Prevalence Trends and Associated Modifiable Risk Factors of Peptic Ulcer Disease among Students in a University Community South-South Nigeria

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ABSTRACT

Introduction: Peptic ulcer disease (PUD) is one of the commonest ailments of the alimentary system. It affects about 4 million of the world’s population annually, with incidence of complications in approximately 10–20%. PUD impacts negatively on the health-related quality of life of affected individuals while employers and healthcare systems are burdened with high economic cost of dealing with the disease. Established risk factors of PUD such as stress, smoking, and use of alcohol, coffee, and NSAIDs are commonly associated with university students and could impact on the disease prevalence. Therefore, determining the prevalence trends of established PUD and associated risk factors in risk populations is essential for clinical and epidemiological decision making.

Objective: To investigate the prevalence trend and associated modifiable risk factors of PUD among students in Niger Delta University (NDU), Amassoma Bayelsa State, Nigeria.

Methods: A hospital based retrospective survey design was employed. The medical records of students who accessed the NDU Medical Centre from January, 2014 to December, 2019 were assessed. Relevant data extracted from students’ case files were analysed with the aid of the Statistical Package for Social sciences (SPSS) version 23 and described statistically in terms of frequencies and percentages.

Results: A total of 988 students were diagnosed of PUD from January, 2014 to December, 2019. More Christians (74.7%) and first year students (30.4%) had PUD. More females (55.6%) than males (44.4%) were diagnosed of PUD. Females had PUD than males in 2014 (64.1%), 2015 (61.5%), 2016 (56.2%) and 2018 (54.0%); while males had PUD than females in 2017 (52.0%) and 2019 (51.4%). Prevalence was highest among students within 17-21 years in 2014 (33.5%), 2015 (43.2%), and 2017 (32.4%) while in 2016, 2018 and 2019, prevalence was highest among 22-26 (33.3%), 27-31 (30.3%) and 34.3%) respectively. Starvation, stress, NSAID use, alcohol consumption and cigarette smoking were the major modifiable risk factors of PUD documented. Starvation and stress were most common (100%) among students.

Conclusion: PUD prevalence is low but risk factor association is enormous. Education aimed at reducing risk factor association may help change future prevalence trend in the positive direction.

Keywords: Prevalence trends, Peptic Ulcer Disease, Risk Factors, Niger Delta University
1. INTRODUCTION

Peptic ulcer disease (PUD) is one of the commonest ailments of the alimentary system. [1] It affects about 4 million of the world’s population annually, with incidence of complications in approximately 10–20% [2–5] PUD is clinically described as a disruption of the continuity of the gastrointestinal mucosal lining which appear as sores of at least 0.5 cm in diameter in endoscopic studies. [5] It is largely classified as gastric ulcers (GU) or duodenal ulcers (DU) based on the affected section of the gastrointestinal tract (GIT). [6] The chief symptom is epigastric pain which may subside when food or alkali is consumed. [5]

PUD is predominantly caused by the activities of Helicobacter Pylori (H. Pylori) and/or Non-Steroidal Anti-inflammatory Drugs (NSAIDs). While the activities of H. Pylori creates imbalance in acid production and regulation through inflammation-induced increased gastrin secretion and decreased somatostatin secretion, NSAIDs tend to influence the Cyclo-Oxygenase (COX) pathways, resulting in the production of prostanoids (prostaglandins, prostacycline, and thromboxane) which alters the mucosal protection mechanism and subsequent damage of the mucosal surface of the affected region. [5,7,8]

Apart from the activities of H. pylori and NSAIDs, studies have identified risk factors of PUD which are mostly modifiable. The modifiable risk factors include the use of corticosteroids, anticoagulants, coffee, alcohol, smoking, stress, spicy foods, use of unclean water sources and fasting; while non-modifiable risk factors include genetics, age, gender and past history of PUD. [6,9–13]

Although, more than three decades ago, Nigeria was considered one of the countries with high PUD prevalence, [14] a more recent information about the prevalence of PUD in Nigeria is dearth. However, with the epidemiology of H. pylori infection, the prevalence of PUD can be estimated, [15] since almost 100% of duodenal ulcer patients and 82% of gastric ulcer patients in Nigeria are H. pylori positive. [16] Generally, studies in Nigeria show that H. Pylori infection is high. In Kano, Northern Nigeria, Bashir and Ali [17] reported H. pylori prevalence of 81%. Malu, Ani and Bello also reported a prevalence of 87% in Jos, [18] while Aboderin, Abdu, Odetoyn, and Okeke, reported 73% in South-West, Nigeria. [19] These information on H. pylori infection suggest that a similar trend could exist for PUD. Nevertheless, for the purpose of clinical and epidemiological decision making, it is essential to directly determine the prevalence of established PUD among risk populations.

Although, Eniojukan and colleagues, [6] reported 40% and 60% prevalence rates of GU and DU respectively, in a university community in Delta State Nigeria, to the best of our knowledge, no study has considered prevalence trends and associated modifiable risk factors of PUD in a student population alone. Risk factors of PUD such as stress, fasting, smoking, use of alcohol, coffee, and NSAIDs are commonly associated with students and therefore, could impact on the prevalence of PUD. More so, significant number of host communities of higher institutions in Nigeria where most students live, do not have clean source of water and because unclean source of water is a risk factor of PUD, [11] prevalence rate may rise.

PUD impacts negatively on the health-related quality of life of affected individuals. Employers and healthcare systems are also burdened with high economic cost of dealing with the disease. [20] Thus, investigating the prevalence trends and modifiable risk factors of PUD is expedient, especially in a student population; as such information could provide a guide for decision making and development of prevention strategies.

2. MATERIALS AND METHODS

2.1. Study Design, Setting and Population

A hospital-based retrospective survey design was employed to assess the medical records of students who accessed...
the Niger Delta University (NDU) Medical Centre Amassoma, from January, 2014 to December, 2019; in order to determine the prevalence trends and associated modifiable risk factors of PUD. NDU is located in Wilberforce Island Amassoma, Southern Ijaw Local Government Area of Bayelsa State, Nigeria. It was established in 2000 by the laws of the State House of Assembly. The NDU which comprised of three campuses: Glory Land (main campus) and College of Health Sciences (CHS) in Amassoma and the temporary campus of Faculty of Law in the capital city of Yenagoa, has over 16000 students. The NDU medical centre is located in the Glory Land campus. It has a 4-bedded male and female wards, a 4-bedded emergency room, a medical laboratory, ophthalmology unit, pharmacy unit, X-ray unit and a theatre.

2.2. Data Collection/Analysis

Medical case files of students who accessed the NDU Medical Centre Amassoma, from January, 2014 to December, 2019 were assessed to determine the prevalence trends and associated modifiable risk factors of PUD. Data extraction which lasted for a period of 7 weeks, was done only from the case files certified by the Health Records Department. Case files with incomplete information were excluded. The data obtained were analysed with the Statistical Package for Social sciences (SPSS) version 23 and described in terms of frequencies and percentages.

2.3. Ethical Approval

Ethical clearance was obtained from the Research and ethical committee of NDU while administrative permit was obtained from the Chief Medical Director (CMD) of the NDU Medical Centre.

3.0. RESULTS

Students’ medical records were accessed and analysed based on sex, age, religion and year of study from 2014 to 2019. A total of 988 students were diagnosed of PUD within the 6-year period under review. Assessment showed that the highest number of PUD diagnosis (198) was made in 2018. More females than males had PUD in 2014 (64.1%), 2015 (61.5%), 2016 (56.2%) and 2018 (54.0%), while more males had PUD in 2017 (52.0%) and 2019 (51.4%). Prevalence was highest among students within 17-21 years in 2014 (33.5%), 2015 (43.2%), and 2017 (32.4%). In 2016, PUD prevalence was highest among students aged 22-26 (33.3%) while in 2018 (30.3%) and 2019 (34.3%), prevalence was highest among students aged 27-31. The students with PUD comprised of Christians, Muslims and Eckists. Prevalence was highest among Christians than Muslims and Eckists in 2014 (70.0%), 2015 (83.3%), 2016 (87.6%), 2017 (67.6%), 2018 (69.2%) and 2019 (74.3%). Analysis based on year of study showed that PUD was most prevalent among first-year students (30.4%), followed by second (19.2%) and third-year (20.4%) students. In terms of associated modifiable risk factors of PUD, the 6-year review revealed that all the students (100%) with PUD, from 2014 - 2019, were associated with starvation. Other modifiable risk factors based on highest annual prevalence were stress (100%), use of NSAIDs (92.4%), alcohol consumption (74.3%), smoking (51.4%) and depression (15.7%). From 2014 to 2019, females were more associated with stress and depression than males, while males were more associated with NSAIDs, smoking and alcohol than females. Female association with stress (68.8%) and depression (80.0%) was highest in 2014, while male association with NSAIDs, smoking and alcohol were highest in 2015 (66.0%), 2014 (91.9%) and 2017 (81.3%) respectively.
Table 1: prevalence Trend of PUD based on Sex, Age, Religion and Year of Study  
(N = 988)

<table>
<thead>
<tr>
<th>Variables</th>
<th>2014 (n= 170)</th>
<th>2015 (n= 192)</th>
<th>2016 (n= 105)</th>
<th>2017 (n= 148)</th>
<th>2018 (n= 198)</th>
<th>2019 (n=175)</th>
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<td>freq/%</td>
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<td></td>
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<tr>
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<td>77 (52.0)</td>
<td>91(46.0)</td>
<td>90 (51.4)</td>
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<td>109(64.10)</td>
<td>118 (61.5)</td>
<td>59 (56.2)</td>
<td>71 (48.0)</td>
<td>107(54.0)</td>
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<tr>
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<td>17-21</td>
<td>57 (33.5)</td>
<td>83 (43.2)</td>
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<td>22-26</td>
<td>40 (23.5)</td>
<td>48 (25.0)</td>
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<td>29 (19.6)</td>
<td>56 (28.3)</td>
<td>38 (21.7)</td>
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<td>27-31</td>
<td>45 (26.5)</td>
<td>41 (21.4)</td>
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<td>20 (10.4)</td>
<td>22 (21.0)</td>
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<td></td>
<td></td>
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</tr>
<tr>
<td>Christianity</td>
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<td>160 (83.3)</td>
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<td>100 (67.6)</td>
<td>137(69.2)</td>
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<td>Eckist</td>
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<td>Year of Study</td>
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<td></td>
<td></td>
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<tr>
<td>1st Year</td>
<td>46 (27.1)</td>
<td>50 (26.0)</td>
<td>37 (35.2)</td>
<td>42 (28.4)</td>
<td>75 (37.9)</td>
<td>50 (28.6)</td>
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<td>2nd Year</td>
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<tr>
<td>4th Year</td>
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<td>5th Year</td>
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Table 2: Associated Modifiable Risk Factors of PUD according to Year  
(N = 988)

<table>
<thead>
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<th>Modifiable Risk Factors</th>
<th>2014 (n=170)</th>
<th>2015 (n=192)</th>
<th>2016 (n=105)</th>
<th>2017 (n=148)</th>
<th>2018 (n=198)</th>
<th>2019 (n=175)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>freq/%</td>
<td>freq/%</td>
<td>freq/%</td>
<td>freq/%</td>
<td>freq/%</td>
<td>freq/%</td>
</tr>
<tr>
<td>Starvation</td>
<td>170(100.0)</td>
<td>192 (100.0)</td>
<td>105 (100.0)</td>
<td>148 (100.0)</td>
<td>198 (100.0)</td>
<td>175 (100.0)</td>
</tr>
<tr>
<td>Male</td>
<td>61 (35.9)</td>
<td>74 (38.5)</td>
<td>46 (43.8)</td>
<td>77 (52.0)</td>
<td>91 (46.0)</td>
<td>90 (51.4)</td>
</tr>
<tr>
<td>Female</td>
<td>109 (64.10)</td>
<td>118 (61.5)</td>
<td>59 (56.2)</td>
<td>71 (48.0)</td>
<td>107 (54.0)</td>
<td>85 (48.6)</td>
</tr>
<tr>
<td>Stress</td>
<td>125 (73.5)</td>
<td>180 (93.8)</td>
<td>105 (100.0)</td>
<td>129 (87.2)</td>
<td>176 (88.9)</td>
<td>168 (96.0)</td>
</tr>
<tr>
<td>Male</td>
<td>39 (21.2)</td>
<td>70 (38.9)</td>
<td>46 (43.8)</td>
<td>58 (45.0)</td>
<td>84 (47.7)</td>
<td>83 (49.4)</td>
</tr>
<tr>
<td>Female</td>
<td>86 (48.8)</td>
<td>110 (61.1)</td>
<td>59 (56.2)</td>
<td>71 (55.0)</td>
<td>92 (52.3)</td>
<td>85 (50.6)</td>
</tr>
<tr>
<td>NSAIDs</td>
<td>90 (52.9)</td>
<td>100 (52.1)</td>
<td>88 (83.8)</td>
<td>116 (78.4)</td>
<td>173 (87.4)</td>
<td>131 (74.9)</td>
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<tr>
<td>Male</td>
<td>52 (57.8)</td>
<td>66 (66.0)</td>
<td>46 (52.3)</td>
<td>69 (59.5)</td>
<td>88 (50.9)</td>
<td>75 (57.3)</td>
</tr>
<tr>
<td>Female</td>
<td>48 (42.2)</td>
<td>44 (44.0)</td>
<td>42 (47.7)</td>
<td>47 (40.5)</td>
<td>85 (49.1)</td>
<td>56 (42.7)</td>
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<tr>
<td>Smoking</td>
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<td>62 (32.3)</td>
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<td>76 (51.4)</td>
<td>55 (27.8)</td>
<td>69 (39.4)</td>
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<tr>
<td>Male</td>
<td>34 (91.9)</td>
<td>51 (82.3)</td>
<td>18 (81.8)</td>
<td>64 (84.2)</td>
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<tr>
<td>Female</td>
<td>3 (8.1)</td>
<td>11 (17.7)</td>
<td>4 (18.2)</td>
<td>12 (15.8)</td>
<td>7 (12.7)</td>
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</tr>
<tr>
<td>Alcohol</td>
<td>30 (29.4)</td>
<td>93 (48.3)</td>
<td>78 (74.3)</td>
<td>84 (43.2)</td>
<td>100 (50.5)</td>
<td>44 (25.1)</td>
</tr>
<tr>
<td>Male</td>
<td>33 (66.0)</td>
<td>65 (69.9)</td>
<td>46 (58.9)</td>
<td>52 (81.3)</td>
<td>76 (74.3)</td>
<td>31 (70.5)</td>
</tr>
<tr>
<td>Female</td>
<td>17 (44.0)</td>
<td>28 (30.1)</td>
<td>32 (41.0)</td>
<td>12 (18.7)</td>
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<td>13 (29.5)</td>
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<tr>
<td>Depression</td>
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<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>31 (15.7)</td>
<td>20 (11.4)</td>
</tr>
<tr>
<td>Male</td>
<td>3 (20.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>7 (22.6)</td>
<td>5 (25.0)</td>
</tr>
<tr>
<td>Female</td>
<td>12 (80.0)</td>
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<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>24 (77.4)</td>
<td>15 (75.0)</td>
</tr>
</tbody>
</table>

4.0. DISCUSSION

4.1. Prevalence of PUD

In the 6-year retrospective review, medical records showed that only 988 students were diagnosed with PUD. Considering the number of years and the total student population of about 16000, this figure appears relatively small. Specifically, the 988 affected students represent only 6.25% of the entire population and an average number of 165 diagnosed cases per year. This may, however, not represent the true situation because, it is likely that some students would have sought healthcare outside the institution’s medical facility and therefore, not included in the institution’s medical records. Earlier, practices among PUD patients that suggest care consultations outside healthcare facilities have been reported. They include the buying of PUD drugs from the open markets, hawkers and supermarkets and the use of herbal medicines for the treatment of PUD. [6]

These practices contradict conventional facility-based recommendations and indicates that care consultations might have been made outside healthcare facilities. Thus, encouragement through education is
needed to make healthcare facilities students’ choice for health-illness consultations.

4.1.1. Prevalence Trends Based on Gender

Generally, PUD prevalence was higher in females than males in 4 out of the 6 years being reviewed. Even the two years when prevalence was highest among males, it was only 2% and 1.4% above the female prevalence in the respective years. The higher PUD prevalence in females observed in the population may not be unconnected with increased female association with modifiable risk factors of PUD. Females were found to be more associated with modifiable risk factors of starvation, stress, and depression than their male counterparts. Though the proportion of females associated with the use of NSAIDS, alcohol and smoking were less than males, the difference in magnitude was minimal and therefore, could play a role in increasing their risk for PUD. While this finding contrast with Bello, et al. and Omosor, et al., which reported higher prevalence of PUD among males in Kano and Delta states of Nigeria respectively, [21, 22] it supports Jemikajah et al, which reported higher prevalence in females than males in Warri, Nigeria. [11] Eniojukan and colleagues also reported higher percentage of female (60%) in their study. [6] Decreasing female association with risk factors of PUD may help reduce prevalence.

4.1.2. Prevalence Trends based on Age

PUD was most prevalent among students aged 17-21. Although, this study did not consider gastric and duodenal ulcers as separate entity, the age group of 17-21 fall within the age range Eniojukan et al reported for duodenal ulcer in Delta state, Southern Nigeria. According to Eniojukan et al, higher prevalence was observed for duodenal ulcer among their respondents aged 16-35 years while prevalence was higher for gastric ulcer among respondents older than 35 years. [6] Considering also, the earlier research report of Tijjani and Umar which found highest PUD prevalence among individuals less than 35 years in Kano, Nigeria, [15] it could be inferred that more young individuals are now having the disease. This may not be unconnected to increased association with risk factors of the disease such as smoking, alcohol and NSAIDS; as records indicate multiple association with risk factors which may have increased their chances of developing the disease. There is, therefore, need to provide risk factor education tailored towards younger students’ specific profile to help change the trend.

4.1.3. Prevalence Trends Based on Religion

Prevalence according to religious affiliation indicates that Christians were more affected than Muslims and Ekists in all 6-year records. This may be so because majority of individuals in the study milieu are Christians. In addition, fasting, which is a regularly observed Christian ritual, have been documented as an emerging risk factor for PUD and its complication of perforation, in Nigeria. [23] It is therefore, likely that Christians in this study had higher proportion of PUD patients partly because of their involvement in religious fasts. The finding is, however, consistent with that of Eniojukan et al which also recorded 70% as Christians in their study sample in Delta state, southern Nigeria. [6]

4.1.4. Prevalence Trends Based on Year of Study

Findings on prevalence based on year of study showed that PUD was most common among first students. The ages of most of the first-year students fall within the age range of 17-21 which was the most affected age group in this study. Higher association with risk factors could still be implicated for higher prevalence among them. Therefore, measures to reduce association with risk factors among young individuals should be instituted to help change the trend. Previous reports on prevalence based on year of study could, however, not be accessed to compare with this finding.

4.2. Modifiable Risk Factors associated with Students with PUD
Starvation was the commonest modifiable risk factor of PUD found among the students. The medical records of all the students indicated that they had starved themselves before the emergence of signs and symptoms that brought them to the medical centre. According Hung and Neu, starvation not only aggravates acid-induced gastric damage but also influence greater acid back-diffusion, oxygen radical generation and low production of mucus and mucosal glutathione which increase the risk for ulcer formation. [24] The reason for a 100% experience of starvation across sample is not clear. However, it is likely that most of the students became starved because they could not find right time to eat due to congested academic schedules or lack money to buy food for themselves. Specifically, for females, it may be part of practices aimed at reducing stomach fat. Notwithstanding the factors influencing starvation, providing information on the relationship between starvation and ulcer formation may help university students prevent the experience.

Stress was among the modifiable risk factors associated with university students with PUD. More female than males were affected. This may probably be due to higher proportion of females in the population of diagnosed PUD patients or lower threshold for stress compared with males. University education is usually viewed as stressful. Full time students are commonly scheduled for academic activities from 8am-5pm and have to attend to assignments and personal study during the night. When such activities are routinely observed, there is tendency for stress levels to increase and impact negatively on the gastrointestinal system.

There are, however, contrasting reports on the relationship between stress and PUD. For example, while Song, Jung and Jung found no difference in stress level between peptic ulcer patients and controls using the stress severity scale, [25] Anda and colleagues found an increased risk of peptic ulcers (OR 1.8) in individuals with self-perceived stress during the month before baseline. [26] More so, while both Rosenstock, et al and Johnsen, et al found no evidence of peptic ulcers as a psychosomatic disease, [27, 28] Deding and colleagues indicated that stress should be considered a determinant of peptic ulcer disease. [29]

A major difference in these studies is how stress was defined. For example, Rosenstock et al and Johnsen et al did not define stress as everyday life stress, while Deding and colleagues did. Rosenstock et al used psychological vulnerability and Johnsen et al used mental depression and coping problems. Considering stress as everyday life stress, Deding and colleagues established that high levels of perceived everyday life stress raises more than twice the risk of either receiving triple treatment or being diagnosed with peptic ulcer compared with individuals with lowest level of perceived stress. [29] Comparatively, the stress associated with university students appear to be similar to the everyday life stress reported by Deding and colleagues. It is, therefore, essential to equip university students with strategies to cope with everyday life stress.

The use of NSAIDS, alcohol and smoking were associated with university students with PUD. Specifically, more males were associated the use of NSAIDS, smoking and alcohol consumption than females. According to Eniojukan et al, males are thought to be involved in physical activities that are greater and more vigorous than those involved in by females. Hence, males may be prone to consuming NSAIDS as pain reliever than females. NSAIDS are major risk factors for PUD. NSAIDS impact on the mucosal protection through the reduction of the effectiveness of mucus bicarbonate barrier, gastric acid and pepsin, which results to damage of the affected mucosal surface 5. Smoking and alcohol have also long been considered risk factors of PUD because they elevate the risk of ulcers and impairs the process of healing. [6]
Also, in the 6-year retrospective review, only in 2014 (8.8%), 2018 (17.7%) and 2019 (11.4%) that few cases of PUD associated with depression. Nevertheless, the successive report of depression in 2018 and 2019 appears to make it an emerging risk factor in our study population. While depression is thought to be a mental illness, it also plays a huge role in appetite and nutrition. While some individuals cope by overeating or bingeing which can lead to weight gain and obesity related illness such as diabetes, some may lose appetite entirely or fail to eat the right amount of nutritious food. In cases that lead to loss of appetite, starvation may eventually set in and impact negatively on the GIT, creating tenderness for ulcer formation. In a study conducted in 2019, baseline depression associated with subsequent incidence of PUD, which, however, reduced seemingly with increased or continued social engagement. Reciprocal relationship was also established between depression and peptic ulcers in two longitudinal follow-up studies in a Korean population.

Although, causes of depression among students with PUD in our study could not be traced in their medical records, it may not be unconnected with challenges of failure, illness and abuse, socioeconomic factors and relationships issues commonly experienced in university campuses. Strategies targeted towards these aspects may aid in the reduction of depressive levels among university students.

Another finding worthy of note in this study is the higher female association with depression. In all the three years when depression was reportedly associated with PUD, females were more than twice associated with depression than males. The finding is not inconsistent with previous reports on prevalence differences between females and males. The prevalence of major depression have long been reported to be higher in women than in men. Patten, et al and Pearson, et al also reported a more than twice prevalence of depression in young women than men. Globally, annual prevalence was 5.5% for women and 3.2%, for men, representing a 1.7-fold greater incidence in women.

The reasons for the difference in depression between women and men have not been clearly delineated. However, biological sex differences have been implicated and less emphasis is placed on race, culture, diet, education and many other potentially social and economic factors. Specifically, Women experience some unique depression-related illness that could contribute to higher prevalence over men. Such illnesses include premenstrual dysphonic disorder, postpartum and postmenopausal depression and anxiety, which are associated with changes in ovarian hormones. Thus, it could be inferred that female students in our study population associated more with depression than their male counterpart, partly due to existing biological sex differences.

5. CONCLUSION

PUD prevalence is generally low. However, risk factor association is enormous. More females, Christians, and first-year students within 17-21 years had PUD. Starvation, stress, use of NSAIDs, alcohol and smoking are predominant modifiable risk factors of PUD among university students. Education discouraging association with modifiable risk factors may help change prevalence trends in the positive direction. A prospective prevalence study on trends and associated risk factors of PUD should be done among university students as this would provide a more accurate data for insightful analysis.

Authors’ Contributions
This work was done collaboratively by the authors. Author Soupriye B. Zibima generated the original concept, designed the project, wrote the first draft, contributed to drafts, collected data, and did statistical analysis. Juliet I. Oniso involved in data collection, contributed to drafts, data input and analysis.

Conflict of Interest
No conflict of interest exist among authors.
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