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Research Article

Maximum Outer Diameter of Appendiceal Lesions: An Histopathological Approach

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Abstract

The average maximal outer diameter (MOD) of the appendix in adults is 0.6 cm and in children, it is between 0.21-0.64 cm. Most of the assessment of MOD of the appendix has been from radiological diagnosis. We aim to determine the correlation between the MOD and lesions that occurred in the appendix from 2012 to 2022 in Bowen University Teaching Hospital, Anatomic pathology laboratory. The study was a retrospective one in which 315 participants with cases of appendiceal lesions were analysed in the lab. All reports containing complete biodata of patients, histopathological diagnosis including acute appendicitis, acute appendicitis with peritonitis, ruptured acute appendicitis and neoplasms from right hemi-colectomy specimen were included. Chronic granulomatous inflammation, haemorrhagic necrosis of the appendix in association with right hemicolectomy specimens were also included. All reports with incomplete biodata, histopathology lab number, samples whose dimensions were omitted, samples with irregularity in the lab number and date of submission of samples, or of reporting the results; unsigned reports and results not extracted from the archives were excluded. Also, appendixes with normal diagnosis, and follicular hyperplasia were excluded. Also excluded were reports whose sample blocks (formalin fixed paraffin embedded), and haematoxylin & eosin slides were not found. Convenience sampling was used and the lesions were categorized into 3 main groups based on their dimensions, group 1 (0.4-0.5cm), group 2 (1-1.5cm) and group 3 (2cm and above). Based on histopathology diagnosis, the samples were classified as acute appendicitis, acute appendicitis with peritonitis, and neoplasms and others. Appendiceal samples constitute about 56% of the GIT samples received. Only 3 neoplastic lesions were recorded. This constitute 0.01% of the lesions seen. The age group 20-29 had the highest number of participants (90) and the least participants were in the age range of 70 years and above. The median age of the group was 41.1 and the median age of the participants was 26.5 years. The category 1-1.5cm had the highest number of participants and this was not significant when compared to the other groups, p= 0.06824. There is also no significant association between age group and dimensions using loglinear test, AIC criterion and Poisson regression test. There is a slight occurrence of all the dimensions of the lesions in the male participants with a p value-0.0108. There is no significant difference between the appendiceal lesions in males and females. MOD of the appendix is an important feature of the appendix and the dimensions cuts across several age group and sex.

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1. Introduction

The vermiform appendix is a small worm-like organ, extending from the base of the caecum; it is tubular in nature with a blind end, and it is located in the right iliac fossa [1]. The average length of the normal appendix is 8-10cm with a range of 2-20cm [2]. The average maximal outer diameter (MOD) of the appendix to be considered as normal in adults is 0.6 cm [3]. In children, MOD to be considered as normal is between 0.21-0.64 cm [4].

Acute appendicitis (AA), which is a disease of the appendix, is the most common cause of abdominal pain that requires surgery [5]. There are other appendiceal lesions like torsion of the appendix, mucinous adenocarcinoma of the appendix, adenocarcinoma of the appendix, low grade appendiceal mucinous neoplasm of the appendix (LAMN), and carcinoid tumour of the appendix [6–10]. They all present with signs similar to acute appendicitis. These signs include vague mid-abdominal pain, anorexia, nausea, right lower quadrant abdominal pain, guarding and leukocytosis from full blood count (FBC) [5]. However, some of these neoplasms are known to present with larger MOD's [7–9]. Although in one study, a non- neoplastic lesion was reported with a larger maximal outer diameter of 2.6cm [6]. It is a known fact that non-neoplastic lesions are smaller and more often likely to present with features of acute appendicitis than neoplasms [11]. Radiological investigations like ultrasound and computerized Tomography (CT) have helped in playing a key role in providing a conclusive diagnosis of AA before surgery, which has led to a reduction of the number of cases of AA in the theatre [10]. In one study, the MOD of the appendix in acute appendicitis, when examined at the cut-up table of the surgical pathology laboratory correlated well with the diagnosis on CT with the appendix specimen [12].

Most of the assessment of MOD of the appendix in literature has been from radiological diagnosis. There is a paucity of data on the histopathological assessment of MOD of the appendix. This is so despite the fact that the "gross" appendectomy specimen usually ends up with the pathologists even in resource rich centers. In addition, other histopathologically examined appendiceal lesions asides AA, often presents with various gross dimensions as mentioned above and cuts across different age groups. We therefore, sought to determine the correlation between the MOD and the various types of lesions that occurred in the appendix, from 2012 to 2022 in Bowen University Teaching Hospital, Anatomic pathology laboratory.

2. Materials And Method

Study Location: The study was conducted at Bowen University Teaching Hospital, Ogbomoso, South-West Nigeria, a missionary Hospital, which serves as a referral centre for primary, and secondary government owned healthcare facilities and private hospitals around the region.

Study Design: The study was a descriptive cross-sectional retrospective one in which 324 cases of appendiceal lesions reported in the lab was extracted from the register and pass-worded computer in the Anatomic pathology laboratory, from 2012 to 2022 (ten years) and subjected to statistical analysis. This number is close to the calculated sample size (356) and fit for statistical analysis. Nine participants had incomplete data and did not meet the inclusion criteria. Thus, they were removed from the set. A total of 315 participants were then subjected to statistical analysis.

Sample size calculation: Formula for sample size (finite population) is

$$n = \frac{n_o}{1 + n_o - \frac{1}{N}} \tag{1}$$

n= adjusted sample size
n_o= initial sample size (for finite population)
N= population less than 10000 in this case 5000

$$n_o = \frac{z^2 \times p \times (1-p)}{E^2} \tag{2}$$

Z=z-score based on confidence level
p= estimated proportion of population taken as 0.5
E= margin of error taken as 0.05
N= population size
Therefore,

$n_o = \frac{1.96^2 \times 0.5 \times (1-0.5)}{0.05^2}$
n_o=384.16
n=$\frac{384.16}{1.0766}$ = 356

Inclusion criteria: All reports containing complete biodata of patients, the various histopathological diagnosis recorded including acute appendicitis, acute appendicitis with peritonitis and neoplasms (low-grade appendiceal mucinous neoplasm (LAMN), invasive adenocarcinoma, and mucinous adenocarcinoma) from right hemi-colectomy specimen. Ruptured appendix was categorized as acute appendicitis with peritonitis because that was the histopathologic diagnosis. Lesions like chronic granulomatous inflammation, haemorrhagic necrosis of the appendix in association with right hemicolectomy specimens were also included.

Exclusion criteria: All reports with incomplete biodata such as age, sex, histopathology lab number, and name of the patient. Appendiceal samples whose dimension was omitted by the attending pathologist or the assistant. Samples with irregularity in the lab number and date of submission of samples, or of reporting the results; unsigned reports and results not extracted from the archives were excluded. In addition,

appendixes with normal diagnosis or just follicular hyperplasia were excluded. Also excluded were reports whose sample blocks (formalin fixed paraffin embedded (FFPE)), and haematoxylin & eosin slides were not found.

Sampling Technique: Convenience sampling method was used. All available cases were targeted and a population of participants (324), which was close to the calculated sample size (356) within the specified time frame (2012-2022) were selected. About 315 cases were eventually analysed after screening for exclusion criteria. The data was extracted from histopathology reports taken from the routine register and or digital archives of the anatomic pathology laboratory. The data retrieved include, sociodemographic data, the gross dimensions of the appendiceal samples submitted by the surgeons for histopathological examination. The appendiceal lesions were categorized into 3 main groups based on their dimensions, group 1 (0.4-0.5cm), group 2 (1-1.5cm) and group 3 (2cm and above). Based on histopathology diagnosis, the samples were also classified as acute appendicitis, acute appendicitis with peritonitis and, neoplasms and others.

Data collection: Data was collected by well trained staff of the medical records department from passworded computers at the anatomic pathology laboratory. The selected slides which are haematoxylin and eosin stained (H&E), of the participants were retrieved and reviewed by the attending pathologists. Slides that were damaged or unavailable were re-cut from the formalin fixed paraffin embedded blocks in the archives of the lab.

Study variable: The MOD of the various selected appendiceal lesions, the age, sex and histopathological diagnosis.

Data Analysis: The data obtained was analysed using the statistical packages for social sciences (SPSS) 25.0 and R-programming version 4.4.1. Proportions and frequencies, as categorical variables were compared using Chi-square or Fisher's Exact test, Loglinear model and Poisson Regression model. The p-value was taken as $p < 0.05$, which is considered as statistically significant, in the multivariate model.

Null Hypothesis: Is that there is no correlation between the dimensions of appendiceal lesions and MOD.

Alternate Hypothesis: Is that there is a correlation between the appendiceal lesions and MOD

Ethical approval was received from the Bowen University Teaching Hospital Ethical Committee before the commencement of the research with the following reference number; Registration number NHREC/12/04/2012, and approval number BUTH/REC-26811. This study was conducted in compliance with the Helsinki Declaration on biomedical research on human subjects. All the data obtained were stored in a password-protected computer thereby maintaining participants' confidentiality.

3. Results

About 577 gastrointestinal (GIT) surgical samples were received in the anatomic pathology lab in the study period of ten years. Appendiceal samples constitute about 56 % of the GIT samples received. Only 3 neoplastic lesions were recorded. This constitute 0.01% of the lesions seen, while, non-neoplastic lesions made up 99.1% of the remaining lesions.

The age group 20-29 had the highest number of participants (90) and the least participants were in the age range of 70 years and above Table 1. Also, the median age of the group was 41.1 Table 1 and the median age of the participants was 26.5 years. The age group 10-19 and 20-29 had the highest number of patients,176 Table 1. The category 1-1.5cm had the highest number of participants and this was not significant when compared to the other groups, p= 0.06824. In addition, there were 51 participants with MOD of 1-1.5cm in the age group 10-19 Table 2 There is also no significant association between age group and dimensions using loglinear test, AIC criterion and Poisson regression test Table 3. There was no significant difference between the participants with acute appendicitis and those with acute appendicitis with peritonitis, p-value = 0.6537 Table 4. All kinds of appendiceal lesions can occur in any age group but their incidences are fewer in the extremes of age groups Table 4. In-addition, acute appendicitis and acute appendicitis with peritonitis are the commonest disease in the appendix. There is a slight occurrence of all the dimensions of the lesions in the male participants with a p value-0.0108 using chi square test Table 5. There were slightly more males than females presenting with various kinds of appendiceal lesions Table 6. Neoplasms were barely seen in the early extreme of life, when compared with the older extreme of life Figure 1. These neoplasms were only three (mucinous adenocarcinoma, invasive adenocarcinoma and low grade mucinous neoplasm), and had a MOD greater than 2 cm. There is no significant difference between the appendiceal lesions in males and females Figure 2. There were slightly more females presenting with the dimensions of 0.4-0.5cm Figure 3.

Table 1: Frequency distribution table

Age group	Frequency	Percentage
0-9	13	4.1
10-19	86	27.3
20-29	90	28.6
30-39	53	16.8
40-49	47	14.9
50-59	15	4.8
60-69	5	1.6
70-79	3	1
80-89	3	1
Total	315	100

Table 2: Frequency table for MOD by age

Age	Dimension	Count
3-9	0.4-0.5cm	4
10-19	0.4-0.5cm	37
20-29	0.4-0.5cm	26
30-39	0.4-0.5cm	13
40-49	0.4-0.5cm	9
50+	0.4-0.5cm	3
3-9	1-1.5cm	8
10-19	1-1.5cm	51
20-29	1-1.5cm	45
30-39	1-1.5cm	29
40-49	1-1.5cm	28
50+	1-1.5cm	14
3-9	2cm & above	2
10-19	2cm & above	14
20-29	2cm & above	9
30-39	2cm & above	11
40-49	2cm & above	10
50+	2cm & above	10

Using Poisson' s regression model, estimate = 1.3832 & $p < 0.001$ for age range 3-9 cm
Using Poisson' s regression model, estimate =1.9859 & $P < 0.001$ for age range 10-19

Table 3: Age Category by MOD

Age Group	0.4–0.5 cm	1–1.5 cm	2 cm & above
3–9	4	8	2
10–19	29	55	18
20–29	23	43	14
30–39	15	29	9
40–49	13	26	8
50+	8	15	5

Pearson's Chi-squared test
X-squared = 17.288, df = 10, p-value = 0.06824

Table 4: Frequency table for Diagnosis by age

Age	diagnosis	count
3-9	Acute appendicitis	8
10-19	Acute appendicitis	56
20-29	Acute appendicitis	44
30-39	Acute appendicitis	25
40-49	Acute appendicitis	21
50+	Acute appendicitis	9
3-9	Appendicitis + peritonitis	5
10-19	Appendicitis + peritonitis	39
20-29	Appendicitis + peritonitis	27
30-39	Appendicitis + peritonitis	24
40-49	Appendicitis + peritonitis	22
50+	Appendicitis + peritonitis	14
3-9	Neoplasms & others	1
10-19	Neoplasms & others	7
20-29	Neoplasms & others	9
30-39	Neoplasms & others	4
40-49	Neoplasms & others	4
50+	Neoplasms & others	4

Table 5: Sex vs Dimension

Sex	0.4–0.5 cm	1–1.5 cm	2 cm & above
Female	42.15480	80.18576	25.65944
Male	49.84520	94.81424	30.34056

Pearson's Chi-squared test Check if there's a significant association between Sex and Appendix Dimension.
X-squared = 9.0546, df = 2, p-value = 0.01081

Table 6: Sex and Diagnosis

Sex	Acute Appendicitis	Appendicitis with Peritonitis	Neoplasms & Others
Female	74.68731	60.02477	13.28793
Male	88.31269	70.97523	15.71207

Pearson's Chi-squared test
X-squared = 7.6111, df = 2, p-value = 0.02225

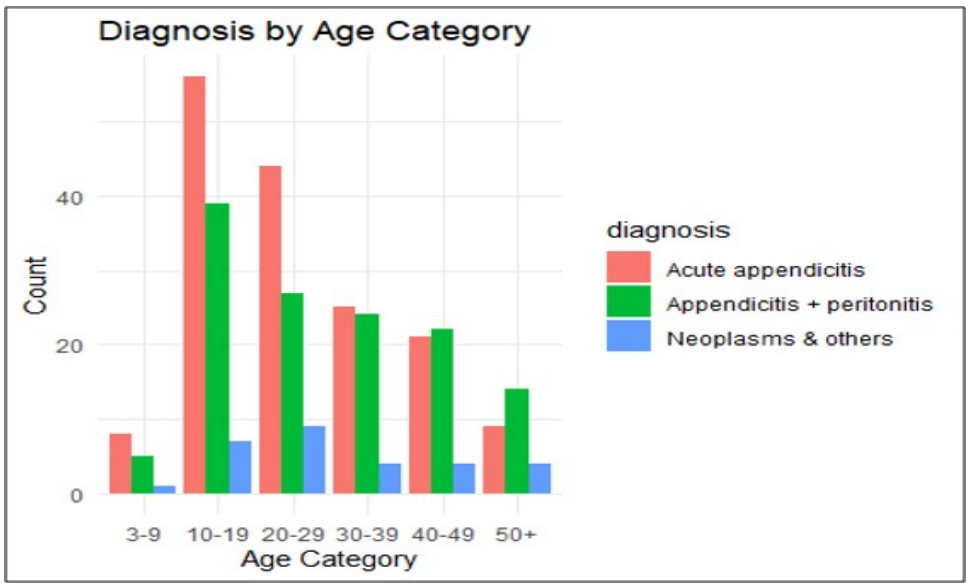

Figure 1: Multiple Bar Plot showing Diagnosis vs Age category

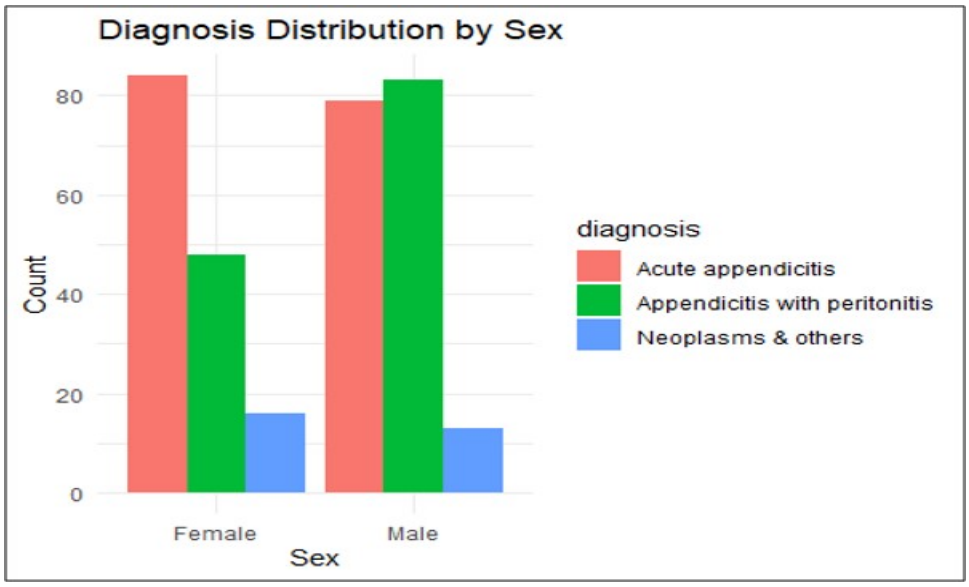

Figure 2: Multiple Bar Plot Visualizes Appendix diagnosis vs sex

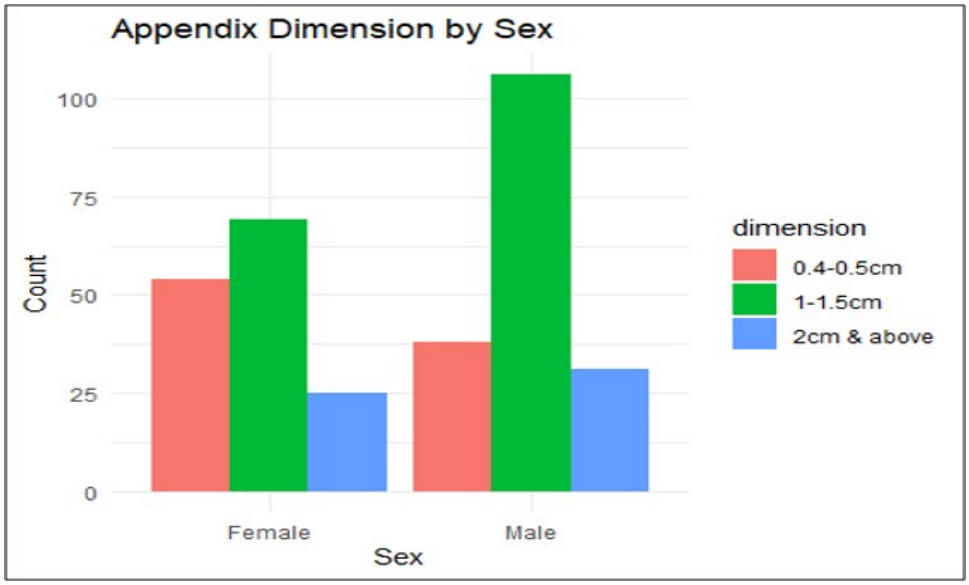

Figure 3: Multiple Bar Plot showing the distribution of dimensions by sex

4. Discussion

Appendicectomy is a common surgical procedure and histopathological examination is the gold standard for diagnosis of lesions of the appendix; it not only confirms the diagnosis but also reveals the pathologies which have significant impact on further patient management [13]. This observation, mirror's our findings in this study, as appendectomy specimen constituted 56% of the total GIT specimen received within the study period. The median age of the participants was 26.5 and the median group age was 41.5. which is similar to the median age of 26.08 reported [10]. This study is also in agreement with the observation of [14], that appendiceal lesions are commoner in the young [14]. It also mirror's the finding of [15] in which the median age of the participants in their study was 30. 6 ± 2.17.

As pathologists, part of the process towards making a diagnosis in histopathology is the gross examination of the specimens submitted by the surgeons. These gross dimensions are very important in histopathological examinations. Pathologists routinely take the dimensions of the tissue at the surgical cut-up table during the gross examination of received samples, and for tubular structures like the appendix, fallopian tube and intestines, only two dimensions are recorded. The length and the breadth of the specimen [15]. The breath corresponds to the MOD, which is what was assessed in this study [15], also reported that the MOD of the appendix in cases with confirmed inflammation was 4.22 ± 2.1mm, while cases without inflammation was 3.37 ± 1.4 mm at a significant level of $p =< 0.01$. They also found out that the cut-off value for appendiceal diameter was 6.5 mm with very high-class prediction, and peri-appendiceal inflammation. While, other workers like [16] got a range of 3.4 mm to 14mm on CT studies. Got a MOD of 0.5 -1.2 cm diameter in their study [17]. This is similar to our study, in which most of the cases of acute appendicitis and acute appendicitis with peritonitis had a MOD between the range of 0.4 to 0.5 cm and 1 to 1.5 cm among the participants in the age range between 10 and 29 years. However, the difference in the number of participants within the dimensions of 0.4 to 0.5cm and the participants with MOD of 1 to 1.5 cm is not significant at p = 0.068; and this mirror's the findings of [18] also found out that appendiceal MOD is higher in acute appendicitis than in normal appendix [18]. At ultrasonography, a MOD of 6 to 10 mm is a clear pointer to a diagnosis of acute appendicitis [17]. As regards to AA in this study, the participants within the age range of 10-19 years had the greatest number of cases across all the dimension groups with $p < 0.001$ using the Poisson's regression model. This is also the same for the age group of 3-9 with $p < 0.001$. Further buttressing the fact that AA is a disease found in the young.

The MOD in the case of the appendix, is a pointer to the nature of the disease at the surgical cut-up table and inflammation has been known to pose a direct effect on the length and MOD of the appendix [15]. These dimensions are sometimes helpful to the pathologists in determining the nature of the disease. Therefore, in order to make the job of the statistical analysis easy, we divided the total number of cases seen into 3 major groups, based on the histopathological diagnosis and MOD. The groups based on diagnosis are acute appendicitis, acute appendicitis with peritonitis, and neoplasms and others. The groups based on MOD are 0.4-0.5cm, 1 to 1.5 cm and greater than or equals to 2cm. Only three participants with neoplasms were recorded and these cases have been reported in literature. They include mucinous adenocarcinoma, invasive adenocarcinoma and low-grade appendiceal mucinous neoplasm (LAMN) [7–9]. Their MOD's are 4cm, 6cm and 2cm, respectively. Other lesions seen includes, chronic granulomatous appendicitis due to tuberculosis, schistosomiasis, trichuriasis; chronic appendicitis with fibrosis, congestion, and haemorrhagic necrosis. All with MOD of $\geq$ 2cm. The presence of fibrosis with attachment to the mesentery and adjacent structures was responsible for the MOD that was observed in these lesions. Although, Hashimi and Barthel have reported a case of torsion of the appendix in a 16-year-old boy with the gross findings showing a MOD of 2.6cm [6]. This supports our reason for grouping other lesions alongside with neoplasms as there would have been several other classes and statistical analysis would have been awkward.

Acute appendicitis is the commonest lesion in the appendix; eventhough, histopathological examination also reveals that there are other similar lesions like acute suppurative appendicitis, acute appendicitis with peritonitis, ulcero-phlegmonous appendicitis, transmural inflammation of the appendix with or without presence of fecolith and gangrenous perforated acute appendicitis [18]. Hence, we grouped ruptured acute appendicitis along with acute appendicitis with peritonitis. Acute appendicitis with peritonitis and ruptured acute appendicitis have similar features on microscopy except for the area of perforation on the wall of the appendix. Even though, we know clinically that the management of ruptured acute appendicitis takes a different course. In this study, both cases of acute appendicitis and acute appendicitis with peritonitis were seen more in the younger participants between the ages of 10 and 29 years old. However, it has been reported that both

diseases can occur in all age group [14].

In developed countries, most appendectomy specimen are submitted for histopathological examination [18]. This is unlike in our resource challenged setting, where physicians are often persuaded and encouraged to send samples of their clients for histopathological examination [8].

In this study, there is a slightly more male preponderance of the participants over the female participants, when the sex was compared to the dimensions at a statistical level of p =0.010; and in terms of the disease categories versus sex, there are more male participants with a slight significance of p= 0.022. This mirror's the findings of [19–21]. In a study by [17] the MOD of the appendix in males was between 5-10mm with average of 7.45mm. While in females, the MOD was between 5-12mm with an average of 6.87mm.

Primary neoplasms of the appendix constitute less than 2% of lesions seen in the appendix [22]. This is similar to our findings in this study, in which neoplasms were just 0.01% of the lesions seen. In addition, non-neoplastic lesions were 99.1% of the lesions seen and it is in congruence with the study of [19], in which non-neoplastic lesions constituted 99.34% of the appendiceal lesions reported [19].

The range of dilatation of LAMN in a study was 2.4cm [23] but mucocele of the appendix rarely have diameter greater than 2cm as reported by [24–26]. This observation is similar to ours whereby the only case of LAMN was 2 cm in diameter. The other neoplasms mucinous adenocarcinoma of the appendix(4cm) and invasive adenocarcinoma of the appendix (6cm), both had their MOD greater than 2cm. This can be attributed to the invasion of the wall of the appendix and surrounding structures, which was reported at the surgical cut-up table. The 3 neoplasms occurred in the 5th and 6th decade; invasive adenocarcinoma and LAMN occurred in males and mucinous adenocarcinoma occurred in a female. Although, mucinous neoplasms occur four times more in females than males [27]. The sample size of the neoplasms in this study and other lesions is not adequate enough for proper correlation with previous research that has been done. In addition, some of the mucocele have been reported to coexist with acute appendicitis and other lesions [13].

Limitations:

1. Lack of adequate data or research material on the MOD carried out by Anatomic pathologists.
2. Presence of several lesions in the appendix that makes grouping as an entity difficult for statistical analysis.
3. Most studies conducted are radiological research.
4. Most of the diseases or lesions cut across the various age groups and dimensions.

Recommendation: We recommend that

1. All appendectomy specimen be submitted for histopathological examination.
2. Pathologists should take proper dimensions, especially the MOD and do proper dissections in line with laid down techniques for grossly suspected lesions.
3. Other pathologists should conduct more research on the MOD of the appendix. This will enable pathologists have their own compendium on MOD of lesions in the appendix.

5. Conclusion

MOD of the appendix is an important feature of the appendix and the dimensions cuts across several age group and sex. It aids the pathologists in the histopathological examination and diagnosis of samples received in the laboratory. Therefore, a proper record of the MOD is important at the surgical cut-up lab.

Article Information

Disclaimer (Artificial Intelligence): The author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.), and text-to-image generators have been used during writing or editing of manuscripts.

Competing Interests: Authors have declared that no competing interests exist.

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