**TITLE PAGE**

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**TITLE: CLINICOPATHOLOGICAL REVIEW OF APPENDICECTOMY SPECIMEN IN A TROPICAL MISSION HOSPITAL: A CROSS-SECTIONAL COHORT STUDY**

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**ABSTRACT**

**BACKGROUND:** Acute appendicitis remains a common surgical condition and the importance of specific elements in the clinical diagnosis remain controversial. It is a disease of the young presenting in children and early adolescents although no age group is exempt. This clinicopathological study aims to determine the various lesions of the surgically removed appendix in a resource constrained mission hospital setting, northwestern Cameroon.

**METHOD:** This retrospective cross-sectional descriptive study was undertaken to review the histo-pathology reports of all appendectomy specimens submitted to the Pathology department, Central Laboratory of a Mission Hospital; Northwestern region of Cameroon from January 2011 to January 2016. Patient’s socio-demographical data, clinical presentations were extracted from the request form. The data were analyzed using the SPSS version 22 and presented with descriptive and inferential statistics.

**RESULTS:** A total of 683 appendices were received during the 5-year study period constituting about 12% of total specimens. The age range of patients in this study is 14–78 years with a mean of 20.12 ± 5.12 years. Acute appendicitis was found in 86.9% of our cases while other lesions constitute 13.1% and negative appendectomy occurred in 4.5% of the cases.

**CONCLUSION:** The incidence of acute appendicitis remains low especially in the rural communities of Africa. We therefore conclude that the current study spanned the entire gamut of pathological processes that involve the appendix and provides a fair idea about the clinicopathological correlation in appendectomy specimens.

**KEYWORDS: Acute abdomen; Appendix; Appendectomy; Histology; Resource-constrained setting**

**INTRODUCTION**

The diagnosis of acute appendicitis is most commonly a clinical one; many patients present with a typical history and examination findings. The cause of acute appendicitis is unknown but is probably multifactorial; luminal obstruction and dietary and familial factors have all been suggested [1–3].

Appendectomy is the treatment of choice and is increasingly done as a laparoscopic procedure [2]. Acute appendicitis is a disease of the young presenting in children and early adolescents although no age group is exempt. It is the most common cause of acute surgical abdomen worldwide and its incidence varies with geographical location [3]. In the United States, a crude estimate of the incidence of acute appendicitis is 11 cases per 10,000 populations [4]. Studies have shown acute appendicitis to be more common in the whites than non- whites [5]. Appendicitis is the most common abdominal emergency and accounts for more than 40,000 hospital admissions in England every year [6, 7].

There is paucity of data in Cameroon, but a study by Ngowe Ngowe *et al* [8] reported an incidence rate of 4.6% for acute appendicitis. In other sub-Saharan Africa, like Nigeria, incidence of acute appendicitis is relatively low with varying reports of average annual frequencies ranging from 22.1 to 49.8 new cases but in other African countries, annual frequencies are relatively higher ranging from 22.9 to 129 new cases per 100,000 persons [7, 9–13]. Not only has the pathologic diagnosis of acute inflammation, at times unusual findings such as incidental tumors highlighted the importance of pathologic analyses of every single resected appendix. Clinicopathological studies of appendiceal lesions on the African continent are relatively few and this study was conducted to determine the various lesions of surgically removed appendix in our center and compare our findings with other studies elsewhere.

**Objectives of the Study:** These include: 1) To evaluate the clinical presentations of acute appendicitis in a tropical rural African setting, Cameroon. 2) To correlate such clinical features with the pathological findings of resected appendix specimens.

**Research Question**: 1) What are the various lesions of surgically removed appendix in our center? 2) Do such lesions compare relatively with findings with other studies elsewhere?

**Hypothesis:** There are no significant differences in the clinicopathological features of appendiceal lesions in the contemporary tropical African population with other studies elsewhere.

**PATIENTS AND METHODS**

**Study Design and Setting**

This retrospective cross-sectional descriptive study was undertaken to review the histopathology reports of all appendectomy specimens submitted to the Pathology department, Central Laboratory of a Mission Hospital; Northwestern region of Cameroon from January 2011 to January 2016. The Central Laboratory is a referral center for several government district hospitals, private hospitals and other mission hospitals in the northwestern region and its environs.

**Study population and procedure**

The Northwestern region is a rural community with a population of 1,753,460 people (2016 Cameroon Population-Census). A pretested proforma which was developed by the researcher was used for data collection. Patient’s socio-demographical data, clinical presentations were extracted from the request form. Routine haematoxylin and eosin (H&E) staining and where necessary histochemical studies were carried out. Alcian blue/Periodic Acid Schiff stain was done for a case of suspected mucocoele. **Validity of Instrument:** The proforma were validated by the experts in that area. **Reliability:** Test retest method was used for the reliability of the instrument. The result was 0.8.

**Statistical Analysis**

All data were entered in an excel database (Excel 2007, Microsoft corporation®) and analyzed using the Statistical Package for the Social Sciences (SPSS) version 22 (IBM Corp, Armonk, NY, USA). In addition, subsequently presented with descriptive and inferential statistics in terms of frequency, age and sex distribution, nature of clinical signs and symptoms as well as histological characteristics of pathologic lesions (normal, acute appendicitis with or without peritonitis, lymphoid hyperplasia, eosinophilic appendicitis and schistosomal appendicitis)

**Ethical Considerations**

Ethical approval was obtained from the Institutional Ethical Committee. Confidentiality was ensured by not writing the names of patients on the proforma in accordance with Helsinki declaration of 1964.

**Reporting:** The STROBE / STROCSS guidelines were used in reporting this study [14, 15].

**RESULTS**

During the study period of five years between January 2011 and January 2016, a total of 683 appendices were received in the Histo-pathology department, Central Laboratory of the Mission Hospital, constituting about 12% of total specimens. There were 273 males and 410 females constituting a male to female ratio of 1:1.5. The age range of patients in this study is 14–78 years with a mean of 20.12 ± 5.12 years. Acute appendicitis was found in 86.9% of our cases while other lesions constitute 13.1% and negative appendectomy occurred in 4.5% of the cases. The number of cases per year for the 5 years was 96, 98, 102, 106, and 108 respectively.

**Age and sex distribution**

The age and sex distribution of the patients is shown in Table 1. The peak age of occurrence in this study is 20–29 years closely followed by 10–19 year age group both constituting over 60% of the cases. The least number of cases (12 patients) were seen in the age group 60–78 years constituting 1.8%.

**Clinical presentation**

The most common form of presentation by our patients was right iliac abdominal pain (92%) which later became generalized in 24.8% of cases. The other symptoms include fever (72%), vomiting (58%), and loss of appetite (46%). The mean duration of symptoms was 4.05 days. Twelve patients had perforation at surgery and 2 out of these presented primarily in shock. The average hospital stay post operation was 5.5 days with a range of 4–14 days. No record of mortality in this study.

**Histological diagnosis**

The distribution of histological diagnosis is as shown in Table 2. Thirty-one cases (4.5%) were found to be normal. Uncomplicated acute appendicitis was seen in 174 patients constituting 60% and acute appendicitis with peritonitis constitutes 20%. Submucosal fibrosis, schistosomiasis, lymphoid hyperplasia and subacute appendicitis constitute 5.5%, 1.0%, 3.4% and 4.4%, respectively. Others include eosinophilic appendicitis (1.0%), both endometrosis and mucocoele was seen in seven patients (1.1%); Neoplastic lesions of the appendix in 3 patients (0.5%). The histology of acute appendicitis, acute appendicitis with lymphoid hyperplasia, schistosomal appendicitis and carcinoid tumor is shown in Figures 1–4. Table 3 shows the distribution of the appendectomy specimen with respect to their nature (non-neoplastic and neoplastic lesions). Acute appendicitis with peritonitis (Figure 2) occurs more in males than females with a ratio of approximately 2:1. The peak age of occurrence is 20–29 years, constituting 33.1% and closely followed by age groups 10–19 years and 30–39 years constituting 29.5% and 15.8% respectively.

The distribution of patients with histological diagnosis of acute appendicitis and acute appendicitis with peritonitis showed that acute appendicitis occurs more in females (63.8%) than males (36.2%) while acute appendicitis with peritonitis occurs more in males (65.7%) than females (34.3%). The peak age of occurrence for both is the 3rd decade of life.

**DISCUSSION**

**Epidemiologic considerations**

Acute appendicitis is a very common disease and appendix is a common specimen received in the histopathology laboratory worldwide [1, 2]. The incidence varies widely from region to region with higher incidence among the whites than blacks [1, 2]. Appendix is one of the most common specimens received in our central laboratory during the study period. This is exemplified by the fact that it constituted about 12% of the total histological specimens received in our hospital during the 5 year period. The standardized annual incidence rate of appendicitis was 3.85 per 100,000 which are similar to that reported in suburban population of Sagamu, South-west, Nigeria [16].

**Predisposing factors**

The incidence of acute appendicitis is increasing in many other African populations probably due to urbanization as reported in Abuja, Nigeria which is occupied by the affluent in the society [16]. The diet in this region is westernized and consists of low fiber [17]. It is believed that high fiber diet which increases the bowel motion reduces the incidence of acute appendicitis [17]. Therefore in Cameroon and other regions of Africa and South-East Asia where high fiber diet is the staple food, the incidence of acute appendicitis is less [18]. The male to female ratio of 1:1.5 in this study compares favorably with the studies by Ali et al [19] in Maiduguri and Blair et al [20] in Canada where the male to female ratio was 1:1.2 but contrasts other reports in which males predominate[ 7,9,16].

Maximum number of patients (33.1%) who underwent appendectomy was in the age group of 20-29 years. The peak age of occurrence in our study is the 3rd decade of life. Most reports showed peak age of occurrence in the 2nd and 3rd decades of life. Our finding compares with that of Fashina *et al* [21] in Lagos, Alatise *et al* [22] in Ile-Ife while Ohene-Yeboa *et al* [11] in Ghana and Ali *et al* [17] in Maiduguri, Nigeria reported peak age in the 4th decade of life. Some studies especially in the developed world reported peak age in the 2nd decade of life [23, 24]. Humes and Simpson [2] in a clinical review of acute appendicitis in England reported peak age incidence of occurrence as 10–20 years and male to female ratio of 1.4:1 although they acknowledged variations in incidence across geographical zones as no age is exempt from acute appendicitis. The frequency of occurrence of acute appendicitis decreases with increasing age. This is similar to this and most other reports from outside our country [9–11, 23].

**Diagnostic and therapeutic considerations**

The diagnosis of acute appendicitis is mainly through history and physical examination. The findings in this study concur well with what was obtained in other studies. The mean duration of symptoms in our study was 4.05 days which compares favorably with other reports locally and internationally [10, 11]. Twelve patients had perforation at surgery and two (2) out of these presented primarily in shock. This is probably due to late presentation at the emergency room. Fear of surgical operation and relatively high cost of treatment are the main reasons for late presentation in our environment [16]. The two (2) patients who presented in shock were adequately resuscitated and had appendectomy. The average hospital stay post operation was 5.5 days with a range of 4–14 days. This is comparable with other studies [10, 11]. No mortality was recorded in the patients studied. This study showed a wide range of histological diagnosis. The negative appendicectomy rate of 4.5% is low compared with most studies reviewed which reported a range of 8.6–35.8% [9, 10, 21, 24–27]. This low rate may not be unconnected with the growing clinical acumen of our surgeons coupled with radiological investigations. The abdominal pains in these patients were mainly due to pelvic inflammatory diseases and urinary tract infection.

Acute appendicitis constituted 86.9% in this study which is comparable with the study of Abudu *et al* [16] in Sagamu, Nigeria. Ojo *et al* [9] and Abdulkareem *et al* [10] reported slightly lower rates of 69.9% and 70.3%, respectively. Most studies from outside Nigeria reported a range of 45.7–82.5% which compared favorably with this study [11, 24]. **Immunological considerations**

Lymphoid hyperplasia constituted 4.4% which compares with the study conducted in the UK by Singhal and Jadhav in 2007 [28] and contrasts that of Abdulkareem [10]. Lymphoid hyperplasia slide is presented as figure 1. Some authors have suggested that immunological factors may play roles in the pathogenesis of appendicitis [29, [30]](http://www.ssajm.org/article.asp?issn=2384-5147;year=2014;volume=1;issue=4;spage=185;epage=190;aulast=Ahmed#ref30). Barker and colleagues have championed the belief that appendicitis is a disease that prevails in communities with good public health services and housing in place and, by implication, lower in those without these social indices [31-34]. This suggests an explanation for the observed low population incidence of appendicitis from developing countries in Asia and Africa [[3](http://www.ssajm.org/article.asp?issn=2384-5147;year=2014;volume=1;issue=4;spage=185;epage=190;aulast=Ahmed#ref16)5, [36]](http://www.ssajm.org/article.asp?issn=2384-5147;year=2014;volume=1;issue=4;spage=185;epage=190;aulast=Ahmed#ref22). Surgeons with working experience in sub-Saharan countries like Cameroon are made empirically aware of this difference in the incidence of appendicitis when they move to developed countries in Western Europe and North America. With the relative rarity in the first decade and progressive decline after the third decade, it may be inferred that the peak incidence seems to coincide with the age endowed with the most active lymphoreticular activity in the mucosa-associated lymphoid tissues, which make up most of the appendix [37, 38].

Schistosomal appendicitis constituted 1.0% of the total patients studied as seen in figure 2. The high prevalence of intestinal parasites in the developing world could also account for some cases of appendicitis, as it has been noticed to be initiated by or associated with them. The commonly associated parasites are *Schistosoma mansoni, Schistosoma haematobium, Enterobious vermicularis, Ascaris lumbricoides, Entamoeba histolytica,* and pin-worm, among others. Badmus *et al* [[39]](http://www.annalsafrmed.org/article.asp?issn=1596-3519;year=2010;volume=9;issue=4;spage=213;epage=217;aulast=Oguntola#ref25), and Adebamowo *et al* [[40]](http://www.annalsafrmed.org/article.asp?issn=1596-3519;year=2010;volume=9;issue=4;spage=213;epage=217;aulast=Oguntola#ref26), have reported some cases of schistosomal appendicitis from south western Nigeria. All these cases were associated with varying degrees of fibrosis in the submucosa. This lends credence to the fact that schistosomal appendicitis is associated with inflammation, repair, and deposition of fibro-connective tissue as well as subsequent obliteration of the appendiceal lumen which will result in the typical presentation of acute abdomen [20, 41].

**Pathological considerations**

Chronic fibrosing appendicitis was seen in 5.5% of cases in the present study. In contrast Edino *et al* [12] in their study reported 17% cases of chronic fibrosing appendicitis. Obstruction of the appendiceal lumen seems to be essential for the development of appendiceal gangrene and perforation [42]. Yet, in many cases of early appendicitis, the appendix lumen is patent despite the presence of mucosal inﬂammation and lymphoid hyperplasia [42]. The histology of acute appendicitis is as demonstrated in Figure 3. In the present study, diagnosis of mucocele was made in 6 (0.9%) of cases. Papaziogas *et al* [43] also made such an observation in their study spanning over 20 years. Diagnosis of endometriosis was made in just 1 (0.2%) cases in the present study. Gustofson *et al* [44] studied 133 female patients and found endometriosis to be present in 4 (3%) cases. Only a single case of Mucinous cystadenoma was diagnosed in the present study accounting for 0.2% of the total cases. Similarly, Marudanayagam *et al* [45] in their retrospective analysis of 2660 cases reported mucinous cystadenoma to be present in 0.6% of the cases. A diagnosis of carcinoid tumor was made in 1 (0.2%) cases as seen in figure 4. Similarly Hof *et al* [46] found carcinoid in only 7(0.47%) cases. Giant cell lymphoma of the appendix was the only malignant lesion encountered in the present study seen in a single case of 55 years old male thus confirming the view that appendix is mostly involved by benign conditions. No single case of cystadenocarcinoma was seen in our study. This is in sharp contrast to the series by Jones and Paterson [47] who reported that primary malignant tumors of the appendix i.e. cystadenocarcinoma were found in only 0.1% of all appendectomies.

**CONCLUSION**

The incidence of acute appendicitis remains low especially in the rural communities of Africa like our study has shown. Acute appendicitis is one of the most common surgical emergencies in our environment therefore prompt and adequate intervention will go a long way in reducing its morbidity and mortality. Finally, the current study spanned the entire gamut of pathological processes that involve the appendix and provides a fair idea about the clinicopathological correlation in appendectomy specimens.

**LIMITATIONS OF THE STUDY**

1. Retrospective nature of the study could be marred by poor record keeping as noted in the incomplete data in less than 10% of the total patients managed.
2. Lack of Electronic Medical Record System in one of the hospital data studied in the past years until January 2018 with resultant loss of data.
3. Delay in patients’ presentation, and compounded by the on-going anglophone- crisis
4. Poverty, ignorance, false beliefs and insufficient health infrastructure, in the sub-region of Cameroon are amongst the lists of possible limitations of this study.

**RECOMMENDATIONS**

1. Full implementation of Electronic Medical Record System in all our local hospitals in the sub-regions for a comprehensive data base will support improved future research on the disease.
2. There is an urgent public health concerted effort aimed at improving health care seeking habit of the population.
3. Educating the populace on early and prompt diagnosis, adequate resuscitation as well as early surgery in patients with acute appendicitis to keep the morbidity and mortality low.
4. Patients who are misguided by false beliefs can be better educated by public enlightenment.
5. Effective government legislation on indiscriminate consumptions of herbal remedies, as substitutes for orthodox medicine.
6. It is imperative for prompt and early resolution of ongoing Anglophone crisis and in resource constrained setting as ours, an improvement of existing health infrastructure.
7. There is also a strong need for collaboration and integration of the Traditional medicine and Biomedical practices as advocated by the WHO; so as to harness the gains by all and sundry.
8. Functional health insurance for all citizens is mandatory.

**DECLARATIONS**

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**AVAILABILITY OF DATA AND MATERIALS:** The datasets generated and/or analyzed during the current study are available from corresponding author.

**DISCLOSURES:** This Clinical Research is an Extract from the Author’s Doctorate Dissertation.

**AUTHORS’ CONTRIBUTIONS:** The Author conceived of the study and participated in its design and coordination as well as helped to draft the manuscript; the author also read and approved the final manuscript.

**ETHICS APPROVAL AND CONSENT TO PARTICIPATE:** Ethical approval was obtained from the Institutional Ethical Committee. Confidentiality was ensured by not writing the names of patients on proforma in accordance with the Helsinki declaration of 1964. A copy of the written Approval is available for review by the Editor-in-Chief of this journal.

**INFORMED CONSENT:** Informed consent was not sought for this article because this study is a retrospective study; therefore there was no direct human participant.

**COMPETING INTERESTS:** The Author declares that there is no conflict of interest.

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**FIGURE 1: APPENDIX SHOWING LYMPHOID NODULES**



**FIGURE 2: SCHISTOSOMAL APPENDICITIS**



**FIGURE 3: ACUTE APPENDICITIS**



**FIGURE 4: CARCINOID APPENDIX**



**TABLE 1: DISTRIBUTION OF CASES ACCORDING TO AGE GROUPS & SEX**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **AGE GROUP (YEARS)** | **MALE** | **FEMALE** | **SUBTOTAL** | **PERCENTAGE****%** |
| **0-9** | 13 | 10 | 23 | 3.4 |
| **10-19** | 72 | 130 | 202 | 29.5 |
| **20-29** | 78 | 148 | 226 | 33.1 |
| **30-39** | 51 | 57 | 108 | 15.8 |
| **40-49** | 29 | 42 | 71 | 10.4 |
| **50-59** | 24 | 17 | 41 | 6.0 |
| **>60**  | 6 | 6 | 12 | 1.8 |
| **TOTAL** | **273** | **410** | **683** | **100** |

**TABLE 2: DISTRIBUTION OF CASES ACCORDING TO HISTOLOGICAL**

**DIAGNOSIS**

|  |  |  |
| --- | --- | --- |
| **HISTOLOGICAL DIAGNOSIS** | **NO OF CASES****(N=683)** | **PERCENTAGE****%** |
| **Acute appendicitis** | 410 | 60 |
| **Lymphoid hyperplasia** | 30 | 4.4 |
| **Eosinophilic appendicitis** | 7 | 1.0 |
| **Subacute appendicitis**  | 13 | 1.9 |
| **Normal**  | 31 | 4.5 |
| **Appendicitis with peritonitis**  | 137 | 20.1 |
| **Submucosal fibrosis**  | 38 | 5.6 |
| **Endometrosis**  | 1 | 0.15 |
| **Mucocele**  | 6 | 0.9 |
| **Schistosomiasis**  | 7 | 1.0 |
| **Carcinoid tumor**  | 1 | 0.15 |
| **Mucinous cystadenoma** | 1 | 0.15 |
| **Giant cell lymphoma** | 1 | 0.15 |
| **Total**  | **683** | **100** |

**TABLE 3: DISTRIBUTION OF THE APPENDECTOMY SPECIMENS AS PER THEIR NATURE**

|  |  |  |
| --- | --- | --- |
| **SPECIMEN**  | **NO OF CASES****(N= 683)** | **% PERCENTAGE** |
| **NON-NEOPLASTIC** | **680** | **99.5** |
| **NEOPLASTIC** | **3** | **0.5** |