is however higher than 22.4% quoted by other authors in Ghana [13]. Disturbing values of 50.5%, 63.0% and 65.3% have been reported previously [5,7,15].The variation in the rates of appendicitis noted at different localities may reflect the differences in demographics, study design and socio-cultural practices of the study population. Despite these variations in the reported frequencies, appendicitis remains the leading cause of surgical abdomen in the respective centres.

Our study revealed that while the rate of appendicitis doubled within the five years under survey, that of adhesive bands and trauma geometrically increased over the same period. In tandem, there was significant decrease in the prevalence of external hernias and peptic ulcer perforations (table 1). Previous data from Nigeria [5,6,17] and Ethiopia [4] conform with the above reports. Awareness of these variations is crucial to formulation of proper management guidelines and subsequent planning of prevention, advocacy and intervention strategies.

The crux of the matter with appendicitis lies in its propensity towards rupture or gangrene and subsequent intra-peritoneal sepsis.The high rate of complicated appendix (perforation, gangrene) in this study is comparable with previous reports in the sub-region namely Ghana [20,21]and Nigeria [5]. The problem with this form of the disease is grave and as noted in this study, has been quoted to be the commonest cause of peritonitis in Nigeria [7], Ghana [20] and second to duodenal perforation in India [22]. Nevertheless, it has been cited that the perforated appendix may be a different disease from the non-perforated counterpart and that the disease may start in the perforated form ab initio [21]. The overall high negative appendectomy rate (22.7%) documented in this series agrees with reports of previous studies [5,21] and the relative differences in males (2.9%) and females (40.0%) reflect the higher differential diagnoses of appendicitis in the female population as cited elsewhere [7]. It has been reported that majority of negative appendectomies are contributed by an

entity called “none specific abdominal pain” (NSAP) that were misdiagnosed as appendicitis [5,21].

In the elderly population, the spectrum of abdominal surgical emergency differs. In India [23], the most common indication for emergency abdominal operation in the elderly cohorts is perforated peptic ulcer while appendicitis assumed the fifth position. Curiously, in southeast Nigeria, Njeze [24] reported no cases of appendicitis among the 119 elderly patients recruited over a 16-year period. Previous authors have cited that in the elderly, appendiceal lumen is almost obliterated, giving less room for appendicitis [7]. Perhaps, this may justify the paucity of the condition in the elderly.

In advanced economy, laparoscopy and an emerging technology – Natural Orifice Transluminal Endoscopic Surgery (NOTES) are rapidly assuming the preferred approaches for emergency abdominal surgeries [14, 19]. At Mayo clinic, USA, it was reported that appendectomy is the second most frequently performed NOTES procedure after cholecystectomy [19]. Indeed, with laparoscopy and NOTES, the yield of negative appendectomy will be negligible. As the population of elderly patients increases, minimally invasive techniques will be necessary to improve outcomes in those with diminished physiological reserve [14, 19]. Njeze working in southeast Nigeria reported that 40.0% of fifteen elderly patients treated with emergency laparotomy died, most of the deaths were attributed to hemorrhage, infection and cancer [24]. Nevertheless, majority of the abdominal surgical emergencies in that series [24] are amenable to minimally invasive surgery (MIS), but facilities for MIS are scarcely available in southeastern Nigeria. Without prejudice, therefore, current authors agree with their colleagues in Ghana [20] who reported that surgeons in developing countries are not facing surgical challenges similar to those of their counterparts in developed nations.

In this report, adhesive intestinal bands represent the commonest cause of intestinal obstruction and the second leading cause of abdominal surgical emergency in our environment. The decrease in the prevalence of strangulated external hernias in this study and other African communities has been attributed to wider availability and acceptability of elective hernia repair in these settings [5, 25]. A recent publication in Abakaliki [25] Nigeria showed that an impressive 73.5% of 355 inguinal hernia patients had their hernias repaired electively. In our study, malignant bowel obstruction, intussusception, volvulus, internal hernias and abdominal tuberculosis constitute minor causes of intestinal obstruction. The relative rarity of these conditions in our study may lend credence to a recent report in Ibadan [9], Nigeria that intussusception once the commonest cause of intestinal obstruction in that region, is now a myth, coming after external hernia and intestinal bands.

Abdominal trauma, the third major cause of abdominal surgical emergency in this study has steadily evolved and gained prominence in the developing world largely due to increased human movements, proliferation of five arms, widespread political instability and use of military style assault weapons [5,11,26]. In a multi-centre study in South Africa, however, trauma was the overall most common cause of emergency abdominal operation. In Uganda [26] use of alcohol, over-

speeding, overloading, use of motorcycle as means of transportation have been implicated as predisposing factors for abdominal trauma. These observations in Uganda may reflect the state in our environment where the percentages of both penetrating and blunt abdominal traumas from road traffic accident outstripped the causes from civilian violence, fall from height, industrial and domestic accidents put together. Similar pattern was reported in Zaria [5] Nigeria, but differ from findings in Ethiopia [4] and Sudan [15] where stab injuries were the major causes of abdominal trauma.

The wide range of length of hospital stay (LOS) recorded in this study is consistent with data reported by previous authors [5,7,11]. Post-operative morbidities principally after operations for generalized peritonitis and intestinal obstruction were responsible for majority of the prolonged stay. The overall wound infection rate of 15.8% recorded in this study is higher than figures of 2-5% reported in USA and Europe ( $P < 0.05$ ), but comparable to results from India [18, 22] and Pakistan [27]. The reason adduced for higher infection rate in the developing nations include poor hospital designs and lack of attention towards basic infection control measures [18].

The mortality rate of 4.8% in this study, though lower than rates of 8.5% in Sudan [15] and 10.4% in sierra leone [16] is significant. These deaths were mostly from sepsis after operation for peritonitis and gangrenous bowel. Mortality was also higher in patients with delayed presentation, multiple comorbidities, severe pre-operative haemorrhage and intra-abdominal malignancy. Previous studies in Nigeria [5], India [22] and Sierra Leone [16] support the above results. Surprisingly, similar studies in Enugu [17] and Ile-Ife [7] both in Nigeria revealed low mortality rates of 0% and 1.1% respectively. In South Africa, it was determined that hospital location is an independent risk factor for risk-adjusted adverse outcomes following emergency intra-peritoneal surgery [11]. The authors identified patients' demographics, comorbidities, disease spectrum, presence of specialist surgeons and anaesthetist during surgery and availability of computed tomography scans as important predictors of outcome in the six hospitals surveyed [11]. Adamu *et al* in Zaria, Nigeria identified long operation waiting time as important contributor to poor outcome in patient with abdominal surgical emergencies [12]. Majority of the delays in that study [12] were due to financial constraints (53.8%), delayed investigation results (24.1%) and other institutional organization problems (22.1%).

## CONCLUSION

Emergency abdominal surgery constitute significant disease burden in our environment with appendectomy being the commonest emergency procedure performed. Due to westernization of life style, increased human movements, availability and acceptance of elective inguinal hernia repair, an epidemiological transition has evolved in our setting. Prevention strategies, advocacy and prompt interventions are needed at auspicious time to reduce the burden of this problem. The establishment of National health insurance scheme (NHIS) in Nigeria is salutary as long waiting time before operations mainly due to financial constraints and other hospital bureaucratic bottlenecks have been implicated for poor outcome.

**Author's contributions:** OAU conceptualized the study and performed the literature search, coordinated the manuscript writing, data collection and analysis. He participated in manuscript editing and did the submission. ESCO participated in data analysis, manuscript writing and editing. The two authors read and approved the manuscript for submission.

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