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Original Articles

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Prof. Ezekiel E. Ugiagbe
MB;BS, FMCPath, MD, Ph.D.
Editor-in-Chief, Annals of Medical and Surgical Practice
Department of Pathology, University of Benin Teaching Hospital, PMB 1111, Benin City, Nigeria

Evaluation of analgesics and co-analgesic prescriptions at a General Practice Clinic in Southern Nigeria.

[1] Opadeyi AO,' PhD, FWACP, Ayinbuomwan SA FMCP [1,]

[1] Department of Clinical Pharmacology and Therapeutics, University of Benin, Benin city, Nigeria

ABSTRACT

Background: The WHO analgesic ladder provides guidance to healthcare providers in the prescription of appropriate analgesics to alleviate pain. However, access, safety, and tolerability considerations of these agents may influence their prescriptions. This study sought to determine the prescription pattern of analgesics and co-analgesics in a general practice clinic.

Methods: A retrospective analysis of dispensed analgesics and co-analgesics in the general practice clinic of a tertiary hospital was undertaken, from February 2021 to January 2022. The type of analgesic prescribed, formulation, number of analgesics per prescription, co-analgesics, and presence of a proton pump inhibitor (PPI) per prescription was evaluated. Prescriptions were selected by a systematic sampling method and evaluated using the WHO analgesic ladder. Descriptive and inferential statistics were conducted.

Results: A total of the 2229 analgesic products were prescribed in1188 patient encounters. Majority of the patients 941(79.2%) obtained more than one analgesic and co-analgesic. Furthermore, most were categorized as being on Step I WHO analgesic ladder 1161(97.8%)., Paracetamol was the most prescribed non-opioid, 612(27.5%), then Celecoxib 493(22.2%) for NSAIDs, paracetamol with codeine, 26(1.2%) was most prescribed opioid, while tizanidine was the most prescribed co-analgesic227(10.2%). PPIs were co-prescribed in 22.5% of the 583 patients on NSAIDS.

Conclusion: Non-opioids remain the most frequently prescribed medications for pain in general practice. Also a large number of co-analgesics was also noticed. The paucity of opioid prescriptions in this study underpins the urgent need to address the concerns and inertia of prescribers with opioid agents. Furthermore, prescribers should be educated on the importance of utilizing the WHO analgesic ladder in the management of pain.

Keywords: Analgesics; Pain management; Prescriptions; Anti-inflammatory agents, Non-steroidal; Nigeria

INTRODUCTION

In the pharmacologic management of various types of pain, analgesics and other agents are utilized. Globally, the WHO pain ladder was designed to aid the initiation and maintenance of therapy depending on the severity.[1] However, in Nigeria, following the recognition of a need to domesticate management practices which may improve the quality of life in those with pain in Nigeria, the guideline for the management of pain in Nigeria was released in 2018.[2]

Corresponding author
Dr. Abimbola O. Opadeyi,
Department of Clinical Pharmacology and Therapeutics, University of Benin
Benin city
Email: abimbola.opadeyi@uniben.edu

The guideline suggests medications appropriate to the varying intensities of pain, enumerates escalation and de-escalation procedures and outlines the potential adverse effects of these medicinal products for use in Nigeria. The guideline prescribes the use of non-opioids- such as paracetamol, Non-Steroidal Anti-Inflammatory Drugs (NSAIDS), opioids and different drugs collectively referred to as adjuvants for pain management.[2]

These medicines, though useful have also been associated with adverse reactions such as NSAIDs- induced gastropathy, paracetamol associated hepatotoxicity and other cardio-renal morbidities[3], abuse and misuse potentials with the opioids, and increased cardiovascular morbidities with selective cyclooxygenase (COX) 2 inhibitor, [4,5]. They have also been used as agents for intentional poisoning. [6]Drug -induced gastropathy has also been observed in this setting previously as a common cause of emergency admission. [7,8] Furthermore, studies suggest that patient often resort to self-care practices and polypharmacy after obtaining an initial prescription.[9,10]

Studies in Nigeria have shown that analgesics are commonly prescribed in general practice settings ranging from 8.7% to 74%[11–14] and the commonest analgesic prescribed from these studies were paracetamol and diclofenac with very few opioids prescribed namely tramadol and pentazocine. They were largely conducted prior to the release of the Nigerian pain guideline. In a study on elderly patients attending general practice 92% of the elderly patients had gastroprotective agents prescribed as recommended in various practice papers and the Nigerian guideline[2,15] However, the co-prescription of gastroprotective agents in general practice setting in Nigeria has not been well evaluated.

Globally up to 50% of patients with low back pain received opioids[16] and the use of adjuvants such as muscle relaxants have been shown to have a modest efficacious effect in the management of acute low back pain.[17] Again, there are very few studies in the Nigeria general population describing the use of opioids and adjuvants for pain relief in general practice.

This study sought to determine the prescription pattern of analgesics and co-prescribed medicines in a Nigeria general practice clinic which may aid the revision of the pain management and treatment guidelines, revision of the essential medicines list and help in understanding self-medication practices of patients for pain. The impact of pain on the physiological and psychological well-being of these individuals cannot be under-emphasized.

Objectives: to describe the prescription pattern of analgesics and adjuvants and other co-prescribed medications in a general practice clinic.

Methods

Study Design- This was a cross sectional retrospective study of patients who had attended the general practice clinic (GPC) of the University of Benin Teaching Hospital(UBTH) Benin-City from February 1st 2021 to January 31st 2022. Approximately 23,000 patients are attended to yearly by the UBTH GPC. The dispensing records of the pharmacy department was utilized for this study. Only patients who purchased their medications at the GPC pharmacy were included in this study.

Sampling:

For a patients' dispensing record to be included in the evaluation, an analgesic needed to be in the prescription. All prescriptions containing analgesics (specifically drugs belonging to the Anatomic Therapeutic Chemical classification (ATC)[18]- N02- Analgesics:

(N02A- Opioids; N02B- Other analgesics and antipyretics); M01A: Antiinflammatory and antirheumatic products, non-steroids; M02B: Topical products for joint and muscular pain were evaluated in the study. The data collection form also included name of the drug, dosage form and amount dispensed where available. Generic names of the stocked different brands of antipyretics and analgesics in the hospital pharmacy used in the sales records was used to identify drugs written in the brand form. Acetylsalicylic acid of the 75mg strength was excluded as this is not used for analgesia.

Sample size: The medicines were selected using the patient encounters according to the WHO Drug use Indicators[19] which recommended a minimum of 600 prescriptions for evaluating current treatment practices in a cross-sectional survey using retrospective data. The sample size was increased to 1000 to improve the reliability of the study. After obtaining legible prescriptions of patients' dispensed analgesics for the period, a systematic random sampling was used to select the prescriptions.

Data analysis: The medicines were classified using the ATC classification as above, In addition, patients who were prescribed more than 1 analgesic as well as other analgesics such as amitriptyline, gabapentin and pregabalin were noted, categorized and analyzed. The drugs were also classified using the WHO pain ladder.[1,2]Step 1 for mild pain- non-opioids +/- adjuvants (Ibuprofen or other NSAIDs, paracetamol, or aspirin), Step 2- Moderate pain : weak opioid +/- non-opioid, +/- adjuvant (codeine, tramadol, low dose morphine), step 3- Severe pain: strong opioid +/- non-opioid, +/- adjuvants (morphine, fentanyl, oxycodone, hydromorphone, buprenorphine). Adjuvants listed include: antidepressant, anticonvulsant, antispasmodic, muscle relaxant, bisphosphonate, or corticosteroid). The use of proton pump inhibitors (PPI) was noted in each prescription.

Statistical analysis; Data was analyzed using SPSS version 21 and presented descriptively using means and frequencies. Chi square was used to analyze the associations between categorical variables. Statistical significance was set at $p < 0.05$.

Ethical approval (ADME/E/22/A/VOL. VII/148311669) was obtained from the UBTH Health Research and Ethics committee. The data obtained was anonymized and securely kept.

Results

A total of 1188 complete patient dispensing records were analyzed in the study. The mean number of medicines dispensed per patient was 3.8(1.4) medicines, the mean number of analgesics prescribed were 1.9(0.5) analgesics per prescription. The total number of analgesic products prescribed in this study were 2229 medicinal products. Of which, non – opioids were the most prescribed, especially paracetamol 612(27.5%). The most prescribed opioid prescribed was codeine with paracetamol 26(1.2%), no strong opioid was prescribed in this study (Table 1). Regarding the WHO Pain ladder, most of the patients 1161(97.8%) were on Step 1, while only 26(2.2%) were on Step 2. Most of the preparations were prescribed for the oral route 1926(86.4%), 215(9.6%) topical preparations and 88(4.0%) were prescribed as injectables. Most of the patients had 2 analgesics prescribed 853(71.8%), while 247(20.7%), 77(6.5%) and 11(0.9%) had 1, 3, 4 or more analgesics prescribed respectively.

Of the 88 injectable analgesics, paracetamol accounted for the highest proportion 73(83%), diclofenac 14(15.9%) and pentazocine 1(1.1%).

Table 1: Prescription pattern (WHO Pain Ladder Classification) of analgesics in a general practice clinic in Southern Nigeria

Medication	ATC code	n/N=2229 (%)
Non- Opioids		
Paracetamol	N02BE01	612(27.5)
Celecoxib	M01AH01	493(22.2)
Diclofenac(Including combination preparations)	M01AB05/ M01AB55	207(9.2)
Diclofenac(Topical)	M02AA15	170(7.6)
Ibuprofen	M01AE01	59(2.6)
Methylsalicylate (Topical)	M02AC	58(2.6)
Glucosamine/chondroitin sulphate	M01AX25/ M01AX05	59(2.6)
Aceclofenac	M01AB16	8(0.4)
Naproxen	M01AE02	1(0.04)
Ketorolac	M01AB15	1(0.04)
Trypsin-Chymotrypsin	M09AB52	1(0.04)
Opioids		
Codeine with paracetamol	N02AJ06	26(1.2)
Tramadol	N02AX02	1(0.04)
Pentazocine	N02AD01	1(0.04)
Adjuvants		
Tizanidine	M03BX02	227(10.2)
Pregabalin	N02BF02	121(5.4)
Amitriptyline	N06AA09	107(4.8)
Gabapentin	N02BF01	75(3.4)
Orphenadrine citrate	M03BC01	1(0.04)
WHO PAIN LADDER		
STEP 1		1161(97.8)
STEP 2		26(2.2)

ATC: Anatomical Therapeutic Chemical Classification

Regarding the use of oral/parenteral NSAIDs, majority of the patients, 713(60%) had one or more NSAIDs prescribed and this was significantly higher in those prescribed 2 or more analgesics/adjuvants (chi square - likelihood ratio 98.36,p<0.001).Also among those prescribed NSAIDs, those on selective cyclooxygenase 2 inhibitors (COX-2) 96 (50.5%) were more likely to be prescribed a proton pump inhibitor (PPI) and this was also statistically significant (chi square =8.88, p=0.01).

Table 2: Association between co-prescription of Non-Steroidal Anti-Inflammatory Drugs (NSAIDS) and PPI at a general practice clinic in Nigeria

Medications	PPI(No) n=998(84%)	PPI(Yes) n=190 (16%)	Chi-square (p-value)
No NSAIDs	415(41.7)	59(31.1)	8.88(0.01)
Non-selective NSAIDs	186(18.6)	35(18.4)	
Selective NSAIDS	397(39.8)	96(50.5)	

NSAIDs- Non Steroidal Anti-inflammatory Drugs (Non-selective COX-1&COX2 and -Selective COX2 Inhibitors), Topical NSAIDs not included. PPI-Proton Pump Inhibitors.

Discussion

In this study of analgesics and co-prescribed medications. Non-opioids mainly paracetamol and celecoxib were the most prescribed medications. Opioids prescriptions were very few and consisted mainly of paracetamol with codeine, the use of adjuvants specifically tizanidine was evident in the study. Patients were more likely to receive an NSAID prescription once they are prescribed multiple analgesics and attention to gastroprotection was poor in patients prescribed NSAIDs, It appeared that majority of the pain were adjudged to be mild as only Step 1 of the WHO pain ladder was the most prescribed. Paracetamol was also the most prescribed injectable, this was noted in a previous study,[20] patients with fever, and acute pain do present to general practice clinics and may require immediate therapy. It is however encouraged to prescribe oral medications to patients presenting with pain rather than injections.[2]

Previous in-country studies had shown that paracetamol was the most commonly prescribed analgesic[12,14] closely followed by diclofenac and even in the community, patients who self-medicate, are most likely to use these medicines.[10,21]Paracetamol was equally the most prescribed in our study and in a recent systematic review , it was found to be efficacious in knee or hip osteoarthritis, episodic tension type headaches, dental procedures, otitis media in children, common cold related headaches, and abdominal pain, but not efficacious for low back pain or sore throat.[22] This may explain the continued high rate of prescription of paracetamol. However, paracetamol is not without adverse effect,[3] and considering the bulk of paracetamol being prescribed, ongoing research into its safety in this setting is required.

The second most prescribed medication in our study was celecoxib, reflecting a shift from findings in previous studies where non-selective COX inhibitors were the second most prescribed medicines.[12,14]Although, celecoxib has a safer gastrointestinal tolerability profile compared with the traditional NSAIDs,[23]a proportion of patients on celecoxib still received PPI in this study. Furthermore, PPIs were offered mainly to those on NSAIDs, as also noted in a study of elderly patients in a general practice clinic where 92% of them were co-prescribed analgesics and PPIs.[24]Although, the proportion of patients on PPI was lower in this study, the results implies some recognition of some need for gastroprotection in patients who may be at risk. [15]

Glucosamine and chondroitin sulphate prescriptions as noted in the study suggests that medications used for long term management pain and osteoarthritis are increasingly being needed. This is opposed to the 0.1% of analgesic prescriptions in a Colombian study,[25] also a systematic review showed their efficacy in reduction of joint space narrowing[26]An increased attention to this co-analgesic will be required due to its increasing prescriptions seen in the study and not observed from earlier in-country studies.[12,24]

Other cross-sectional study of analgesics utilization in the south-western part of Nigeria had shown that analgesics were commonly prescribed with over 70% of prescriptions containing an analgesic, and up to 35% having multiple analgesics.[12]While our study found a higher rate of multiple analgesic prescriptions, there was a high proportion of topical analgesic agent prescriptions which suggests that a comprehensive approach to pain management is currently being utilized by the physicians.

The high rates of multiple analgesic prescriptions in this study may also be due to the use of adjuvants hitherto not fully evaluated in Nigeria. Adjuvants such as the gabapentinoids, muscle relaxants are increasingly being prescribed for pain, from 5% to 12% in a decade seen in American patients with osteoarthritis.[27]Adjuvants have indirect analgesic effect that target neuropathic pain and visceral pain in combination with other analgesics.[2]There is a need to explore the rationality of these prescriptions given the growing trends in use.

Opioids were not prescribed in large amounts in this study as observed in a recent review of opioid consumption in Sub – Saharan Africa,[28]and as distinctly different from the developed nations.[16,29] Opioids are shown not to be easily accessible, proneness to misuse and abuse has also been noted to be on the rise globally, this may have influenced the decision of the physicians. Again, it was noted that more patients were on the first step of the WHO pain ladder in this study suggesting that patients presented more with mild pain, but the multiplicity of analgesic (up to 4 analgesics and adjuvants) implies otherwise. Objective pain assessment using pain scales is not routinely carried out in Nigeria mainly due to unawareness[12] and as such, determination of the severity and type of pain which ought to direct appropriate measures for pain relief is absent. There is a need to elucidate the reasons that the factors influencing paucity of opioid prescriptions in this setting.

Limitations: the study reviewed dispensing records over a one year period allowing for a good representation of the practices in the clinic. However, the clinical diagnoses were unavailable for review. Also, the results may not be generalizable to other general practices in the country.

Conclusion: There appears to be a shift in the prescriptions of NSAIDs from the non-selective to the selective while paracetamol remains the single most prescribed analgesic. More patients were on multiple medications for pain, with an increasing prescription of different adjuvants emphasizing increasing recognition of neuropathic pain. Weak opioids were primarily prescribed and in low quantities. Gastroprotection with PPI is considered for a proportion of the patients placed on NSAIDS and multiple analgesics. Further studies into the use of co-analgesics are required.

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Conflicts of Interests: The authors have no conflicts to declare.

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Effect of parenteral iron therapy in iron- deficient anaemic pre-dialysis chronic kidney disease patients in a Nigerian tertiary hospital: a cross-sectional study

Imuetinyan R Edeki,[1] Nosakhare T Idubor[2]

[1]Department of Internal medicine, University of Benin Teaching Hospital, Benin City, Edo State, Nigeria

[2]Department of Haematology, University of Benin Teaching Hospital, Benin City, Edo State, Nigeria

ABSTRACT

Background: Iron deficiency anaemia is common in chronic kidney disease (CKD) patients, with iron deficiency being the commonest cause of anaemia. Treatment with iron therapy can correct the deficiency, reduce overall cardiac death and hospitalization rates, improve cognitive function and quality of life, as well as, delay the need for commencement of erythropoiesis stimulating agents.

Aim: This study sought to determine the effect of parenteral iron therapy in iron deficient pre-dialysis CKD patients, as well as factors influencing response to parenteral iron therapy.

Method: Ninety- five pre-dialysis patients with CKD were screened from March 2021 to January 2022. Twenty-three (24.2%) participants found to have iron deficiency anaemia were subsequently studied. 200mg of intravenous iron sucrose was given to each participant weekly for 5 weeks (total dose of 1g). Pre-intervention tests included-full blood count (FBC) including red cell indices, serum ferritin, transferrin saturation (TSAT), folate, vitamin B12, erythropoietin and C-reactive protein. These tests were repeated 2 weeks after last dose of parenteral iron.

Results: The mean packed cell volume (PCV) increased from 28.4±4.7% to 30.4±3.7% ($p<0.001$) after iron therapy. There was also significant increase in mean corpuscular volume (82.0±8.4 vs. 85.1±4.9fl; p=0.003), mean corpuscular haemoglobin (27.1±2.8 vs. 28.4±2.2pg; p=0.006), ferritin (120.4±46.9 vs. 211.2±36.7ng/ml; p=0.001) and TSAT (20.5±6.0 vs.27.9±16.9%) following parenteral iron therapy. Thirteen percent of participants had optimal response, 69.6% had inadequate response while 17.4% had no response to parenteral iron therapy. Adequate response to iron therapy was associated with lower baseline PCV.

Conclusion: The mean PCV, red cell indices, serum ferritin and TSAT significantly improved in iron deficient anaemic pre-dialysis patients with CKD after 5 weeks of parenteral iron therapy, response to parenteral iron therapy was generally inadequate.

Key words- chronic kidney disease, pre-dialysis, iron deficiency anaemia

INTRODUCTION

Anaemia is a frequent complication of CKD, with iron deficiency being the commonest cause of anaemia.[1,2]Iron supplementation whether oral or parenteral, is essential in treatment of anaemia in CKD.[3]

Intravenous iron therapy is used when rapid haemoglobin response is required and this may delay the need for commencement of erythropoiesis stimulating agents (ESA).[4] Iron therapy

Corresponding Author: Imuetinyan R Edeki, Department of Internal medicine, University of Benin Teaching Hospital, PMB 1111, Edo State, Nigeria.

teeidubor@yahoo.com

when used alone may be effective in treatment of anaemia in pre-dialysis CKD patients.[5]Parenteral iron is reported to be more effective than oral iron supplementation in CKD patients due to better systemic absorption and improved bioavailability.[5]Oral iron therapy is associated with some gastrointestinal side effects,[6] reduced intestinal absorption due to gut oedema,[7] increased degradation by gastric juices and limited bioavailability due to hepatic first-pass effect.[5]

In pre-dialysis patients with CKD, the choice of route of iron administration is based on severity of iron deficiency, availability of venous access, response to prior oral iron therapy, cost, patient compliance and side effects of prior oral or intravenous iron therapy.[5] However, oral therapy is not recommended for use in patients with CKD on dialysis.[5]

Parenteral iron therapy may rarely be associated with anaphylactic reactions, increased risk of infection, iron deposition in tissues and renal tubular toxicity when given in excess.[8] Rarely, adverse reactions to intravenous iron administration may include difficulty in breathing, hypotension, hypertension, pruritus, nausea and vomiting, chest pain, fever and dizziness.[9]

The rationale for the use of iron therapy in CKD are to ensure adequate iron stores for erythropoiesis, to prevent iron deficiency as well as to correct iron deficiency anaemia. Various guidelines have stated the need for routine iron therapy in patients with CKD patients.[5,10,11] Several studies have also shown the effectiveness of parenteral iron supplementation over oral administration in CKD with varying limitations.[10,11,12] These limitations include paucity of knowledge on the long-term clinical benefits of iron therapy (aside the direct effect on haemoglobin) and long-term adverse effects of iron therapy when given in excess of what is required-ventricular arrhythmias, heart failure and worsening carotid atherosclerosis.[13,14]

Although knowledge of iron studies will better guide physicians on appropriate dose and frequency of iron therapy, routine iron studies are rarely carried out in Nigerian CKD patients prior to parenteral iron therapy. This is probably because the tests are expensive and are not readily available in most Nigerian hospitals.

There are varying reports on the effectiveness of the standard dosing regimen of parenteral iron therapy used in patients with CKD as calculated iron doses are rarely used locally, thus the purpose of this study.

METHODOLOGY

This was a single-centre cross-sectional study conducted at the Nephrology clinic at the University of Benin Teaching hospital, southern Nigeria from March 2021 to January 2022. Ninety-five pre-dialysis CKD patients were consecutively recruited for the study. Twenty-three (24.2%) patients were found to have iron deficiency anaemia and were subsequently studied. Inclusion criteria were iron deficient anaemic CKD patients aged 18years and above who gave informed consent. Pregnant CKD patients as well as those with haemoglobinopathies, human immunodeficiency virus, known malignancies, chronic infections, recent blood transfusion in the preceding 4 weeks and those on ESA were excluded. A researcher administered questionnaire was used to obtain socio-demographic and clinical information from each participant.

Pre-intervention tests included-full blood count (FBC) including red cell indices, serum ferritin, transferrin saturation (TSAT), folate, vitamin B12, erythropoietin (EPO) and C-reactive protein, while post-intervention tests (FBC, serum ferritin and TSAT) were repeated 2 weeks after last dose of parenteral iron.

Iron deficiency anaemia was defined as iron deficiency with PCV less than 30%or Hb concentration<10g/dl.[5,15]

Iron deficiency was defined as TSAT <20%.[5]Participants with iron deficiency anaemia were given iron sucrose 200mg as an intravenous infusion (given in 200 millilitres of normal saline over 20 – 30 minutes, after a negative test dose) weekly for 5 weeks (a total dose of 1g), following which a repeat of investigations was done 2 weeks after. Resuscitation drugs were available prior to commencement of parenteral iron therapy and a trained medical personnel present to observe participants.

Adequate response to intravenous iron sucrose therapy was defined as increase in haemoglobin concentration by at least 1g/dl (or PCV rise of 3%) from baseline level at end of study.[16]

Inadequate response to iron therapy was defined as increase in PCV > 1% but < 3% post iron therapy while no response to iron therapy was defined as increment in PCV < 1% post iron therapy.

Data were analysed using IBM SPSS version 20, with normally distributed data expressed as means and standard deviation. Categorical data were expressed as frequency and proportion while chi-square and Fisher's exact test were used in determining significant association between categorical variables. Paired t test was used to compare mean values of two related groups for unskewed data, while one way analysis of variance was used to determine statistically significant differences between the means of at least 3 independent groups. P value < 0.05 was set as level of significance.

RESULTS

The 23 pre-dialysis CKD patients in this study had a mean age of 58.1±14.9years, comprising of 9(39.1%) males and 14(60.9%) females. Majority were aged 50 years and above with secondary level of education. There was 1(4.3%) participant in CKD stage 2, 6(26.1%) in stage 3, 10(43.5%) in CKD stage 4 and 6(26.1%) in CKD stage 5. Diabetes mellitus (47.8%) was the most common cause of CKD followed by hypertension (39.2%) and chronic glomerulonephritis (8.7%). Table 1

The mean PCV pre-parenteral iron therapy and post-parenteral iron therapy in iron-deficient patients with CKD was 28.4 ± 4.7% and 30.4 ± 3.7% respectively (p<0.001). The mean PCV change following parenteral iron therapy was 2.0± 1.8%. There was also significant increase in mean haemoglobin concentration (9.5 ± 1.6 vs. 10.3 ± 1.4 g/dl) and red blood cell count (3.6 ± 0.8 vs. 3.8 ± 0.6 x 10^6 cells/mm^3) following parenteral iron therapy (p<0.001). Mean MCV (82.0 ± 8.4 vs. 85.1± 4.9 fL; p =0.003) andMCH (27.1 ± 2.8vs. 28.4 ± 2.2 pg; p= 0.006) were also increased following iron therapy.

Ferritin levels increased significantly from 120.4± 46.9 to 211.2 ± 36.7 µg/L post therapy (p = 0.001). Similarly, TSAT levels increased significantly (20.5 ± 6.0 to 27.9 ± 16.9%) following parenteral iron therapy. (p- 0.011) Table 2

Three (13%) of iron - deficient subjects with CKD had optimal response to iron therapy. Sixteen (69.6%) had inadequate response while 4 (17.4%) had no response to iron therapy. Table 2

Mean baseline PCV and EPO in those with adequate response to iron therapy was lower than those who had inadequate and no response but this did not reach statistical significance (p = 0.143). A comparison of baseline PCV of those with adequate, inadequate and no response in a post-hoc analysis using Fisher's least significance difference test, showed that those that had adequate response had significantly lower haematocrit (p = 0.13). Table 4

Age, gender, CKD stage, folate, vitamin B12 and EPO levels did not significantly affect response to parenteral iron therapy. Table 3 and 4

DISCUSSION

This study assessed the effectiveness of parenteral iron therapy in pre-dialysis iron deficient anaemic patients with chronic kidney disease. Although the mean PCV, Hb concentration, red blood cell count serum feritin and TSA significantly improved in iron deficient anaemic patients with CKD following parenteral iron therapy, PCV response was generally inadequate.

There was a significant mean PCV increase of 2.0± 1.8%. This is similar to a mean PCV increase of 2.42± 1.98% following intravenous iron therapy reported by Arogundade et al.[17]This could be explained by the fact that similar total doses of parenteral iron was used in both studies.

Similarly, there was no statistically significant difference in total white blood cell and platelet count. These findings are in consonance to findings by Fish bane et al[18] and Silverberg et al[19] in hemodialysis and pre-dialysis CKD patients respectively. However, contrary to this finding, iron therapy is known to reduce total white blood cell count as it transiently causes leucopoiesis and megakaryopoiesis decline.[20,21]

Serum ferritin and TSAT were also increased among participants and is similar to findings of the FIND-CKD[11] and DRIVE[12]studies. Parenteral iron is known to rapidly improve iron stores as well as circulating iron and delays the need for commencement of erythropoiesis stimulating agents (ESA) as well as reducing ESA dose when required.[22]Parenteral iron therapy has also been reported to improve cardiac health in heart failure which is a common complication in CKD.[23]Iron sucrose used is safe with little or no reported incidence of adverse drug event and is comparable in safety to newer iron formulations.[24] In this study, one (4%) participant reported nausea during parenteral iron administration which was noticed 20 minutes after commencement of the first iron dose, this is in contrast with the study by Arogundade et al[17]who reported moderate adverse drug events in 24.9% of study participants. The reason for this may be the use of iron dextran in the study by Arogundade et al,[17]which has poor tolerability compared to iron sucrose and its use is now obsolete.[25]

Parenteral iron administration in this study was given as an intravenous bolus injection which involved administering small doses of iron over a period of 5 weeks. On the other hand, parenteral iron administered in the study by Arogundade et al[17] was by total dose infusion, where calculated iron required for each patient is given in a single hospital visit. The advantage of the total dose infusion over the intravenous bolus injection is lower cost in terms of time spent in the hospital and transportation. On the other hand, the incidence of adverse drug reactions will be increased with the total dose infusion.

Age, gender, stage of CKD, baseline PCV, folic acid and vitamin B12 did not significantly influence the response to parenteral therapy. A 2-year retrospective study in the United Kingdom (UK) reported better Hb response following parenteral iron therapy in those with lower baseline PCV and later CKD stages 3-5 compared to those with stages 1-2.[26]This report is different from the finding of this present study. This difference may be explained by the relatively small sample size compared to the study done in UK. However, Chukwu et al[26] did not find significant influence of age and gender on Hb response as seen in this study. Iron deficiency affects metabolic pathways of vitamin B12 and

folate and their serum levels has been reported to increase following iron therapy in non-CKD population.[27]

The higher mean EPO among non-responders may be related to poor iron utilisation due to the effect of hepcidin and will need further exploration.

In conclusion, the mean PCV, red cell indices, serum ferritin and TSAT significantly improved in iron deficient anaemic pre-dialysis patients with CKD after 5 weeks of parenteral iron therapy, response to parenteral iron therapy was generally inadequate. The use and safety of parenteral iron sucrose therapy in pre-dialysis CKD patients cannot be over-emphasized. It is however recommended that total iron dosage be calculated for individual patient so as to achieve optimal response.

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Table1: Socio-demographic characteristics, stage and Aetiology of CKD

	CKD WITH IDA (n=23)
Age group (years)	
<50	7 (30.4)
≥50	16 (69.6)
Mean age	58.1±14.9
Gender	
Male	9 (39.1)
Female	14 (60.9)
Education	
Primary	3 (13.0)
Secondary	12 (39.2)
Tertiary	8 (34.8)
CKD Aetiology	
DM	11 (47.8)
HTN	9 (39.2)
CGN	2 (8.7)
ADPKD	1 (4.3)
CKD Stage	
Stage II	1 (4.3)
Stage III	6 (29.1)
Stage IV	10 (43.5)
Stage V	6 (26.1)

IDA- iron deficiency anaemia, DM-diabetes mellitus, HTN- hypertension, CGN- chronic glomerulonephritis, ADPKD- autosomal dominant polycystic kidney disease

Table 2: Pre- and Post- Iron Therapy parameters (N= 23)

	Pre - Iron therapy n = 23 Mean ± SD	Post - Iron therapy n = 23 Mean ± SD	P value
Hb (g/dl)	9.5 ±1.6	10.3 ± 1.4	<0.001
PCV (%)	28.4 ± 4.7	30.4 ± 3.7	<0.001
RBC (x 10^6cells/mm^3)	3.6 ± 0.8	3.8 ± 0.6	0.027
MCV (fl)	82.0 ± 8.4	85.1 ± 4.9	0.003
MCH (pg)	27.1 ± 2.8	28.4 ± 2.2	0.006
MCHC (g/dl)	33.7 ± 1.4	33.2 ±1.8	0.067
RDW (%)	16.6 ± 3.1	13.8 ± 2.2	0.001
WBC (x 10^3cells/mm^3)	5.8 ± 2.3	5.6 ± 1.6	0.525
GRA (%)	61.0 ± 11.5	65.4 ± 6.7	0.002
Lymphocyte (%)	31.4 ± 11.1	28.2 ± 6.9	0.015
Monocytes (%)	7.8 ± 2.7	6.6 ± 2.7	0.020
Platelets (x 10^3cells/mm^3)	249.0 ± 129.5	248.8 ± 95.5	0.991
Ferritin (ng/ml)	120.4 ± 46.9	211.2 ± 36.7	0.001
TSAT (%)	20.5 ± 6.0	27.9 ± 16.9	0.011

Hb- haemoglobin, PCV- packed cell volume, RBC- red blood cell, MCV- mean corpuscular volume, MCHC- mean corpuscular haemoglobin concentration, MCH- mean corpuscular haemoglobin , RDW- Red cell distribution width, WBC- white blood cell, GRA-granulocytes, TSAT-transferrin saturation

Table 3: Association between age, gender, stage of CKD and response to iron therapy (N= 23)

	Optimal responders n= 3	Inadequate responders n= 16	Non responders n= 4	*P value*
Age group(years)				
<50	2 (66.7)	5 (31.3)	0 (0.0)	
≥50	1 (33.3)	11 (68.7)	4 (100.0)	*0.228*
Gender				
Male	1 (33.3)	6 (37.5)	2 (50.0)	*0.685*
Female	2 (66.7)	10 (62.5)	2 (50.0)	
Stage of CKD				
II	0 (0.0)	1 (6.3)	0 (0.0)	
III	0 (0.0)	6 (37.5)	0 (0.0)	*0.237*
IV	0 (0.0)	7 (43.8)	3 (75.0)	
V	3 (100.0)	2 (12.5)	1 (25.0)	

CKD-chronic kidney disease

Table 4: Factors influencing response to iron therapy (N=23)

	Optimal responders n=3 Mean ± SD	Inadequate responders n=16 Mean ± SD	Non responders n=4 Mean ± SD	P value
Baseline PCV (%)	26.4 ± 1.7	31.0 ± 3.8	31.1 ± 3.0	0.143
CRP (ng/ml)	5.1 ± 3.6	4.6 ± 2.4	7.0 ± 0.4	0.203
Folate (ng/ml)	2.5 ± 2.0	3.8 ± 3.5	2.6 ± 3.1	0.702
Vitamin B_{12} (pg/ml)	210.8 ± 33.6	219.5 ± 155.3	178.1 ± 76.0	0.867
EPO (miu/l)	124.0 ± 12.0	143.9 ± 56.2	281.9 ± 308.4	0.161

PCV- packed cell volume, CRP-C reactive protein, EPO- erythropoietin

Ethical Consideration

Ethical Committee of University of Benin Teaching Hospital approved the study protocol with a reference number of ADM/E 22/A/Vol.VII/148220. Written informed consent was obtained from all study participants and information obtained was treated with utmost confidentiality.

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The Prevalence Of Intestinal Helminthic Parasitic Infections Among Patients Attending The University Of Benin Teaching Hospital , South-south Nigeria: A Retrospective Study.

*Lofor P, *Ebeigbe E

*Department of Medical Microbiology, University of Benin Teaching Hospital Benin City, Nigeria.

ABSTRACT

Background: Intestinal parasite infection is one of the main Public health issue, particularly in developing countries like Sub-Saharan Africa. Around 450 million people, primarily children, are believed to be unwell as a result of such diseases, with an estimated 3.5 billion people affected globally. Intestinal helminths infections have continued to occur in Nigeria as a result of low living standards, unsanitary surroundings, and a lack of knowledge about fundamental health-promoting behaviours. The majority of those afflicted are children, and Children in developing nations are most often affected because of their typical hand-mouth conduct, uncontrolled faecal activity, and immature immune systems. These diseases are more common in the less affluent neighbourhoods. They share several characteristics, including poor household income, filthy living circumstances, crowded living quarters, limited access to potable water, tropical weather, and low altitude.Among the top 10 most common infections in the world are intestinal parasitic disorders, including trichiuriasis, ascariasis, and hookworm infestation. The severity of intestinal parasite infections and their determinants among patients at University Of Benin Teaching Hospital, Benin-city, Nigeria, are poorly understood.

Aims: To estimate the prevalence of intestinal helminthic parasites among patients attending University Benin Teaching hospital, Benin-city.

Method: The study is a Retrospective Cross Sectional Study. It involved a review of Case notes of Patients that were admitted in UBTH and managed for Intestinal parasitic diarrhoea diseases from June 2016 to December 2019. Also a review of their Medical microbiology laboratory test records during management especially their Stool Microscopy results was done. Patients with incomplete or missing medical data were excluded from the study. Data were analyzed using SPSS version 26.0 statistical software.

Results: A total of 200 stool samples were processed during the period under review, and 40(20%) Stool samples were positive for intestinal helminths,28 (14%)stool samples were positive for Protozoa, while 132(66%) stool samples showed no parasites .

The Prevalence of intestinal parasite over these three year and 7 months period was 20% (40/200). With Male prevalence 13%(26/200) and Female 7%(14/200).

Of the Forty(40) intestinal helminths isolated,Twenty-six (65%) were from male Stool samples, while 14 (35%) were from female stool samples.

Hookworm (*Ancyclostoma duodenale* and *Necator americanus*) was the most isolated intestinal parasite accounting for8 (20%) of the total intestinal isolates. This was followed by *Ascaris lumbricoides* which accounted for 6(15%) of the total intestinal helminths isolated. In Male stool samples Hookworm and Ascaris lumbricoides were the most isolated intestinal parasite, while *Schistosoma haematobium* and *Ascaris lumbricoides* were the most isolated intestinal parasites in female stool samples. The least identified intestinal parasite were *Hymenolopsisnana* and *Schistosomajapanicum.* Seven different kinds of intestinal helminths were identified.

There was no significant relationship between the Sex of patients and the acquisition of intestinal parasites (as P= 0.460)

There was a significant relationship between the age group of patients and the Species of intestinal parasites isolated (P= 0.000).

Conclusion: In adults and school-age children, intestinal parasite infections were highly prevalent. The findings suggest that in order to reduce intestinal parasite infections, coordinated eradicated measures must be strengthened. The results of this study will be a valuable contribution to any modifications made to intestinal parasite prevention and control programmes by the federal, state or local governments.
Keywords: **Intestinal helminths, Patients, University of Benin Teaching Hospital, Prevalence, Benin-city**

INTRODUCTION

Intestinal parasite infection is one of the main public health issues, particularly in developing countries like Sub-Saharan Africa. Around 450 million people, primarily children, are believed to be unwell as a result of such diseases, with an estimated 3.5 billion people affected globally [1].

Corresponding author
Ejime Ebeigbe
Department of Medical Microbiology, University of Benin Teaching Hospital, Benin City Nigeria
Email:ejimenicholas@gmail.com

Intestinal helminths infections have continued to occur in Nigeria as a result of low living standards, unsanitary surroundings, and a lack of knowledge about fundamental health-promoting behaviours [2, 3]. Kids attending school have a higher probability of acquiring intestinal helminths infections, and they also tend to have them more frequently [4, 5, 6]. The majority of those afflicted are children, and Children in developing nations are most often affected because of their typical hand-mouth conduct, uncontrolled faecal activity, and immature immune systems(7).

Parasitic illnesses have been associated with a higher risk of nutritional anaemias, protein energy shortages, and stunted child growth. They may also result in a high risk of morbidity and mortality [10], as well as physical illness and subpar academic performance among pupils [8, 9]. Parasitic diseases are regulated by behaviour. Key components of health systems include biological, environmental, and social elements. The probability of disease transmission, infection, and associated death and morbidity is influenced by social and professional factors like education, local circumstances like well-maintained residential and rural infrastructure, and economic factors like monthly income [11, 12].

These diseases are more common in the less affluent neighbourhoods. They share several characteristics, including poor household income, filthy living circumstances, crowded living quarters, limited access to potable water, tropical weather, and low altitude. Among the top 10 most common infections in the world are intestinal parasitic disorders, including trichiuriasis, ascariasis, and hookworm infestation [13].

Intestinal helminths have a major role in the development of gastrointestinal problems, including dysentery, vomiting, diarrhoea, anorexia, haematuria, abdominal distension, and sometimes cognitively associated disorders. [14, 15]. Malnutrition and anaemia can be caused by severe chronic infections with *Ascaris lumbricoides* and hookworms (*Ancylostomadoudenale*or *Necator americanus*) in high-risk individuals. [16, 17, 18].

The severity of intestinal parasite infections and their determinants among patients at University Of Benin Teaching Hospital, Benin-city, Nigeria, are poorly understood.

In order to ascertain the types and prevalence of human intestinal helminthic parasites among patients arriving at the University of Benin Teaching Hospital in Benin City,the current retrospective Study was carried out.

MATERIAL AND METHODS

Study setting:

The study was conducted in UBTH and the department of medical microbiology of the University of Benin Teaching Hospital, a

900-bedded tertiary centre located in Benin-city, south south Nigeria. The hospital is dedicated to teaching, research and specialist services and serves Lagos State and neighbouring States in south south Nigeria.

Study design:

The study was a Retrospective Cross Sectional Study. It involved a review of Case notes of patients that were admitted in UBTH and managed for Intestinal parasitic diarrhoea diseases from June 2016 to December 2019. Also, a review of their medical microbiology laboratory test records during management especially their Stool Microscopy results was done.

Patients with incomplete or missing medical data were excluded from the study.

Ethical considerations

Ethical approval for the study was obtained from University of Benin Teaching Hospital Research and Ethics Committee, with PROTOCOL NUMBER: ADM/E22/A/VOL.VII/14830112981. As data were retrospectively obtained from the laboratory records and did not involve contact with patients nor was recruitment of patients done, informed consent was not deemed necessary. However, privacy and confidentiality of patients' data were protected in accordance with the Declaration of Helsinki.

RESULTS

A total number of 200 stool samples were processed during the period of review(Table 1). 40(20%) Stool samples were positive for intestinal helminths,28 (14 %) stool samples were positive for Protozoa, while 132(66%) stool samples showed no parasites. (Table 2)

The Prevalence of intestinal parasite over these three year and 7 months period was 20%(40/200). With Male prevalence of intestinal parasite of 13%(26/200) and Female prevalence of intestinal parasite of 7%(14/200).

Of the Forty (40) intestinal helminths isolated , Twenty-six(65%) were from male Stool samples, while 14 (35%) were from female stool samples. (Table 3, Fig1)

Table 1: Socio-demographic characteristics of subjects

VARIABLE	TOTAL NUMBER OF STOOL SAMPLES				NUMBER OF STOOL SAMPLES POSITIVE FOR HELMINTHS ISOLATION			
AGE GROUPS	MALE		FEMALE		MALE		FEMALE	
	(n)	(%)	(n)	(%)	(n)	(%)	(n)	(%)
1-5	13	10.83	7	8.75	0	0.00	0	0.00
6-10	17	14.17	10	12.5	6	5.00	3	3.75
11-15	6	5.00	5	6.25	3	2.50	2	2.50
16-20	5	4.17	5	6.25	2	1.67	0	0.00
21-25	18	15.00	15	18.75	3	2.50	2	2.50
26-30	19	15.83	10	12.5	4	3.33	2	2.50
31-35	16	13.33	10	12.5	5	4.17	3	3.75
36-40	5	4.17	8	10.00	0	0.00	1	1.25
41-45	11	9.17	5	6.25	3	2.50	0	0.00
46-50	10	8.33	5	6.25	0	0.00	1	1.25
Total	120	100	80	100	26	21.67	14	17.5

Table 2: Isolates from stool sample and their percentages

PARASITE IN STOOL SAMPLE	NUMBER	%
Intestinal helminth	40	20
Protozoan	28	14
No parasite	132	66
Total stool sample	200	100

Table 3: Age and Sex

		STOOL SAMPLE WITH INTESTINAL HELMINTHS	
		MALE	FEMALE
Age range	6-10	6	3
	11-15	3	2
	16-20	2	0
	21-25	3	2
	26-30	4	2
	31-35	5	3
	36-40	0	1
	41-45	3	0
	46-50	0	1
	Total	26	14

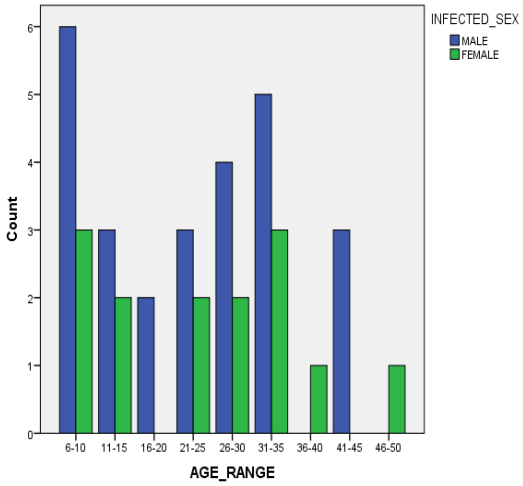

Figure 1: Age and sex of patients with helminths infected stool sample.

Hookworm (*Ancyclostoma duodenale* and *Necator americanus*) was the most isolated intestinal parasite accounting for 8 (20%) of the total intestinal isolates. This was followed by *Ascaris lumbricoides* which accounted for 6(15%) of the total intestinal helminths isolated. In Male stool samples, Hookworm and Ascaris lumbricoides were the most isolated intestinal parasite, while *Schistosoma haematobium* and*Ascaris lumbricoides* were the most isolated intestinal parasites in female stool samples. The least identified intestinal parasite were *Hymenolopsis nana* and *Schistosoma japanicum.*Seven different kinds of intestinal helminths were identified. (Figure 4)

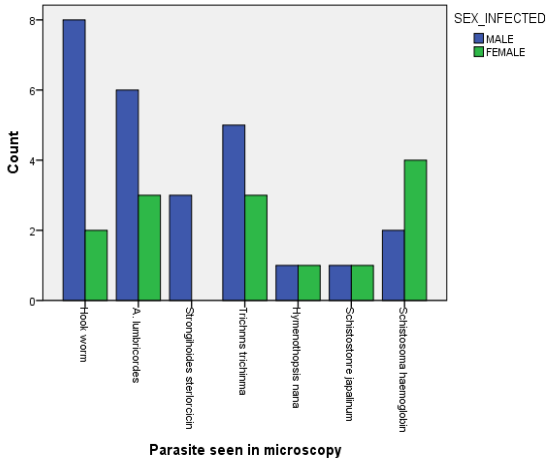

Figure 4: Gender and parasites isolated

There was no significant relationship between the Sex of patients and the acquisition of intestinal parasites (as P= 0.460). (Table 4)

Table4: Gender and Parasite isolated.

		INFECTED STOOL SAMPLE MALE	FEMALE	X^2	P-VALUE
Parasite seen in microscopy	Hook worm	8	2	5.678	0.460
	Ascaris lumbricoides	6	3		
	Strongiloidesstercoralis	3	0		
	Trichuris trichura	5	3		
	Hymenolopsis nana	1	1		
	Schistosoma japanicum	1	1		
	Schistosoma haematobium	2	4		

There was a significant relationship between the age group of patients and the Species of intestinal parasites isolated(P= 0.000). (Table 5)

Table 5. Frequency of parasite species seen across the various age groups

		PARASITE SPECIE							X^2	P-value
		Hook	*A. lumbricord*	*Strongihoi dessterlorc*	*Trichuris trichura*	*Hymenolo psis nana*	*Schistosto nreiapanic*	*Schistoso ma*		
Age range	1-5	0	0	0	0	0	0	0	97.872	0.000
	6-10	5	2	0	1	0	0	1		
	11-15	1	1	0	1	0	0	2		
	16-20	0	0	1	0	1	0	0		
	21-25	1	1	0	2	0	0	1		
	26-30	2	0	0	2	0	0	2		
	31-35	1	5	0	2	0	0	0		
	36-40	0	0	0	0	0	1	0		
	41-45	0	0	2	0	1	0	0		
	46-50	0	0	0	0	0	1	0		
	Total	10	9	3	8	2	2	6		

DISCUSSION

In this Study, the Prevalence of intestinal helminths over the 43months period was 20%(40/200).This Findings were similar to another study done in North eastern Nigeria by Ibrahim

et al(19). Another study done in Irrua reported prevalence of 40% intestinal parasitic infection [20] which was not consistent with the findings in this study.

The Male prevalence of intestinal parasite (13%) was higher than the Female prevalence of intestinal parasite (7%.). This was similar to a study done by Ibrahim at tal (19).

Hookworm (*Ancyclostoma duodenale* and *Necator americanus*) was the most isolated intestinal parasite (accounting for 20%of the total intestinal isolates) in this study. This was followed by *Ascaris lumbricoides*.This was similar to findings of Elemuwa e tal (21) .

The finding that gender doesnot affect the acquisition of intestinal parasite in this study was similar to other previous studies (22-24).

In this Study, Age did not affect the acquisition of intestinal parasites. This was similar to the study by Elemuwa e tal(21), but contrary to some studies which found higher prevalence within the age groups (22, 25).

CONCLUSION

In conclusion, a prevalence of 20% of intestinal Helminthic infections was observed in this study and the parasites that was most frequently isolated from patients accessing care in the University of Benin Tertiary Care centre was Hookworm (Ancyclostoma *duodenale* and *Necator americanus*).

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Gullain – Barre syndrome associated with *Campylobacter jejuni* isolatefrom Rectal swab of a Patient; a University Teaching Hospital, Benin City Experience.

*Lofor P, *Ebeigbe E

*Department of Medical Microbiology, University Of Benin/University of Benin Teaching Hospital Benn City, Nigeria.

ABSTRACT

Background: The unusual immune-mediated acute polyradiculo-neuropathy known as Guillain-Barré syndrome (GBS) is also known as post-infectious polyneuropathy due to the fact that it often manifests after a previous respiratory or gastrointestinal infection.

Although GBS has a wide spectrum of clinical manifestations, the condition most frequently shows up as increasing weakness of the limb, axial, face, or respiratory muscles, along with or without sensory or autonomic abnormality.

Numerous infectious organisms, vaccines, and other circumstances have been found to be GBS triggers.

C. jejuni and *Mycoplasma pneumoniae* are by far the most frequent bacteria associated with GBS.

However there have been several reported cases of GBS triggers which are not as a result of infection or vaccination

This case not only demonstrates the clinical features of Guillain-Barre syndrome but also its severity,

Method: The study was a Retrospective Cross Sectional Study. This involved a review of Case notes of Patients that were admitted in the Children Emergency Room (CHER) of UBTH from January 2019 to December 2019 ,been managed for Gullain-Barre syndrome associated with *Campylobacter jejuni* infection and also a review of their Medical microbiology laboratory test records during management especially their rectal swab Microscopy , Culture and Sensitivity results. It has never being the practice of the Children emergency unit to do rectal swabs for patients with Guillain - Barre syndrome, this was done by the medical microbiology unit upon invitation to see these patients. Patients with incomplete or missing medical data were excluded from the study.

Results: A case report of a male, patient aged 15years. He had recurrent episodes of passage of bloody diarrhoea. The most common initial symptom was weakness in the extremities.

Motor deficit involved all four limbs in this patient. He had ascending progressive paralysis within 48hours of onset of symptoms. There was no history of peptic ulcer disease and no Family history of peptic ulcer disease. No clinical features on examination was suggestive of peptic ulcer disease. There was a history of collection of poultry droppings from a nearby poultry for manure in family farm behind the house. There was history of dyspnoea and tachypnoea respiratory cycle was 63 cycles per minute, Rectal Swab showed Gram negative " gull wing" "s" shape bacilli, urease negative, Catalase positive, Oxidase positive characteristic of *Campylobacter jejuni*. There was heavy growth on Blood agar and Butzler's medium within 6 days of aerobic incubation sensitive to genticin, Erythromycin, Azithromycin and clarithromycin. He was placed on Erythromycin 250 mg 6 hourly for 14 days and recovered fully with Ambulation within 5 days on Erythromycin.

Conclusion: This case report emphasises a relatively inexpensive and straightforward faecal specimen by rectal swab, free of procedural complications like bowel perforation and readily available faecal specimen in the laboratory diagnosis and isolation of *Campylobacter jejuni ,* a cause (among other causes) of Gullain-Barre Syndrome, which is a medical emergency in most cases.Also that with the use of antibiotic therapy, most patients with GBS associated *Campylobacterjejuni* infection if they present early ,make full recover from enteric campylobacter infections.

Keyword: Gullain – Barre syndrome, *Campylobacter jejuni,* Rectal swab, Benin City.

INTRODUCTION

The unusual immune-mediated acute polyradiculo-neuropathy known as Guillain-Barré syndrome (GBS) is also known as post-infectious polyneuropathy because it often manifests after a previous respiratory or gastrointestinal illness [1,2]. It can also be brought on by immunisations and affects both children and adults. Although GBS has a wide range of clinical manifestations, the condition most frequently shows up as increasing weakness of the limb, axial, face, or respiratory muscles, along with or without sensory or autonomic dysfunction [1,2].

Corresponding author
Ejime Ebeigbe
Department of Medical Microbiology, University of Benin TeachingHospital, Benn City, Nigeria.
E-mail: ejimenicholas@gmail.com.

Numerous infectious organisms, vaccines, and other circumstances have been found to be GBS triggers.

Although it might undulate, the disease history is often monophasic. Up to one-third of instances involving respiratory muscles require artificial breathing, and up to twenty percent of those cases do so.

According to reports, the prevalence of GBS is 1-2/100,000/y [3]. Worldwide, an estimated 100,000 new cases are diagnosed each year. Males are afflicted more commonly than females [3). Every 10 years of age increase results in a 20% increase in incidence [2].

The majority of times that GBS occurs, infections are the cause [2].

The pathophysiology of GBS has been linked to bacteria and viruses. Accordingly, in a study in approximately two-thirds of cases, GBS is preceded by a symptomatic infection such as *Campylobacter jejun*i (*C. jejuni*), Epstein-Barr virus (EBV), cytomegalovirus (CMV), or influenza [4). *C. jejuni* and *Mycoplasma pneumonia*e are by far the most frequent bacteria that cause GBS [5]. CMV, Zika, and dengue are the three viruses that cause GBS most frequently [6].Humans typically contract C. jejuni through food consumption, especially through the eating of raw or undercooked poultry meat, tainted, unpasteurized milk, or water-based environmental sources [*7]. C. jejuni* colonises the distal ileum and colon after uptake [7)

Human *C. jejuni* infection post-infectious morbidity is significantly influenced by the shape of the pathogenic Lipo-oligosaccharide (LOS,), which activates the innate immune system via Toll-like receptor (TLR)-4 signalling [8]. TLRs (Toll-Like Receptors) identify specific molecular patterns linked with pathogens. They have a crucial role in inflammation, immune-cell modulation, survival, and proliferation as well as the initial line of defence against invasive infections. TLR1, TLR2, TLR4, TLR5, TLR6, and TLR11 are found on the cell surface, whereas TLR3, TLR7, TLR8, and TLR9 are found in the endosomal/lysosomal compartment. There are currently 11 members of the TLR family known to exist. The "molecular mimicry" between surface LOS antigens and ganglioside antigens (ceramides) on the surface of myelin sheaths or the axolemma is what causes GBS to develop through *C. Jejuni*.(9).

There have been several reported cases of GBS triggers which are not as a result of infection or vaccinations. Angio-immunoblastic T-cell lymphoma was the cause of GBS in a male patient in his 80s [10]. Although the pathophysiological rationale remained obscure, it was hypothesised that a tumour, a paraneoplastic condition, or an autoimmune reaction brought on by a typical exposure could have caused the immunological dysregulation [10]. GBS has also been described as a condition following a kidney donation [11).

Additionally identified as rare GBS triggers are intravenous ganglioside injection for trauma, surgery, stroke, peripheral neuropathy, and surgery [12].

According to culture studies, many Guillain-Barre syndrome patients also have *C jejuni* infection in their stools when their neurologic symptoms first appear. We present a case of Guillain-Barre syndrome linked to a *C.jejuni* infection in the gastrointestinal tract. This case not only demonstrates the clinical features of Guillain-Barre syndrome but also its severity.

CASE REPORT

A 15-year-old boy came to the hospital complaining of weakness in the lower extremities. Ten days earlier he had developed nausea, vomiting, and recurrent bloody diarrhoea associated with fever and chills after collection of poultry droppings from a nearby poultry for manure in family farm behind the house. The gastrointestinal symptoms subsided after 5 days but recurred after 2 days. His gastrointestinal symptoms did not resolve, necessitating his presentation and admission in the Children emergency ward of University of Benin Teaching Hospital. He had ascending progressive paralysis within 48hours of onset of symptoms. There was no history of peptic ulcer disease and no Family history of peptic ulcer disease.

There was history of dyspnoea and tachypnoea respiratory cycle was 63 cycles per minute, When the patient was admitted into the ward, 48 hours after being seen in the emergency department, he was paralyzed in all four limbs. He had grade 2/5 power in his upper extremities and grade 2/5 power in his lower extremities at the time of admission, and all deep tendon reflexes were absent.

Results of laboratory studies at the time of admission included a white blood cell count of 8,700/uL with a normal differential (presumably as a result of previously administered antibiotics).Rectal Swab showed Gram negative " gull wing" "s" shape bacilli, urease negative, Catalase positive, Oxidase positive characteristic of *Campylobacter jejuni* . There was heavy growth on Blood agar and Butzler's medium within 6 days of aerobic incubation sensitive to genticin, Erythromycin, Azithromycin and clarithromycin.

DISCUSSION

Campylobacter jejuni pathogen is highly susceptible to heating, but infections can be acquired by eating undercooked meat or through cross-contamination of kitchen utensils and surfaces. Poultry is the most important reservoir, and several studies indicate that 50 to 70% of sporadic human infections are caused by *Campylobacter species.* (13).

Person-to-person transmission is uncommon, but there are a few exceptions. One is perinatal transmission from mother to child, as a result of the infant's passage through the birth canal.in these instances the mothers are not necessarily symptomatic. (14). The second is when carers are exposed to faeces from infants or other incontinent people. Except for homosexual guys, adults rarely transmit diseases to one another.

Infection with Campylobacter occurs year-round, increasing in the summer in the majority of developed nations. Men and women contract the disease at comparable rates, however some data suggests women may be somewhat more at risk. Young children, especially those under 1 year old, have the highest age-specific attack rates, whereas those between the ages of 15 and 29 see a second wide peak in attack rates. In developing nations, where children may have 10 or more infections in their first two years of life, infection is considerably more prevalent. As people get older, attack rates drop and more infections go clinically quiet.

Bacteremia, which is seldom reported in part because of the organism's fastidious nature and the fact that blood cultures are frequently skipped, it is most frequent in patients who have impaired immune systems and are quite old.(15).Three main patterns have been identified for extraintestinal C jejuni infection. Days after the patient has recovered, the first condition is, transitory bacteremia in a previously healthy host, which is frequently identified by isolation from blood cultures. These patients typically do not require therapy. The second is persistent bacteremia, or seeding to an extraintestinal location in a healthy host together with enteritis. Responses to antibiotic therapy and drainage techniques are typically positive. Third, immunocompromised hosts are susceptible to bacteremia or profound infections. Some of these infections are fatal, and they frequently last for a long time or come back. For Campylobacter infections Meninges, endovascular tissue, including the heart valve, peritoneal fluid, and soft tissues are a few of the other frequent extraintestinal locations,

but many other sites have been documented as well.

Hepatitis, interstitial nephritis, reactive arthritis in those who are HLA-B27 positive (16), a truncal macular rash, and Guillain-Barre syndrome are nonsuppurative consequences of *C.jejuni* infections.

In 1984, the first instance of *C .jejuni*-related Guillain-Barre syndrome was reported; since then, numerous other reports have been made public.(17,18). The only bacterial infection that consistently precedes Guillain-Barre syndrome is *C .jejuni*, which is currently believed to be the most frequent antecedent infection to the condition. (19) According to the description, the organism is a gram-negative bacterium belonging to the Campylobacter genus and related genera. This species seems to commonly colonise the intestines of people, other mammals, and birds. The likelihood that C jejuni infections play a part in the development of Guillain-Barre syndrome is supported by the high prevalence of these infections as well as by their propensity to penetrate tissue and cause inflammation. (20, 21).

In 50 and 75 percent of all instances of Guillain-Barre syndrome, jejuni infection has been found to be responsible. (20,21) Anecdotal reports are the first type of proof that Campylobacter infection causes Guillain-Barre syndrome. Serologic tests have revealed anti-C .jejuni antibodies in serum from Guillain-Barre syndrome patients, a finding that is consistent with a recent infection. This is the second line of evidence. A large percentage of Guillain-Barre syndrome patients had *C jejuni* in their faeces at the time of the onset of neurologic symptoms, according to culture studies. (22,23) Additionally, it has been noted that when C jejuni infection precedes Guillain-Barre syndrome, neurologic symptoms are more severe and more likely to be curable. (24). The risk of developing Guillain-Barre syndrome might be higher after infection with *C.jejuni* type 0: 19.(25).

In the treatment of Campylobacter-associated Guillain-Barre syndrome, plasma exchange was found to reduce the requirement for hospital treatment, with cost savings that outweighed the price of the medication.

Several antibiotics, such as macrolides, tetracyclines, quinolones, the aminoglycosides, chloramphenicol, and nitrofurantoin are effective against C jejuni in vivo. (26,27). Whether the infections arise naturally or as a result of antibiotic therapy, almost all patients make a full recovery from enteric Campylobacter infections. There have occasionally been fatalities in developed nations, particularly in elderly or immunocompromised people. The high morbidity and mortality rates linked to diarrheal diseases in underdeveloped nations are likely caused by a significant proportion of infections that occur very early in life before immunity takes over. This case highlights several interesting features of Guillain-Barre syndrome and C jejuni infection. Motor deficit involved all four limbs in this patient. He had ascending progressive paralysis within 48hours of onset of symptoms. There was no history of peptic ulcer disease and no Family history of peptic ulcer disease .No clinical features on examination of peptic ulcer disease. There was a history of collection of poultry droppings from a nearby poultry for manure in family farm behind the house before onset of symptoms.

CONCLUSION

This case report emphasizes a relatively inexpensive and straightforward faecal specimen by rectal swab, free of procedural complications like bowel perforation and readily available faecal specimen in the laboratory diagnosis and isolation of *Campylobacter jejuni*, a cause (among other causes) of Gullain-Barre Syndrome, which is a medical emergency in most cases. Also, that with the use of antibiotic therapy, almost all patients make full recovery from enteric campylobacter infections.

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Awareness, knowledge and uptake of human papillomavirus vaccine among female undergraduates in a University in Southwestern, Nigeria

*Oluwole T. O. [1,2], Otaigbe I. I. [1,2], Okangba C. C. [1], Shonekan O.[1], Nwadike V. U.[1], Tayo B.[1], Okunbor H. N.[2], Akeredolu A. A.[1], Omeonu A. C.[1], Opabola T. E.[1], Asaolu I. O.[3], Alomooluwa O. H.[3], Otis-Ehiemuan O. A.[3], Olatunji J. O.[3], Taiwo D. O.[3], Ikuelogbon O. E.[3],Elikwu C. J.[1,2].

[1]Department of Medical Microbiology, School of Basic Clinical Sciences, Benjamin Carson (Snr.) College of Health & Medical Sciences, Babcock University, Nigeria.
[2]Department of Medical Microbiology, Babcock University Teaching Hospital, Nigeria.
[3]Benjamin Carson (Snr.) College of Health & Medical Sciences, Babcock University, Nigeria.

Corresponding author: Oluwole, Temitayo O.
Department of Medical Microbiology, School of Basic Clinical Sciences, Benjamin Carson (Snr.) College of Health & Medical Sciences, Babcock University, Nigeria.
Email: treeyof@yahoo.com

ABSTRACT

Background: Human papillomavirus (HPV) is the most prevalent sexually transmitted infection globally. HPV-associated cervical cancer is the second most common cancer among women in Nigeria. The HPV vaccine has been demonstrated to be highly effective against the HPV types implicated in 70% of cervical cancer cases. The HPV vaccine was approved in Nigeria in 2009. However, there have been reports of low vaccine uptake especially in young people.

Aim: This study sought to investigate the level of information regarding HPV infection, HPV vaccine and possible reasons for vaccine hesitancy among female undergraduate students in a University in Southwest, Nigeria.

Methods: This was a cross-sectional, descriptive study of 242 female undergraduate students of Babcock University, Nigeria. Self-administered questionnaires were used to obtain participants' socio-demographic characteristics, assess their knowledge of HPV infection and HPV vaccine, self-reported HPV vaccination status, and possible reasons for vaccine hesitancy.

Results: The majority, 68.2% and 64% of the participants had heard about HPV infection and HPV vaccine respectively. However, less than half of the participants knew the diseases associated with HPV, the occurrence of asymptomatic infection and the unavailability of a cure. Only 12.7% (n=29) reported that the vaccines are effective. Only 3.7% (n=9) of the participants had received HPV vaccine. No reason (41.8%), inadequate information about the vaccine (23.9%), and complications due to vaccination (16.4%) were some of the reasons for vaccine hesitancy.

Conclusion: There was a low level of knowledge of HPV infection and HPV vaccine. Hence, educational intervention is crucial to improve the knowledge and attitude towards the HPV vaccine.

Keywords: Human papillomavirus, HPV knowledge, HPV vaccine, HPV prevention, Vaccine hesitancy, University students.

INTRODUCTION

Human papillomavirus (HPV) is the most common sexually transmitted organism in humans with about 75% of sexually active men and women acquiring the infection at some point in their lives.[1–3] It is easily transmitted by skin-to-skin or skin-to-mucosa contact through oral, vaginal and anal sex and it can be transmitted by asymptomatic individuals.[4,5] The global prevalence of HPV is about 11-12% with considerable regional variation; the highest prevalence is seen in sub-Saharan Africa (24%), Eastern Europe (21%) and Latin America (16%).[6–8] Over 200 HPV genotypes have been described and they have subsequently been classified into high-risk or low-risk based on their oncogenic potential. High-risk HPV has been attributed to 4.8% of the cancer burden worldwide.[4,6,9] High-risk HPV genotypes have been implicated in 99.7% of cervical cancers.[9] Infections caused by the low-risk HPV genotypes rarely cause cancer. The most prevalent HPV genotypes worldwide are high-risk genotypes 16 (3.2%), and 18 (1.4%).[8,10] HPV 16 and 18 contribute to 70% of cervical cancers.[11,12]

Cervical cancer is the fourth most common cancer globally and is estimated that a woman dies from cervical cancer every 2 minutes.[13] It disproportionately affects women in low- and middle-income countries (LMICs) as the majority of the cases and deaths occur in these countries.[13] In Nigeria and Africa in general, cervical cancer is the second most common cancer among women.[14] In Nigeria, the estimated annual incidence and the annual death toll are 12,075 and 7,968 respectively.[15] It is also estimated that about 3.5% of women in the general population have HPV-16/18 cervical infection at a given time.[15]

HPV is usually acquired shortly after sexual debut.[16,17] Over 20% of women have HPV infection within 3 years of coitarche (first sexual intercourse) in Nigeria.[18] The range of median age at coitarche in females is 16.7-17.9 years and about 15.6% of 15-year-old girls have had sexual intercourse.[15] Hence, human papillomavirus infection is most prevalent in the young population with the highest rate between the ages of 18 and 30 years.[18] Furthermore, the period of adolescence and youth is associated with risky behaviours and exploratory sexual practices which further increase the risk of HPV infection and could threaten long-term health and well-being.[16,17] Hence, there is a need to put in place an active prevention program.

Primary prevention of HPV infection and thus cervical cancer through vaccination has been proven as the most effective means of prevention. HPV vaccine was first introduced in 2006 and was available for use in females between the ages of 9-26 years (preferably before sexual debut). This vaccine has been introduced to the childhood immunization program in many countries for girls aged between 9 and 13 years. HPV vaccine was introduced in Nigeria in 2009. However, over a decade later, studies have reported low vaccine coverage since its introduction with factors such as low level of awareness, prohibitive costs and limited availability of the vaccine as major barriers to its uptake.[20–25]In October 2023, the HPV vaccine was integrated into the Expanded Programme on Immunization (EPI) in Nigeria, aimed at vaccinating 7.7 million girls aged 9-14. Hence, female adolescents within this age group, are eligible to receive single-dose HPV vaccine at no cost.[26]

Several studies have reported poor awareness and knowledge of HPV infection and HPV vaccine in Nigeria.[24,27–31] Furthermore, there have been reports of vaccine hesitancy due to widespread misinformation.[32,33] Hence, the need to access the level of information on HPV

infection and HPV vaccine, the willingness for vaccination in unvaccinated participants and possible reasons for vaccine hesitancy.

The study aimed to investigate the level of information regarding HPV infection and HPV vaccine among female University students, the self-reported vaccination rate, vaccine intention in unvaccinated participants and possible reasons for vaccine hesitancy.

MATERIAL AND METHODS

Study Design and Setting

This was a descriptive, cross-sectional study among female undergraduate students of Babcock University, a private University owned by the Seventh-Day Adventist Church. The University is located in Ilishan-Remo, Ogun State, Nigeria and has a student population of about 10,000. The study was conducted over a 6-month, from September 2022 to February 2023.

Study Population

The study was conducted among female undergraduate students between the ages of 16 - 26 years.

3.4 Sample Size Determination and Sampling Method

The sample size was determined using the Fisher formula:

To minimize errors due to non-compliance, 10% was added to the sample size resulting in a final sample size of approximately 213. The study participants were selected by convenience sampling

Inclusion criteria

- Female undergraduate students of Babcock University
- Within the age range of 16 - 26 years of age
- Persons who were willing to fill out the questionnaire

Exclusion criteria

- Female students outside the age range of 16 - 26 years
- Male students
- Female students who were unwilling to fill out the questionnaire

Ethical consideration

Ethical clearance was obtained from the Babcock University Health Research and Ethics Committee before the commencement of the study (BUHREC692/22). Participation was voluntary, written informed consent was sought and consenting female undergraduate students within the age range were recruited into the study. Anonymity was ensured by not obtaining personal information such as names and addresses from participants. Participants' confidentiality was maintained and data collected were saved in a password-protected laptop only accessible by the research team.

Data collection

Pre-tested, self-administered, questionnaires were filled by participants. The questionnaire consisted of three parts. Part 1 explored the socio-demographic characteristics and sexual history of participants. The demographics included the age, school/faculty, year of study and marital status. The sexual history addressed history of sexual intercourse, age at initiation of sexual intercourse, number of lifetime partners, condom use, and history of sexually transmitted infection.

Part 2 consisted of questions regarding HPV infection such as knowledge of the virus, disease caused by the virus, persons at risk of the infection, mode of transmission, presence of cure and effective means of prevention. Part 3 assessed participants' knowledge of the HPV vaccine, who should be vaccinated, the effectiveness of the vaccine, the best age for vaccination, self-reported vaccination status, willingness to receive the HPV vaccine and possible reasons for vaccine hesitancy.

Data analysis

Data collected was analysed using IBM_SPSS Statistics for Windows version 22. Standard descriptive statistics were used to summarise the data.

RESULTS

Socio-demographic and behavioural characteristics

A total of 242 female undergraduate students participated in the study. The mean age of the participants was 19.1 years (SD = 1.3, range 16 – 25). As shown in Table I, the majority (36.4%) of the participants were in the School of Health and Medical Sciences and the majority were in their 3rd and 4th years of study, 34.3% and 32.6% respectively. All the participants were unmarried. About 85.4% of the participants reported never to have had sexual intercourse. The mean age of first sexual intercourse was 18.2 years (SD = 1.6, range 15 – 21). The number of lifetime sexual partners ranged from 1 - 7 with about 48.5% of them having more than one lifetime sexual partner. Only 34.3% reported using a condom during every incidence of sexual intercourse. One of the participants reported a previous history of syphilis. The majority (61.7%, n=132) had no concern about possible HPV infection while 38.3% (n=82) were concerned about possible HPV infection.

Knowledge of HPV

The majority 62.2% of the participants had heard of HPV. As shown in Table II, the most common sources of information about HPV infection among the participants included school (40.5%), social media (30.2%) and seminars (29.3%). About 41% of the participants recognized HPV as the aetiologic agent of genital warts and 38% as the aetiological agent of cervical cancer. Most (83.9%) of the participants correctly identified that HPV is different from HIV. The majority (52.1%) of the participants reported that both males and females are at risk of HPV infection. Most of the participants identified unprotected vaginal sex (75.6%), anal sex (82.2%), and oral sex (42.1%) as modes of transmission of HPV. About 34.3% of the participants reported that HPV is common in society and 41.7% reported that symptoms of HPV infection are not always obvious. Only 27.3% of participants reported that there is no cure for HPV infection while 56.2%, 47.9%, and 46.7% reported that abstinence, vaccination and use of condoms are the most effective means of prevention of HPV infection.

Knowledge of HPV vaccine

Of the 242 participants, 64% were aware of the HPV vaccine. School (40.1%), hospital/health workers (24.0%) and the internet (22.7%) were the three most common sources of information about the HPV vaccine. Table III shows that only 3.7% of the participants had received the HPV vaccine while 96.3% were yet to be vaccinated. About 34% reported that both males and females could be vaccinated against HPV and only 12.7% of the participants reported that the HPV vaccine is effective. The majority (60.4%) were willing to receive the HPV vaccine while 20% were unwilling to receive the vaccine. Reasons for vaccine hesitancy included inadequate information about the vaccine (23.9%), complications due to the vaccine (16.4%), need for parental consent (11.9%) and high cost of vaccine (6.0%). Table 4 shows the awareness of the respondents and the rate of HPV vaccine uptake.

DISCUSSION

The study aimed to assess the level of knowledge of HPV infection and uptake of HPV vaccine among female undergraduate students at Babcock University. In this study, we observed sub-optimal knowledge of HPV infection and HPV vaccines as well as very low vaccine uptake among the students and high levels of willingness to receive the vaccine.

The proportion of participants with awareness of HPV infection and HPV vaccine (68.2% and 64% respectively) is similar to the level of awareness observed in a study among new intake nursing students in Benin City, Nigeria which reported 68.5% and 63% respectively.[32] The level of awareness of HPV was higher than that of a similar study conducted earlier in the same University among female undergraduate students which reported an awareness of 54.5%.[28] It is also higher than reports of other studies about the awareness of HPV infection and HPV vaccine among undergraduate students in Niger (34.8% and 25.0% respectively)[31], Kebbi (29.0% and 29.2% respectively)[29], Edo (5.2% and 17.0% respectively)[24], and Lagos (17.7% and 14.4% respectively)[27]. However, it is lower than that reported in a study among medical and allied health students in Northern Nigeria (80%), and medical students in Lagos, Nigeria (85.4% and 69.3% respectively) which reported the level of awareness as 80%.[34]

Overall, there was a low level of knowledge of HPV infection as less than half of the participants were aware of HPV being implicated in genital warts, cervical and vaginal cancers, less than one-third were aware of HPV being implicated in vulvar, penile and head and neck cancers as well as laryngeal warts. In addition, less than half of the participants were aware of the possible asymptomatic nature of HPV infection and the unavailability of a cure. Although, more than half of the participants reported the role of abstinence from sexual intercourse as an effective means of prevention of HPV and about half of the participants reported the role of vaccination, use of condoms and avoiding multiple sexual partners in effectively preventing HPV infection. Furthermore, about 1 in 4 of the participants, reported a misconception (washing of genitalia after sexual intercourse) as an effective means of prevention of HPV infection.

Some studies have also reported a low level of knowledge about HPV infection among undergraduate students.[34,35,35,36,27,30,29,31,25] The knowledge gaps observed in this study highlight the urgent need for early education on cervical cancer prevention and HPV vaccination at all levels of education in Nigeria. The source of information for over one-third of the participants was school. Thereby, further emphasizing the need for HPV education at all levels of the education system. The internet and social media also play a big role in the education on HPV infection and promotion of HPV vaccines as about one-quarter to one-third of participants obtain information via these channels.

A high proportion of participants had a positive attitude to the HPV vaccine and were willing to be vaccinated. This is similar to reports among students in Benin[36], Lagos[27,37]. However, a low level of vaccine uptake (3.7%) was observed. The low vaccine uptake in this study is a reflection of the low level of knowledge of the HPV vaccine. Lack of awareness of the HPV vaccine negatively impacts the vaccine uptake. Low HPV vaccine uptake has also been reported in several studies in Nigeria such as Gombe (3.7%)[30], Lagos (2.6% and 5.3%)[25,37], Benin (0.9% and 3.7%)[32,36], Port Harcourt (5.1%)[21], Ogun (14.2%)[18]. However, higher rates of HPV vaccine uptake have been reported in studies in Germany (67%)[38] and the United States of America (47.3%)[39].

Factors contributing to vaccine hesitancy among the participants include inadequate information about the vaccine, concerns about possible complications of the vaccine, need for parental consent and high cost of the vaccine, over one-third of the participants gave no reason for vaccine

hesitancy. None of the participants highlighted religious reasons as a possible barrier to HPV vaccine uptake. This is similar to the report from a study in Lagos which highlighted similar reasons for low vaccine uptake among participants. However, some of the participants reported a lack of access to vaccines (40.8%) and religious reasons (17.7%) as barriers to vaccine uptake which was not observed in our study.[37] Adequate information about the HPV vaccines and their effectiveness is necessary to improve vaccine uptake while allaying fears and concerns about vaccine-related complications. There is also a need to extend the free vaccines to older individuals to ease the high cost of the vaccine while attaining a wider vaccine coverage and thereby reducing the prevalence of HPV infection and the incidence of cervical cancer.

Limitations of the study: The study may have been prone to information and recall biases. Furthermore, a more extensive quantitative study and qualitative interviews are desirable to elucidate the observations more substantively.

CONCLUSION

This study showed a low level of knowledge of HPV infection and HPV vaccineand a high level of willingness to receive the HPV vaccine but with an extremely low level of vaccine uptake. There is a need for an intense health promotion programme to raise awareness of HPV infection and educate on the existence of HPV vaccines at all levels of education in the country to combat the scourge of HPV infection and by extension cervical cancer.

Conflict of interest: The authors declare no conflict of interest

Authors' Contribution: All authors contributed to the conceptualization, design, data collection, data analysis/interpretation, preparation and approval of the manuscript for publication.

Running title: Awareness and uptake of HPV vaccine

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Table I: Socio-demographic and behavioural characteristics of the participants

Variables	**Frequency**	**Percentage (%)**
Age range (Years)		
16 – 18	95	39.2
19 – 21	125	51.6
22 – 24	21	8.7
>24	1	0.4
School/Faculty		
Health and medical sciences	88	36.4
Social science	56	23.1
Public and allied health	5	2.1
Management science	10	4.1
Law and security studies	3	1.2
Education and humanities	34	14.0
Science and technology	22	9.1
Nursing science	11	4.5
Computing and engineering science	13	5.4
Year of study		
1st	8	3.3
2nd	54	22.3
3rd	83	34.3
4th	79	32.6

5th	17	7.0
6th	1	0.4
Residence		
On campus	227	93.8
Off campus	15	6.2
Marital status		
Single	242	100
Married	0	0
Separated	0	0
Divorced	0	0
Have you ever had sex?		
Yes	35	14.6
No	205	85.4
Total	240	100
Age at first sexual intercourse		
15-16	5	15.6%
17-18	13	40.6%
19-20	10	31.2
21-22	4	12.5%
Total	32	100
Number of lifetime sexual partners		
1	17	51.5
2	11	33.3
3	2	6.1
4	1	3.0
5	1	3.0
>5	1	3.0
Total	33	100

Use of condoms		
Always	12	34.3%
Sometimes	11	31.4%
Rarely	9	25.7%
Never	3	8.6%
Total		
Positive history of smoking	7	2.9
Positive history of alcohol ingestion	36	14.9
History of use of recreational drugs	8	3.3

Table II: Knowledge of HPV Infection

Variables	**Frequency**	**Percentage (%)**
Heard of HPV		
Yes	165	68.2
No	77	31.8
Source of information		
TV/Radio	28	11.6
Social media	73	30.2
Internet	61	25.2
School	98	40.5
Hospital/health worker	55	22.7
Seminar/public talk	71	29.3
Friends	39	16.1
Print media	39	16.1
Parents	35	14.5
Diseases caused by HPV		
Genital warts	99	40.9
Cervical cancer	92	38.0

Vaginal cancer	84	34.7
Penile cancer	27	11.1
Chlamydia	29	12.0
Diabetes mellitus	30	12.4
Vulva cancer	58	24.0
Head and neck cancer	7	2.9
Gonorrhoea	20	8.3
Laryngeal warts	8	3.3
Syphilis	16	6.6
Are HIV and HPV different		
Yes	203	83.9
No	11	4.5
No idea	28	11.6
Who is at risk of HPV infection?		
Females only	66	27.3
Males only	8	3.3
Both males and females	126	52.1
No idea	42	17.4
Mode of transmission of HPV		
Unprotected vaginal sex	183	75.6
Oral sex	102	42.1
Anal sex	199	82.2
Hand shake with infected person	4	1.6
Sharing of contaminated sharp objects	27	11.1
Blood transfusion	40	16.5
Sharing of toilets with infected person	19	7.8

Kissing an infected person	5	2.1
Mosquito bites	1	0.4
Is HPV infection common in the society?		
Yes	83	34.3
No	65	26.8
No idea	94	38.8
Are the symptoms of HPV infection always obvious?		
Yes	25	10.3
No	101	41.7
No idea	116	47.9
Is there a cure for HPV infection?		
Yes	46	19.0
No	66	27.3
No idea	130	53.7
What is the most effective means of prevention of HPV		
Oral contraceptive use	39	16.1
Use of condoms	113	46.7
Douching	22	9.1
Washing of genitals after sex	59	24.3
Abstinence	136	56.2
Avoid having multiple sexual partners	111	45.9
Regular pap smear	73	30.2
Regular blood test	37	15.3
Vaccination	116	47.9

Table III: Knowledge of HPV vaccine

Variables	Frequency	Percentage (%)
Heard of HPV vaccine		
Yes	155	64.0
No	87	35.9
Source of information		
TV/Radio	13	5.4
Social media	53	21.9
Internet	55	22.7
School	97	40.1
Hospital/health worker	58	24.0
Seminar/public talk	44	18.2
Friends	24	9.9
Print media	7	2.9
Parents	19	7.8
Who can be vaccinated against HPV		
Males only	3	1.3
Females only	72	30.4
Both males and females	80	33.8
No idea	82	35.6
Total	237	100
Is HPV vaccine effective		
Yes	29	12.7
No	68	29.7
No idea	132	57.6
Total	229	100
Best age for vaccination (years)		
9-13	45	18.6

14-20	41	16.9
21-30	30	12.4
Any age	37	15.3
No idea	89	36.8
History of HPV vaccination		
Yes	9	3.7
No	233	96.3
Willingness to receive HPV vaccine		
Yes	142	60.4
No	47	20.0
No idea	46	19.6
Total	235	100
Reasons for vaccine hesitancy		
Inadequate information about the vaccine	16	23.9
Parental consent needed	8	11.9
High cost of vaccine	4	6.0
Complications due to vaccination	11	16.4
No reason	28	41.8
Total	67	100

LIPID PROFILE AND OBESITY IN WOMEN WITH PREECLAMPSIA
RUNNING TITLE : HYPERLIPIDEMIA IN PREECLAMPSIA

*Onovughakpo-Sakpa EO, *Ayinbuomwan E

*Department of Chemical Pathology, University of Benin/ University of Benin Teaching Hospital, Benin City, Edo State.

ABSTRACT

Background: Maternal predisposition to preeclampsia could be explained by abnormal lipid metabolism which may have a role to play in the promotion of oxidative stress and vascular dysfunction seen in preeclampsia and this is avoidable with timely and effective care. One of such care is close monitoring of the lipid profile which would no doubt improve clinical outcome.

Aim : To estimate lipid profile and assess obesity in women with preeclampsia.

Method: This study had a total of 196 respondents. The subjects were registered pre-eclamptic (PE) ante-natal care (ANC) patients of the Obstetrics and Gynaecology Department of Government Specialist Hospital, Benin City, Edo State, Nigeria. The control subjects were registered normotensive ANC patients (NPW) and analbuminuric hypertensive pregnant (AHPW) patients of the same Department, and within the same age range. Ethical clearance was obtained from the Edo State Health Management Board. Structured questionnaires were administered to the study groups. Body mass index (BMI) was calculated from their weights and heights. Standardized colorimetric assay kit was used for lipid profile. Data were analyzed using SPSS version 16.0 and the level of significance was set at 95% ($p < 0.05$).

RESULTS: The results revealed a significantly ($P<0.05$) higher BMI in PE (33.35±0.75Kg/m^2) when compared with NPW (26.57±0.66Kg/m^2) and AHPW (24.84±1.26Kg/m^2. The mean index systolic and diastolic blood pressures were found to be significantly ($p< 0.05$) higher in PE (160.24±9.34mmHg and 108.56±8.02mmHg) than in NPW (106.00±11.23mmHg and 63.38±4.32mmHg) and AHPW (141.38±14.21mmHg and 98.21±4.94mmHg).The mean total cholesterol (TC), triglyceride (TG) and low density lipoprotein (LDL-C) were significantly ($P<0.05$) increased in PE (228.44±3.39mg/dl, 154.73±3.96mg/dl and 146.17±2.85mg/dl) and AHPW (192.13±21.21mg/dl, 134.51±12.62mg/dl and 141.23±10.25mg/dl) when compared with NPW (179.53±5.97mg/dl, 122.92±5.52mg/dl and 116.83±5.48mg/dl). However mean high density lipoprotein (HDL-C) was significantly ($p < 0.05$) lower in PE (38.54 ± 0.61mg/dl) and AHPW (35.63±8.05mg/dl) than in NPW (45.61±1.32mg/dl). TC and TG were significantly ($P<0.05$) increased in the 2ndtrimester in PE (205.76 ± 5.23 mg/dl, and 176.03 ± 6.20 mg/dl,) and AHPW (190.57 ±11.23mg/dl and 165.65±9.44mg/dl) than in NPW (159.44±9.15mg/dl and 113.63±9.16mg/dl) and the 3rdtrimesters(PE: 211.13±4.63mg/dl and 193.43±4.97mg/dl, AHPW: 202.82±10.13mg/dl and 180.94±11.75mg/dl, NPW: 173.82±8.02mg/dl and 130.35±6.12mg/dl) while HDL-C was significantly ($P<0.05$) lower in PE(38.44±0.91mg/dl) and AHPW(33.98±7.55mg/dl) than NPW(45.67±1.17mg/dl) in the 3rd trimester. Mean serum LDL-C and TG were significantly ($P<0.05$) higher in severe (155.61±5.10mg/dl and 160.72±5.20mg/dl) than in mild (142.79±3.43mg/dl and 147.39±5.60mg/dl) PE.

CONCLUSION: This study showed that abnormalities of lipid metabolism and obesity may contribute to the severity of preeclampsia and thus lipid profile can be used as a biomarker for preeclampsia.

KEY WORDS : Preeclampsia, Hyperlipidemia, Obesity, Overweight,

INTRODUCTION

Nearly one tenth of all maternal deaths in Africa and Asia and one-quarter in Latin America are associated with hypertensive diseases in pregnancy, a category that encompasses pre-eclampsia.[1]Pre-eclampsia(PE) is a disorder of pregnancy characterized by high blood pressure and a large amount of protein in the urineand it is one of the leading causes of maternal and perinatal morbidity and mortality worldwide.[2]

Corresponding author
Ekiye ayinbuomwan (Consultant chemical pathologist fmcpath)
Department of chemical pathology, University of Benin/ University of Benin Teaching Hospital, Benin city, Edo state.
Email: ekiyeayinbuomwan@gmail.com

In pre-eclampsia, the systolic blood pressure is≥140mmHg, diastolic ≥90 mmHg and there is proteinuria of at least 300 mg in 24hour urine sample collection. According to the World Health Organization (WHO), the incidence of preeclampsia ranges from 2-10% of pregnancies worldwide with 1.8 – 16.7% occurring in developing countries while developed countries have a rate of 0.4%.In Nigeria, preeclampsia affects 37,000 women annually with a prevalence rate of 5.6% to 7.6% of pregnancies in Southern Nigeria.[3,4,5] Onset of symptoms occur in the late second or third trimester, most commonly after the 32nd week. Some women will experience pre-eclampsia as early as 20weeks, though this is rare and it may also occur in the immediate postpartum period.[6]Women with mild proteinuria generally have no symptoms. However, women with severe pre-eclampsia (blood pressure ≥160/110 mmHg, proteinuria>2.5g/24h) may have symptoms such as renal insufficiency, liver diseases, haematological and neurological disturbances.[2]

During pregnancy, there is increased lipolysis and mobilization of triglyceride from adipocytes. Increased production of VLDL in combination with impaired lipoprotein lipase activity leads to ineffective clearance of triglyceride-rich lipoproteins such as VLDL and VLDL-remnants which eventually result in increased triglyceride levels.[7] Hepatic lipase is responsible for the increased synthesis of TGs whereas the decreased activity of lipoprotein lipase is responsible for decreased catabolism at the adipose tissue level, the net effect of which is increased circulating TGs.[8] There is also accumulation of LDL due to decreased activity of lipoprotein lipase and LDL, total cholesterol and triglyceride levels increase from the second trimester until the third trimester with increasedrisk of development of atherosclerosis.[9,10]

The prevalence of maternal obesity is rising in some antenatal clinics, in line with the prevalence of obesity in the general population with its attendant complications such as gestational diabetes mellitus (GDM), chronic hypertension and preeclampsia.[11]Obesity is considered a risk factor for preeclampsia and there are many mechanisms that link obesity with a higher risk of developing preeclampsia; such as increased level of proinflammatory cytokines and leptin.[12,13]It has been described that leptin reduces cytotrophoblast proliferation. One of the early alterations observed in preeclampsia is poor cytotrophoblast proliferation.[12,14]The increasing prevalence of maternal obesity worldwide is therefore a major challenge in the care of pregnant women from preconception to postpartum. In this study, we intend to assess the relationship between lipid profile and obesity in women with preeclampsia.

MATERIAL AND METHODS

The subjects were registered pre-eclamptic ante-natal clinic (ANC) patients of the Obstetrics and Gynaecology Department of Government Specialist Hospital, Benin City, Edo State, Nigeria. The control subjects were non-pre-eclamptic ANC patients and analbuminuric hypertensive pregnant patients of the same Department and within the same age range. Patients were considered hypertensive when blood pressure (BP)>140/90 mmHg.

Sample size was 196 calculated from the Cochran's formula (Cochran, 1977).[15] Before carrying out the study, ethical clearance was obtained from the research and Ethics Committee of the Ministry of Health, Benin City, Edo State, Nigeria. Verbal informed consent was obtained from all participants. Structured questionnaires were administered to the study groups and used to document their personal data, medical history, social, obstetric and family history. A physical examination was carried out to measure their blood pressure. Fresh Urine samples were collected into sterile bottles in the hospital under supervision. The urine was used for urinalysisusing dipstick to determine those with proteinuria. Blood samples were collected from the antecubutal veins following routine aseptic procedure using a 10ml syringe and dispensed into plain specimen bottles for lipid profile. Samples were centrifuged at 3,000 revolutions/min after allowing the sample to stand for 30 minutes to clot. The serum was harvested with clean pasteur pipettes and stored at 2 - 8^{o}C and analyzed within 48hrs.Total cholesterol (TC) and triglyceride (TG) were analyzed using the enzymatic endpoint method described by Roeschlau et. al.[16]high density lipoprotein (HDL-C) was analysed using the precipitation method described by Roeschlau et. al[16] while thelow density lipoprotein (LDL-C) was estimated from the Friedewald's Equation.[17]

Data was collected and entered into a proforma and analyzed using Statistical package for social science (SPSS) version 16.0. The means and standard deviations of the age, BMI, gestational age and lipid profile were calculated. The Pearson correlation was used in calculating the correlations between any two variables. Univariate analysis were presented as frequencies while bivariate or multivariate analysis were presented as means and standard error of means. The level of statistical significance was set at a p-value of < 0.05 for all tests of statistical significance. Data presentation, tables and charts were done using Microsoft Office.

RESULTS

A total of 196 respondents consisting of 124 pre-eclamptics (PE), 36 normotensive pregnant women (NPW) and 36 analbuminuric hypertensive pregnant women (AHPW) participated in this study. Most of the PE (44%) and Normotensive pregnant women (41.7%) were in the age bracket of 31-35 years while most of the analbuminuric hypertensive pregnant women (40%) were in the age range of 36-40 years (Fig 1). Amongst the PE 39(31.5%) were mild while 85 (68.5%) had severe PE based on a BP> 160/110mmHg(Fig.2).

The results revealed a significant($P<0.05$) higher BMI in PE(33.35±0.75Kg/m^2) when compared with NPW(26.57±0.66Kg/m^2) and AHPW (24.84±1.26Kg/m^2. Majority 71 (57.30%) of PE were overweight and obese (30{24.2%}) while most of the NPW 18(50%) and AHPW 23 (63.9%) were of normal weight. The mean indexsystolic and diastolic blood pressures were found to be significantly ($p< 0.05$) higher in PE (160.24±9.34mmHg and 108.56±8.02mmHg) than in NPW (106.00±11.23mmHg and

63.38±4.32mmHg) and AHPW (141.38±14.21mmHg and 98.21±4.94mmHg). (Table 1&2)
The mean TC,TG and LDL-C were significantly (P<0.05) increased in PE (228.44±3.39mg/dl,154.73±3.96mg/dl and 146.17±2.85mg/dl) and AHPW (192.13±21.21mg/dl, 134.51±12.62mg/dl and 141.23±10.25mg/dl) when compared with NPW(179.53±5.97mg/dl, 122.92±5.52mg/dl and 116.83±5.48mg/dl) However mean HDL-C was significantly ($p < 0.05$) lower in PE (38.54±0.61mg/dl) and AHPW(35.63±8.05mg/dl than in NPW (45.61±1.32mg/dl). (Table 3)
TC and TG were significantly (P<0.05) increased inthe 2nd trimester inPE (205.76 ± 5.23 mg/dl, and 176.03 ± 6.20 mg/dl,) and AHPW (190.57 ±11.23mg/dl and 165.65±9.44mg/dl) than in NPW (159.44±9.15mg/dl and 113.63±9.16mg/dl)and also in the 3rd timester(PE: 211.13±4.63mg/dl and 193.43±4.97mg/dl, AHPW: 202.82±10.13mg/dl and 180.94±11.75mg/dl, NPW: 173.82±8.02mg/dl and 130.35±6.12mg/dl). There was also a significant ($p < 0.05$) increase in TG in the 3rd than in the 2nd trimesters within the PE and AHPW. LDL-C was significantly (P<0.05) higher in PE(145.86±3.76mg/dl and 157.56±4.29mg/dl) and AHPW(130.38±11.42mg/dl and 141.06±10.93mg/dl) than NPW(105.74±0.81mg/dl and 113.40±7.50mg/dl) in the 2nd and 3rd trimester while HDL-C was significantly (P<0.05) lower in PE(38.44±0.91mg/dl) and AHPW(33.98±7.55mg/dl) than NPW(45.67±1.17mg/dl) in the 3rd trimester. (Table 4)
Mean serum LDL-C and TG were significantly (P<0.05) higher in severe (155.61±5.10mg/dl and 160.72±5.20mg/dl) than in mild (142.79±3.43mg/dl and 147.39±5.60mg/dl) PE. LDL-C and TC levels were found to be non-significantly (P<0.05)higher amongst the Obese (150.51±6.55mg/dl and 214.46±7.25mg/dl) and overweight (145.73±3.29mg/dl and 208.69±4.26mg/dl) than in the normal weight (141.96±7.81mg/dl and 203.26±8.69). In the pre-eclamptics, plasma HDL was found to be non-significantly (P<0.05) higher in the normal weight (37.05 1.43mg/dl) than in the overweight (35.46±0.78mg/dl) and Obese (33.85±1.31mg/dl) while mean plasma TG was found to be relatively the same amongst the three groups of pre-eclamptics. (Table 5 & 6)

DISCUSSION

Preeclampsia is one of the most common medical complications during pregnancy with unknown etiology. It is however, characterized by vasoconstriction, metabolic changes, endothelial dysfunction and activation of the coagulation cascade in conjunction with an inflammatory response.[18] In Nigeria, PE has a prevalence rate of 5.6% and it is associated with maternal and fetal morbidity and mortality worldwide.[19,20]
We observed a significantly higher concentration of triglyceride in PE than in the NPW and AHPW which was also reported by Enquobahrie et al[21], Cekmen et al[22] and Phalak and Tilak[23] in their studies of lipid profile in preeclampsia in India. Normal pregnancy results in physiologic hyperlipidemia with an increase in triglyceride and cholesterol due to hyperestrogenemia which induces hepatic biosynthesis of lipids.[7,24]Insulin resistance during pregnancy, leads to increased influx of fatty acids to the liver promoting the synthesis of VLDL with increased TG concentration.[25] There is also an increase in hepatic lipase activity which increases the synthesis of TG in the liver with associated decrease in the activity of

lipoprotein lipase leading to decreased catabolism of adipose tissue. The net effect is an increase in serum TG level.[8] In preeclampsia, there is an additional alteration in blood lipids reflecting disordered lipid and lipoprotein metabolism. The release of free fatty acids and apolipoprotein-CIII from triglycerides promote oxidative stress and proatherogenic responses in macrophages and endothelial cells.[26] VLDL remains in the plasma for a longer time due to a decreased activity of lipoprotein lipase leading to an increase in blood LDL-C and this is associated with development of atherosclerosis. A significant increase in LDL-C was seen in PE and AHPW when compared with NPW in this study. Studies by Gratacos et al and Cassandra et alsupport this finding.[27,28]Also, significantly increased serum total cholesterol in PE than in AHPW and NPW was observed in our study. Abnormal lipid metabolism is not a mere manifestation but is also involved in the pathogenesis of PE and hypercholesterolemia promotes the formation of free radicals which are also implicated in the pathogenesis of preeclampsia.[29,30]

A significantly decreased HDL-C was observed in PE and AHPW than in NPW. HDL-C was lower in the 3rd than in the 2nd trimester in PE and AHPW while the level remained the same in both trimesters in NPW. HDL-C also decreased with severity in PE. This finding is in accordance with studies by Adiga et aland Phalak and Tilak.[29,23] According to Cekmenet al, low HDL-C in PE is due to insulin resistance while Bozkurt et al stated that there is a direct correlation between adipose tissue lipoprotein lipase activity and plasma HDL-C and this may be responsible for the observed low levels of HDL-C.[22,25] Anuradha and Durga also reported significant increases in LDL-C and TC and no significant difference in HDL-C was observed between mild and severe PE.[31]Vidyabati et al observed that the clinical manifestations of PE preceeded dyslipidemia particularly, hypertriglyceridemia and elevated LDL.[32] This indicates that hypertriglyceridemia and high LDL-C may contribute to the aetiologic and pathophysiologic mechanisms responsible for PE.

The association between lipid profile and BMI was not significant, suggesting that maternal lipid levels were independent of overweight or obesity status, similar to findings by Daniel et al.[33]However, we found that more of the preeclamptic women were obesewhen compared to the NPW and the AHPW. Similarly, numerous studies have shown a strong correlation between an increased BMI and the risk of developing preeclampsia.[34,35]

CONCLUSION

Abnormal lipid metabolism particularly high triglyceride and LDL-C and obesity may contribute to oxidative stress and therefore the etiology of PE. Hence, weight control and lipid testing followed by appropriate management pre-conception and during pregnancy would improve the care of women with preeclampsia.

RECOMMENDATIONS

Routine estimation of serum lipids can be useful as a simple screening test to detect dyslipidemia in PE in order to reduce the incidence of complications. Despite the fact that weight loss is not recommended during pregnancy, weight loss should be recommended in women with obesity or overweight that are planning to get pregnant.

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Conflict of interest : nil

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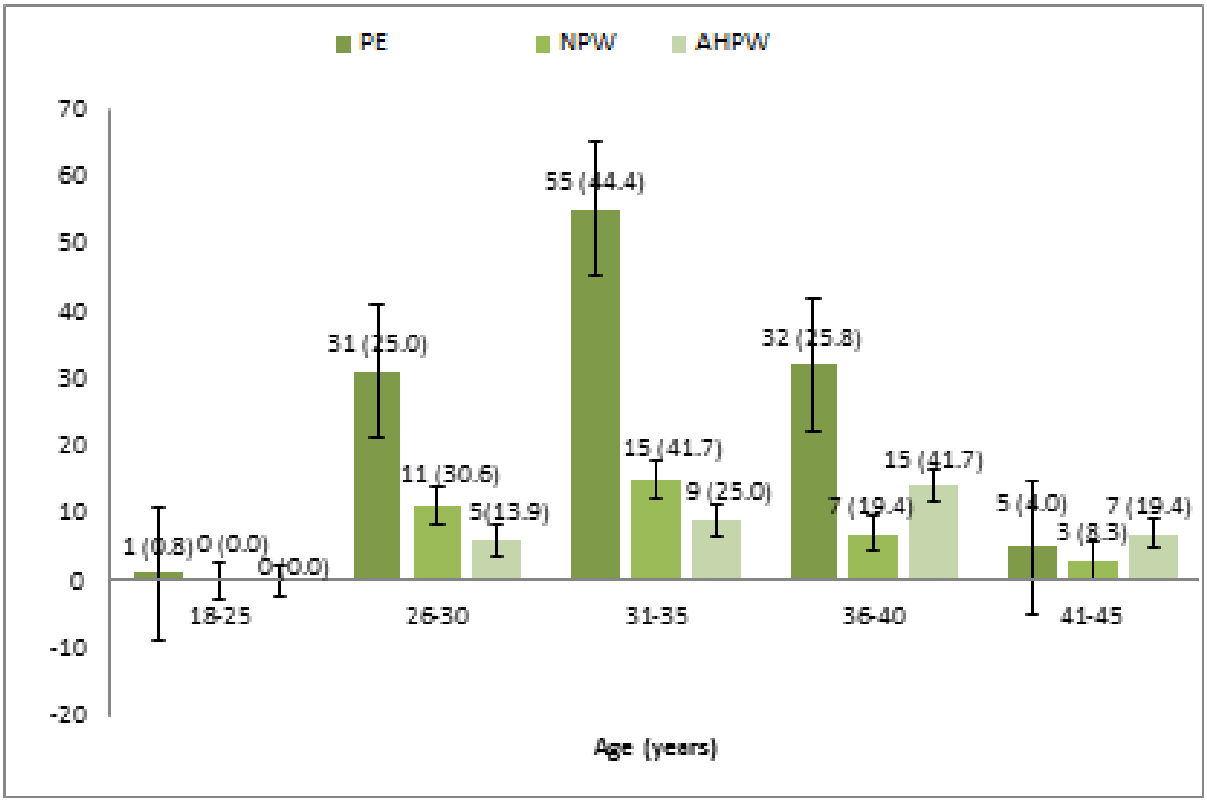

Fig 1:AGE GROUP DISTRIBUTION OF SUBJECTS

Values in parenthesis represent percentage distribution, while the bars on top of the histogram represent standard error.

KEY:

PE Preeclampsia

NPW Normotensive pregnant women

AHPW Analbuminuric hypertensive pregnant women

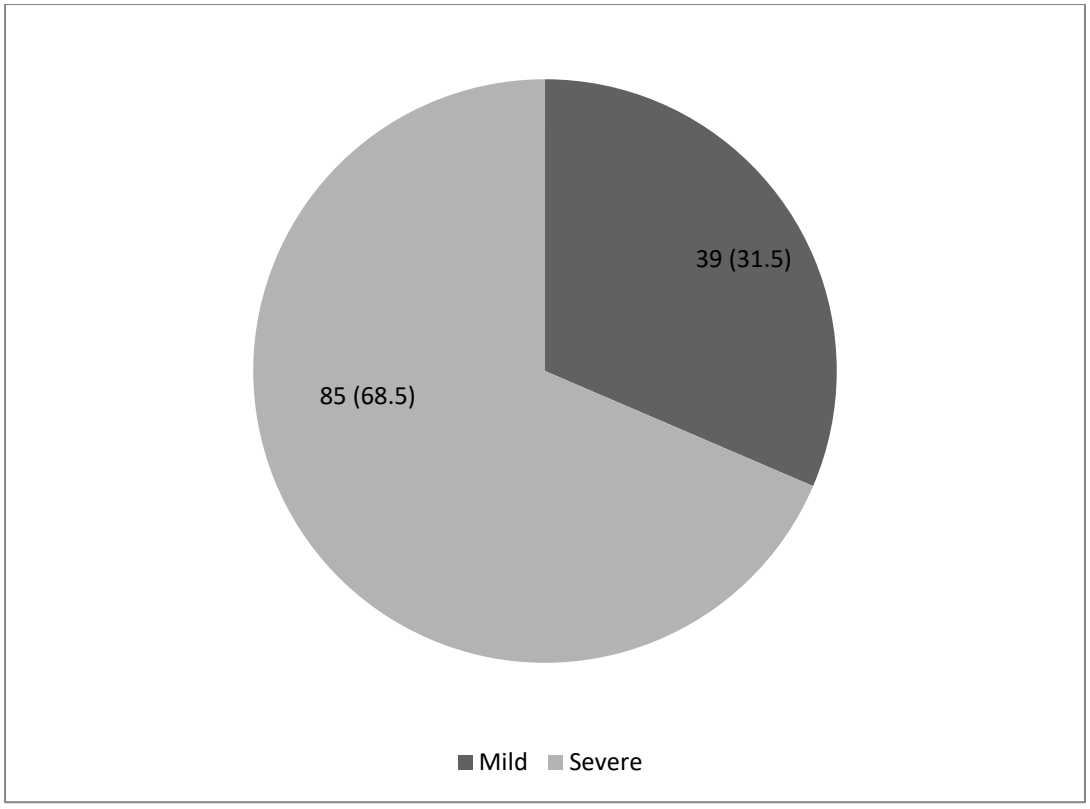

Fig2: SEVERITY OF PRE-ECLAMPSIA

TABLE 1. CLINICAL AND ANTHROPOMETRIC CHARACTERISTICS OF PE, NPW AND AHPW

Clinical/Anthropometric parameter	PE	NPW	AHPW
Booking SBP (mmHg)	136.03 ±23.01[a]	103.05 ± 12.60[b]	140.00 ± 25.52[ac]
Booking DBP (mmHg)	85.08 ± 1.46[a]	62.77 ± 7.01[b]	80.00 ± 5.16[ac]
Index SBP (mmHg)	160.24 ± 9.34[a]	106.00 ± 11.23[b]	141.38 ± 14.21[cd]
Index DBP (mmHg)	108.56 ± 8.02[a]	63.38 ± 4.32[b]	98.21 ± 4.94[cd]
BMI (kg/m^2)	33.35 ± 0.75[a]	26.57 ± 0.66[b]	24.84 ± 1.26[cb]

Values are represented as Mean ± SEM
Values in the same row with different alphabets differ significantly ($p<0.05$)
Key:

SBP Systolic blood pressure
DBP Diastolic blood pressure
BMI Body mass index
PE Pre-eclampsia
NPW Normotensive pregnant women
AHPW Analbuminuric hypertensive pregnant women

TABLE 2. DISTRIBUTION OF PE, NPW AND AHPW SUBJECTS BASED ON BMI

BMI(kg/m^2)	PE (n = 124)	NPW (n = 36)	AHPW (n = 36)
Normal weight (18-24.9)	23 (18.50)	18 (50.00)	23 (63.90)
Overweight(25-29.9)	71 (57.30)	9 (25.00)	6 (16.70)
Obese (>30)	30 (24.20)	9 (25.00)	7 (19.40)
Total	**124**	**36**	**36**

Values in parenthesis represent percentages

Key:

BMI Body mass index PE Pre-eclampsia

NPW Normotensive pregnant women AHPW Analbuminuric hypertensive pregnant women

TABLE 3. LIPID PROFILE STATUS IN PE, NPW AND AHPW, SUBJECTS.

Analyte	PE (n = 124)	NPW (n = 36)	AHPW (n = 36)
Serum TC (mg/dl)	228.44 ± 3.39^a	179.53 ± 5.97^b	192.13 ± 21.21^{ac}
Serum TG (mg/dl)	154.73 ± 3.96^a	122.92 ± 5.52^b	134.51 ± 12.62^{cb}
Serum LDL-C (mg/dl)	146.17 ± 2.85^a	116.83 ± 5.48^b	141.23 ± 10.25^{ac}
Serum HDL-C(mg/dl)	38.54 ±0.61^a	45.61±1.32^b	35.63 ±8.05^{ac}

Values are represented as mean ± SEM

Values in the same row with different alphabets differ significantly ($p<0.05$).

keys: TC Total cholesterol, TG Triglyceride, LDL-C Low density lipoprotein cholesterol HDL-C High density lipoprotein cholesterol, PE Pre-eclampsia,

NPW Normotensive pregnant Women

AHPW Analbuminuric hypertensive pregnant women

TABLE 4. LIPID PROFILEIN VARIOUS TRIMESTERS IN PE, NPW AND AHPW.

Analytes	Trimester	PE n = 124	NPW n = 36	AHPW n = 36
Serum TC (mg/dl)	2nd	205.76±5.23[a]	159.44±9.15[b]	190.57±11.23 [cd]
	3rd	211.13±4.36[a]	173.82±8.025[b]	202.82±10.13[ac]
	p-value	0.19	0.03	0.07
Serum TG (mg/ml)	2nd	176.03±6.20[a]	113.63±9.16[b]	165.65±9.44[ac]
	3rd	193.43±4.97[a]	130.35±6.12[b]	180.94±11.75[cd]
	p-value	0.04	0.14	0.04
Serum LDL-C (mg/dl)	2nd	145.86±3.76[a]	105.74±0.81[a]	130.38±11.42[ac]
	3rd	157.56±4.29[a]	113.40±7.50[b]	141.06±10.93[ac]
	p-value	0.52	0.77	0.53
Serum HDL (mg/dl)	2nd	42.65±2.79[a]	45.80±2.15[b]	43.07±8.33[ac]
	3rd	38.44±0.91[a]	45.67±1.17[b]	33.98±7.55[cd]
	p-value	0.62	0.64	0.02

Values are represented as mean ± SEM

Values in the same row with different alphabets differ significantly ($p < 0.05$)

TC Total cholesterol TG Triglyceride

LDL-C Low density lipoprotein cholesterol HDL –CHigh density cholesterol

NPW Normotensive pregnant women

AHPWAnalbuminuric hypertensive pregnant women PE Pre-eclampsia

TABLE 5. LIPID PROFILE IN PE SUBJECTS AT DIFFERENT PHASES OF PE

	Pre-eclamptics	
Analyte	**Mild (n=39)**	**Severe (n=85)**
Serum TC (mg/dl)	**209.94 ±5.02[a]**	**207.27 ± 4.42[a]**
Serum LDL-C (mg/dl)	**142.79± 3.43[a]**	**155.61 ± 5.10[b]**
Serum HDL-C (mg/dl)	**38.28 ± 1.06[a]**	**35.450 ± 0.73[a]**
Serum TG (mg/dl)	**147.39 ±5.60[a]**	**160.72±5.20[b]**

Values are represented as mean ± SEM

Values in the same row with different alphabets differ significantly ($p < 0.05$)

TC Total cholesterol

TG Triglyceride

LDL-C Low density lipoprotein cholesterol

HDL-C High density cholesterol

PE Pre-eclampsia

NPW Normotensive pregnant women

AHPW Analbuminuric hypertensive pregnant women

TABLE 6. RELATIONSHIP BETWEEN BMI AND LIPID PROFILE IN PE

Analyte	BMI Normal weight N=23	 Overweight N=71	 Obese N=30
Serum TC (mg/dl)	**203.26 ± 8.69[a]**	**208.69±4.26[a]**	**214 ± 7.25[a]**
Serum TG (mg/dl)	**157.08 ±9.41[a]**	**157.00±4.99[a]**	**157.08 ± 9.4 [a]**
Serum LDL-C(mg/dl)	**141.96 7.81[a]**	**145.73±3.29[a]**	**150.51± 6.55[a]**
Serum HDL-C (mg/dl)	**37.05 ±1.43[a]**	**35.46±0.78[a]**	**33.85±1.31[a]**

Values are represented as mean ± SEM

Values in the same row with different alphabets differ significantly ($p < 0.05$)

TC Total cholesterol

TG Triglyceride

LDL-C Low density lipoprotein cholesterol

HDL-C High density cholesterol

PE Pre-eclampsia

NPW Normotensive pregnant women

AHPW Analbuminuric hypertensive pregnant women

Prevalence of Occult Kidney Disease, using EGFR as a screening tool in a rural community in South-South Nigeria.

[1]Ojeh-Oziegbe OE, [2]Aigbavboa HDO

[1]Nephrology Unit, Department of Medicine, College of Medical Sciences, University of Benin and University of Benin Teaching Hospital. [2]Babcock University, College of Health and Medical Sciences.

Abstract:

Background: The early detection of Chronic Kidney Disease (CKD) is of crucial importance in sub-Saharan Africa especially in Nigeria where treatment costs are prohibitive and often out of reach of the vast majority of the patients. Occult Renal disease is defined as a renal dysfunction that cannot be detected by the usual methods of investigations.
This study was part of the World Kidney Day screening in NIFOR, a rural agricultural community in South-South Nigeria.

Method: 168 participants were evaluated, of which 138 had a normal serum creatinine level of ≤1.4 mg/dl. Kidney disease risk factors such as Hypertension, Hyperglycemia, Obesity using Body Mass Index (BMI), Abdominal Obesity using Waist hip ratio (WHR), presence or absence of proteinuria, presence or absence of hematuria, age and gender were documented.
Estimated GFR values were calculated using the CKD Epidemiology (CKD_EPI) 2009 Equation. 138 participants had complete data with a serum creatinine of ≤1.4 mg/dl, and 13 (9.42%) had an eGFR of <60 mls/min despite having a normal creatinine.

Result: 138 participants with a normal serum creatinine of ≤1.4mg/dl were evaluated with the CKD_EPI equation. 13 (9.42%) were found to have an eGFR of <60mls/min.

Conclusion: There is a high prevalence of undetected kidney disease as 9.42% of the participants with normal serum creatinine levels had an eGFR of <60 mls/min. This reveals that serum creatinine values alone may not totally predict the renal functions of these participants. More studies involving a larger population would need to be done.

Key Words: estimated Glomerular Filtration Rate, Occult Renal Disease, Serum Creatinine

INTRODUCTION

The burden of renal disease worldwide appears to be on the increase. It is estimated that kidney disease affects over 8-10% of the general population worldwide, amounting to over 800 million people [1,2].

Corresponding Author:
Dr. Ojeh-Oziegbe Odigie E O
University of Benin/ University of Benin Teaching Hospital, Benin City.
Email: osezuwaonose@yahoo.com

The situation is particularly of concern especially in Sub-Saharan Africa. In the 2016 review of the Global Burden of Kidney Disease, the database showed an 87% rise of CKD and a doubling of CKD deaths between 2000 and 2016 [3]. This is because there is a significant shortage of public health services especially relating to renal case. The issue of renal replacement therapy, especially in established chronic kidney disease (CKD) is a major issue as renal replacement therapy (RRT) with hemodialysis, peritoneal dialysis and kidney transplant is largely unavailable,

and where available, involves a high financial burden to the patients and their relations. This is especially important in Nigeria where the burden of renal replacement therapies fall on the patient and their relations. [4,5]

In Nigeria, hemodialysis is the main method of treatment for those with End Stage Kidney Disease (ESKD). The hemodialysis centers are mainly located in the urban areas of the country. In addition to this, dialysis costs are expensive and largely out of reach to those needing dialytic therapy. Transplant centers are just a few and the cost of transplant extremely prohibitive. [5,6,7,8,9]

Apart from dialytic therapy, CKD patients present with a lot of issues. They have anemia and heart disease, as well as hypertension. The treatment of anemia is also expensive. Kidney disease has been found to be associated with hypertension, diabetes, older age, black race, infection mediated glomerulonephritis and a host of other unidentified etiology.

CKD incidence and prevalence is on the rise. Death from CKD rose by 32.1% from 2015-2016. It is one of the leading causes of mortality and shown a progressive increase in the number of associated deaths in the last 2 decades.

It also represents an exceptionally large economic burden in low income countries, more so as they are the least equipped to deal with its consequences. In resource poor countries like Nigeria, preventive strategies would be a lot more effective.

It is therefore important that kidney disease is identified early and that preventive strategies to avoid and mitigate the course of kidney disease to be implemented as early as possible.

The need for early detection and therefore early intervention cannot be overemphasized. Early detection in our environment has generally included urinalysis to check for proteinuria, electrolytes and urea, and creatinine.[10]

The ability to do basic urea and electrolytes and urinalysis are tools that are readily available, but the observation has been that such tools are rarely used by the generality of populace on their own.

They benefit from these when mass screenings are done. These are regularly not done and when done, are usually as a result of programs like World Kidney Day screening, and the cost of tests are usually borne by the Nephrologists, the nurses and a few pharmaceutical companies involved out of their pocket expenditure.

The value of screening for kidney diseases leading to early detection is an important phenomenon in developed countries. In Nigeria, it is virtually not done as a government outreach towards detection of kidney diseases but sporadically by well-meaning health professionals and they also have to bear the cost.

Treatment of kidney disorders when detected at an early stage is feasible, acceptable, cost effective and generally affordable. Treatment of kidney disease in Nigeria at an advanced stage, when they usually present on the other hand is in many cases not feasible as there are few renal replacement centers and Nephrologists sometimes not acceptable to some groups who do not accept blood transfusion as a mode of anemia management, not cost effective and most importantly, not affordable to the majority of Nigerians as there is no government sponsored or subsidized renal replacement program. [11,12]

Therefore, the mainstay of renal care in Nigeria is for now resting on the base of early detection of kidney disease and also involves screening for kidney disease itself and also for the risk factors of chronic kidney disease such as hypertension and diabetes.

Screening for kidney disease has been done in various communities in Nigeria and has shown a variety of prevalence, all significant, in different communities in Nigeria.

Most of these screenings have mainly been done using urinalysis to detect proteinuria. Other screenings have used urinalysis to try and detect microalbuminia using micral test strips.

Few have used serum creatinine and calculated the estimated Glomerular Filtration Rate (eGFR). This has been found to detect a larger portion of renal disorders, especially in those with normal or borderline serum creatinine values, but the practice of using eGFR has not been used as a screening too in our environment.

Detecting those cases of occult kidney disease would enable us to be able to catch a larger number of kidney disease cases at a much earlier time thus enabling preventive measures to be taken on time to avoid overt kidney diseases.

The immediate way forward is early detection. This will allow for the detection of those with kidney failure and allow for management to slow down the progression of the kidney disease and prolong, for as much as possible, the development of End Stage Kidney Disease (ESKD). Achieving this means screening for kidney disease in various communities and different population groups.[13]

However, there is a downside of using eGFR and certain studies have observed that single eGFR can overestimate prevalence of CKD [14], while others agree on its effectiveness.[15]

This study was carried out as part of the World Kidney Day. The study was done in the Nigerian Institute For Oil-palm Research (NIFOR), in a rural population in South-South Nigeria.

Materials and Methods:

This study was cross sectional and carried out as a part of the World Kidney Day 2014. Data for the study were extracted from the WKD screening of workers from NIFOR with ethical clearance and permission granted by the management of the Nigerian Institute for Oil Palm Research, Benin City. 242 patients, all between the ages of 18-80, were evaluated. Pregnant women were not included in the sample selection. Blood pressure, random blood sugar, height, weight and sociodemographic data were obtained and/or measured. Blood samples were also taken for serum creatinine. As part of the screening for WKD rural screening, chronic kidney disease was defined as a serum $\underline{\geq}$1.5 mg/dL.

Weight was measured in kilograms to the nearest kg, height was measured in centimeters to the nearest centimeter. These were used to calculate the Body Mass Index (BMI), given as weight (kg)/ height squared (m^2).

BP was measured using mercury sphygmomanometers in the sitting position. The average of two BP measurements taken 5 min apart in the left arm was recorded for each participant. HTN was taken as the presence of systolic BP (SBP)≥140 mmHg and/or diastolic BP (DBP)≥90 mmHg. Systolic HTN was defined as SBP≥140 mmHg with a DBP< 90 mmHg, whereas diastolic HTN was defined as DBP≥90 mmHg with a SBP < 140 mmHg. Participants who admitted to being known hypertensives were considered to have good BP control using a cutoff BP value of <140/90 mmHg.

The prevalence of HTN in the study population was taken as the number of self-reported known hypertensives and persons found to have HTN during the study.

Waist–hip ratio (WHR) was determined using the waist circumference (measured at the midpoint between the lowest rib margin and the iliac crests) and the hip circumference (measured at the widest point around the buttocks). Abdominal obesity was taken as WHR > 0.85 for women and WHR > 0.9 for men.

RBS was done using glucose meters and strips (Accu-Chek, Roche diagnostics, Mannheim, Germany). Random blood sugar levels ≥200 mg/dl were considered high and abnormal.

Serum creatinine was determined using the modified Jaffe's method. Serum creatinine of ≤1.4 mg/dL was considered normal. 138 participants with a normal serum creatinine of ≤1.4mg/dl were further evaluated using the 2009 CKD_EPI equation to calculate their eGFR. There were 138 participants with complete results.

Results are presented as follows.

Statistical Analysis:

Data obtained were analysed using IBM SPSS Ver. 21 and Microsoft Excel 2016. Quantitative data were presented as means ± standard deviation, qualitative data are presented as frequencies and percentages.

Results:

Range of serum creatinine for the entire group was 0.2-1.4 mg/dl. Mean serum creatinine was 0.978 ±0.28 mg/dl. For males (N=62) serum creatinine mean was 1.065 ±0.251 mg/dl, and for females (N=76) it was 0.907±0.284 mg/dl. Mean eGFR across the group was 96.69±32.064 mls/min. For males (N=62) mean eGFR was 95.097±27.185 mls/min, and for females (N=76) it was 97.99±35.68 mls/min. For those with an eGFR <60mls/min (N=13), total mean was 56.723±3.67 mls/min, for males (N=2) it is 59.2±0.88mls/min, and for females(N=11) it is 56.27±3.83 mls/min.

Discussion:

The primary definition of chronic kidney disease was estimated Glomerular Filtration Rate (eGFR) less than 60 mls/min per 1.73 m^2 Body Surface Area (BSA)[16].

Serum creatinine only has been found to underestimate GFR, so using equations for calculating the eGFR has been used by researchers and clinicians.

This study showed a prevalence of 9.42% of the study population had an eGFR of <60 mls/min in this population that had a serum creatinine of ≤1.4mg/dl.

It is also important to know that the prevalence of serum creatinine of ≥1.5 mg/dl found in this group of participants were found to be 20.4%. [17]

So it meant that a further 9.42% of the remaining participants adjudged to have a normal renal function had a GFR of less than 60 mls/min. This has been the finding in some other studies and the suggestion had been that prediction equations for GFR should be used more commonly to assess renal function as some individuals with impaired renal function could not be detected by using serum creatinine values alone. While this is in agreement with the Kidney Disease Outcome Quality Initiative (KDOQI) guidelines, some have argued that it is not cost effective. The downside of this argument is that once the serum creatinine is done and the sociodemographic data collected, it does not have additional costs to use a prediction equation to calculate the eGFR.

The added advantages of using eGFR as a tool for early detection of CKD is that it may be possible to detect the disease at an earlier stage and identify the risk factors in those subjects. When such risk factors, which commonly are hypertension and diabetes are known, it would be possible to intervene and mitigate such risk factors thereby possibly stopping the progression of kidney disease.

Even when such risk factors are unknown, as happens in a significant number of kidney disease patients. It would enable clinicians to follow up those at risk for progression of kidney disease and take appropriate action to significantly slow down disease progression.

Certain associations with having a low eGFR found here included abdominal obesity as over 80% of those with reduced eGFR despite having a normal serum creatinine had abdominal obesity. This, for example, is a situation that can be mitigated with lifestyle modification.

Conclusion

This study shows that there is a significant number of kidney disease cases (9.42%) who have an eGFR of ≤60mls/min despite having a normal creatinine level.

It encourages the use of prediction equations, in this case, the CKD_EPI equation to calculate the eGFR so as to identify cases of occult renal disease that cannot be detected by serum creatinine values alone.

For a country like Nigeria with an estimated population of 210 million people, 9.42% would mean a population prevalence of close to 20 million people who may have a normal kidney function by serum creatinine assessment alone.

This is a very large number and more studies would need to be done to ascertain the prevalence of occult kidney disease in the presence of a normal serum creatinine value.

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Table 1: Mean Parameters of Study Participants

Variables (N = 138)	Mean	S.D.
Age (years), of which	46.22	± 14.852
Weight (kg)	65.196	± 13.317
SBP (mmHg)	129.09	± 19.807
DBP (mmHg)	79.16	± 12.222
Serum Creatinine (mg/dL)	0.978	± 0.28
eGFR	96.69	± 32.064
RBS	122.57	± 56.669
Waist/Hip Ratio	0.911	± 0.073
BMI	24.77	± 4.648

Table 2: Comparison of Mean parameters of participants according to gender

Variable	Sex of Patient	N	Mean	Standard Dev.
Age (years)	**Male**	62	52.29	± 15.135
	Female	76	41.28	± 12.703
Systolic BP 1 (mmHg)	**Male**	62	133.02	± 19.264
	Female	76	125.95	± 19.798
Diastolic BP 2(mmHg)	**Male**	62	80.89	± 11.453
	Female	76	77.78	± 12.711
Serum Creatinine (mg/dl)	**Male**	62	1.065	± 0.251
	Female	76	0.907	± 0.284
BMI	**Male**	62	23.007	± 3.102
	Female	76	26.22	± 5.197
Weight (kg)	**Male**	62	64.246	± 11.948
	Female	76	65.98	± 14.382
Waist to Hip Ratio	**Male**	62	0.9311	± 0.073
	Female	76	0.895	± 0.07
RBS	**Male**	62	137.9	± 70.81
	Female	76	110.67	± 39.136
eGFR	**Male**	62	95.097	± 27.185
	Female	76	97.994	± 35.68

Table 3: Further Information on Study Participants (Total N = 138)

	N	**(%) of Total N**
Males	**62**	**44.93%**
Females	**76**	**55.07%**
Haematuria	**6**	**4.35%**
Proteinuria	**7**	**5.07%**
Hypertension	**35**	**25.36%**
DM	**7**	**5.07%**
eGFR<60	**13**	**9.42%**
Abdominal Obesity (WHR)	**101**	**73.19%**
Males	**42**	**30.43%**
Females	**59**	**42.75%**
Obesity (BMI)	**20**	**14.49%**
Males	**2**	**1.45%**
Females	**18**	**13.04%**

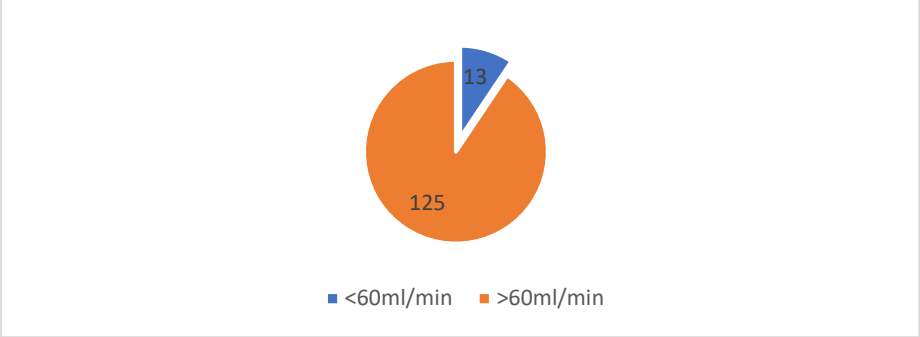

Fig 1: Participants based on eGFR.

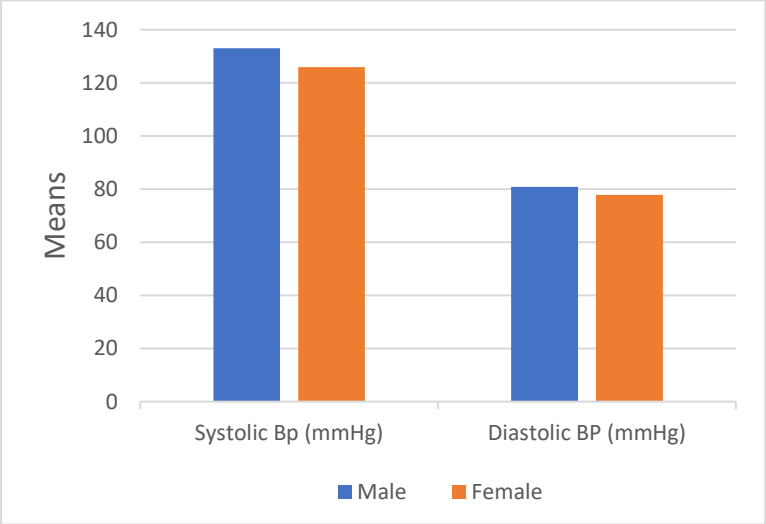

Figure 2: Means comparisons of Blood Pressure between Males and Females

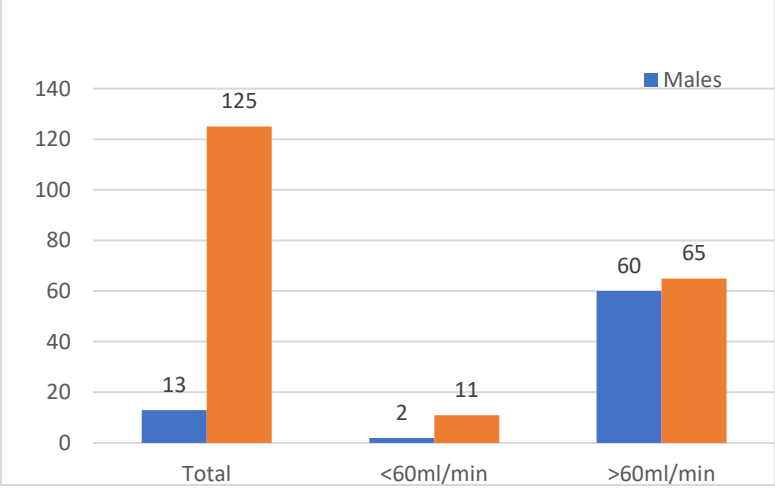

Figure 3: Comparison of eGFR values in patients with Normal Serum Creatinine

EVALUATION OF HISTOPATHOLOGICAL PATTERN OF COLORECTAL CANCERS IN YOLA, NIGERIA.

*Aminu DMC, *Nasiru R, *Appah DL, **Alfa SA

*Department of Anatomic Pathology and Forensic Medicine, Modibbo Adama University/ Modibbo Adama University Teaching Hospital, Yola, Adamawa State, Nigeria, **Department of Pathology, Ibrahim Badamasi Babangida University, Lapai, Niger State

ABSTRACT

Background: Colorectal cancer is the third most common cancer globally with the highest rates in western societies and relatively low rates in Africa, South and Central Asia. However, switch from a fiber diet to high refined carbohydrate and fat diet has led to steady increasing rates in low and middle-income countries.There is no published study on colorectal cancer in our setting, hence this report.The objective of this study was to determine the age, gender, frequency distribution and histopathological spectrum of colorectal cancers in Yola, North-Eastern, Nigeria.

Materials and Methods: This was a 14-year (2010 to 2023) retrospective review of all the histologically diagnosed colorectal cancers in the pathology department of Modibbo Adama University Teaching Hospital, Yola, North-Eastern Nigeria. The analyzed variables included the patient's age, gender, the anatomical location and the histopathological variants.

Results: One hundred and sixty eight histologically diagnosed colorectal cancers were seen during the fourteen year study period, comprising 108 males and 60 females (M : F = 1.8:1). The age range was 10 to 76 years with mean of 44.3 years and highest occurrence in the40 – 49 years age group. Majority of colorectal cancers were in the left-side (67.8%). Well differentiated and moderately differentiated adenocarcinomas were the commonest comprising 39.3% and 34.5% respectively.

Conclusion: This review has shown a rising incidence of colorectal cancer in our environment. There is the need for widespread screening facilities and population-level shifts toward a healthier lifestyle.

Keywords: Colorectal cancer, adenocarcinoma, Yola.

INTRODUCTION

Corresponding Author:
Name: Raheem, Nasiru
Address: Department of Anatomic Pathology and Forensic Medicine, Modibbo Adama University/ Modibbo Adama University Teaching Hospital, Yola, Adamawa
Phone numbers: 07036377054
E-mail address: raheemnasiru@yahoo.com

Colorectal cancer (CRC) is the third most common cancer globally and the second in terms of mortality.The incidence rates are three to four times higher in high-income countries relative to low-income countries, although the regional patterns of mortality rates do not follow those of incidence, with the highest mortality rates found in the sub-Saharan Africa, indicative of disparities in early detection and treatment.[1] In 2022, with an estimated 8,114 new cases and 5,912 deaths in Nigeria, colorectal cancer is the fourth most frequent cancer and the

fourth leading cause of cancer death in Nigeria.[1]

Recent Nigerian studies revealed early-onset and increasing incidence of CRC primarily in urban areas likely attributed to lifestyle modification and switch from a fiber diet to high refined carbohydrate and fat diet.[2-4] As with many other cancers, the mechanism underlying CRC is still not clear, but genetic predisposition, inflammatory bowel disease, consumption of diet low in fiber content, rich in high-fat and red meat, sedentary lifestyle, and obesity are associated with increased risk of developing CRC.[1] The molecular genetic pathways of colorectal tumorigenesis is still evolving, it is well accepted that most CRCs develop from adenomas. The transition from normal epithelium to adenoma to carcinoma is associated with acquired molecular events. Presently, CRC can be separated into three categories based on similar molecular genetic features, suggesting divergent pathways of tumorigenesis: chromosomal instability, microsatellite instability, and CpG island methylator phenotype. These molecular events emerged from important clinical and histological heterogeneity of colorectal polyps and cancers, thus, the chronological evolution of colorectal tumorigenesis and outcome. More than 95% of CRCs are carcinomas, and about 95% of these are adenocarcinomas with a disproportionate distribution in different segments of the bowel.[5]

There is a paucity of information on CRC in our setting despite the steady increasing incidence in Nigeria. There has, however, been no publication on this cancer from Yola, North-eastern Nigeria, hence this review. The objective of this study was to determine the age, gender, frequency distribution and histopathological spectrum of CRC as seen in the pathology department of Modibbo Adama University Teaching Hospital(MAUTH), Yola and to compare our findings with those from the previous series.

MATERIALS AND METHODS

Study design: This was a retrospective review of all histopathological review of colorectal specimen from 2nd January 2010 to 31st December 2023

Study Population: All patients who had CRC within the last fourteen years as confirmed by the pathology department of the MAUTH, Yola

Sample Size: This was a retrospective review of 168 histologically confirmed cases of CRC diagnosed at the pathology department of MAUTH, Yola.

Department of study: Anatomic pathology department of the MAUTH, Yola.

Sample Collection: All CRC recorded in the histology registers of the MAUTH, Yola, Nigeria.

Histology review: Histology slides on all cases were retrieved and reviewed by the study authors. Fresh sections were cut from archival paraffin blocks when slides could not be retrieved. All specimens had been fixed in 10% formal saline, then routinely processed for paraffin embedding. Microtome sections were cut at 4µ and stained with haematoxylin and eosin

Data Analysis: The analyzed variables included the patient's age, gender, the anatomical location and the histopathological variants. The data was analyzed using SPSS version 28(IBM Corp. Released 2021. IBM SPSS Statistics for Windows, Version 28.0 Armonk, NY: IBM Corp), and presented as frequency tables.

Ethical Consideration: Approval for the study was obtained from the Ethical and Research committee of the MAUTH, Yola.

RESULTS

Out of the total 215 histologically diagnosed gastrointestinal tract malignancies, CRC constituted 168 cases which represented 78.1% of all

gastrointestinal malignancies during the fourteen-year study period. The age range was 10 to 76 years, with mean of 44.3 years and highest occurrence in the 40 – 49 years age group.Males were more preponderant with108 males and 60 females (M: F = 1.8:1). Table 1 shows age and gender distributions of Colorectal Cancers. Majorities of colorectal cancers were in the left-side (67.8%).More than half of the cases were in the rectum (52.9%), followed by unspecified site (14.9%), caecum (10.7%), and other less frequent sites. Table 2 shows anatomic site distribution of Colorectal Cancers. Well-differentiated and moderately differentiated adenocarcinomas were the commonest comprising 39.3% and 34.5% respectively. Poorly differentiated adenocarcinomas contributed 6.6% of cases. The other histologic types were signet ring cell carcinoma9.5%, mucinous adenocarcinoma7.1%, small cell neuroendocrine carcinoma and non-Hodgkin's lymphoma constituted 1.2% each and gastrointestinal stromal tumour 0.6%. Table 3 depicts frequency distribution of varioushistological types of Colorectal cancers. Figures 1 and 2 show photomicrographs ofsignet ring cell carcinoma and mucinous adenocarcinoma.

Table 1: Age and gender distribution of Colorectal Cancers

Age group (years)	Male	Female	N (Frequency in %)
10 – 19	2	1	3(1.8)
20 – 29	26	6	32(19.0)
30 – 39	15	15	30(17.9)
40 – 49	21	16	37(22.0)
50 – 59	20	9	29(17.3)
60 – 69	16	8	24(14.3)
70 – 79	8	5	13(7.7)
Total	**108**	**60**	**168(100)**

Table 2: Anatomic site distribution of Colorectal Cancers

Anatomic site	N (Frequency in %)
Caecum	18(10.7)
Ascending colon	7(4.2)
Hepatic flexure	-
Transverse colon	4(2.4)
Splenic flexure	1(0.6)
Descending colon	8(4.74)
Sigmoid colon	7(4.2)
Rectosigmoid junction	9(5.35)
Rectum	89(52.93)
Unspecified	25(14.88)
Total	**168(100)**

Table 3: Histological type of Colorectal cancers

Histologic type	N (Frequency in %)
Carcinomas	
Well differentiated adenocarcinoma	66(39.3)
Moderately differentiated adenocarcinoma	58(34.5)
Poorly differentiated adenocarcinoma	11(6.6)
Mucinous adenocarcinoma	12(7.1)
Signet ring cell carcinoma	16(9.5)
Neuroendocrine neoplasms	
Small cell neuroendocrine carcinoma	2(1.2)
Malignant lymphomas	
Non Hodgkin's lymphoma	2(1.2)
Mesenchymal Tumours	
Gastrointestinal stromal tumour	1(0.6)
Total	**168(100)**

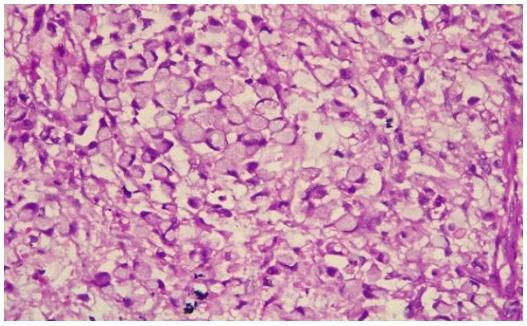

Fig.1: Signet ring cell carcinoma (H&E x40)

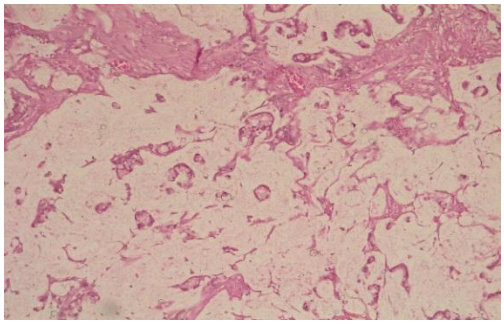

Fig. 2: Mucinous adenocarcinoma (H&E x1

DISCUSSION.

CRC is a gradually increasing lesion in our population with an average frequency of 12 per year in this study. This rate is higher than 3.36 cases per annum in South-South Nigeria, but lower than 14.4 cases per annum in North-Central Nigeria, 18.6 cases per annum in North-West Nigeria and 32.3 cases in Lagos and Sagamu, South-West Nigeria, 27.3 cases per annum in Ghana, and 14.8 cases per annum in Rwanda.[2,4,6-8] In contrast, higher annual frequencies are reported in Europe, Australia/New Zealand, and Northern America.[1] Many reasons can be adduced for the regional variation; consumption of whole grains, dairy products, high fiber diet, minimal transit time of faeces, rarity of inflammatory bowel diseases, and precancerous lesions, among other factors are asserted to be responsible. Nonetheless, the recent steadily rising incidence in Nigeria and other developing countries are related to increase screening, detection, improve documentation, urbanization and westernization. CRC accounted for 78.1% of gastrointestinal malignancies in this study, which conforms with the reports across the globe.[2,7,10-13]

Our review revealed the youngest patient as 10-year-old, and the oldest was 76-year-old,and highest occurrence in the 40 – 49 years age group, with mean age of 44.3 years. While this corroborates studies from Kano 42.8 years, Zaria 38.9 years, Jos 44.3 years, Lagos and Sagamu 50.7 years, all in Nigeria, 49.7 years in Kenya, 54.6 years in Rwanda and 51 years in Egypt, it is lower than many high-income countries where the peak period is between 60 and 79 years and fewer than 50% of the cases occur before 50 years of age except when CRC is

a complication of pre-existing ulcerative colitis or one of the polyposis syndromes, conditions which are rare in our environment.[2,4,13-17]Similarly, 45.8% of cases in this study were seen in 40 years and below. The reasons for early-onset in our setting is unknown but probably environmental factors and genetic susceptibility. Molecular studies on genetic predisposition to familial CRC in our environment is required to establish the association.

Overall, CRC in this series were more preponderant among males (M: F = 1.8:1). This correlated with 1.5:1 in Kano, 1.3:1 in Lagos (Nigeria), 1.3:1 in South Africa and 1.1:1 in Iran, but at variance with female predominance of 2:1 in Ife, 3:1 in Port Harcourt (Nigeria), and 1.1:1 in Ghana.[2,4,6,8,18-20] There is no consistent pattern of gender distribution.

With regard to anatomic location, left-sided (distal tumours) was the most common (67.8%). This is in agreement with most findings of other studies from Nigerian, Rwanda, Iran, and United Kingdom. Conversely, high prevalence of right-sided colonic cancer was reported in Ghana, North American Population.[2,4,6,8,9,19,21,22] The possible explanations for the obvious disparities are; previously there was no colonoscopy for colonic biopsy in our environment, rectal tumour is easily accessible for diagnosis, clinical symptoms of distal tumours are more obvious early for patients.

In this appraisal, adenocarcinomas emerged the most common CRC accounting for 80.4% of all cases. This is the dominant histological variant documented in literature.[2-4,6-15] CRC is predominantly epithelial-derived malignancy. The grading of adenocarcinomas was 39.3% well differentiated, 34.5% moderately differentiated and 6.6% poorly differentiated in this study. The grading distribution pattern is similar to Ibadan and Lagos in Southern Nigeria, and Kumasi in Ghana.[3,8,23] The high-grade tumours were 41.1%, which suggest the need for aggressive treatment regimens among our patients. The mucinous adenocarcinoma is associated with microsatellite instability and comprised 7.1% of cases in this series which is similar to 7.3% in Ife, Nigeria and range of 6 – 20% documented in developed countries, but lower than other Nigerian studies 23.7% in Kano, 33% in Jos, and 21.7% in Ibadan.[3,4,7,20,24-26] The signet ring cell carcinoma accounted for 9.5% which aligns with findings of other Nigerian studies.[3,4] The mucinous adenocarcinoma and signet ring cell carcinoma are common in younger patient and associated with poor prognosis.[24] The small cell neuroendocrine carcinoma contributed 1.2% of cases and it is in tandem with reported incidence of between 0.1% and 3.9%.[27] It is aggressive and associated with poor outcome.[27]

The constraint of this review was that it was a retrospective hospital-based study with the problems of inadequate clinical information such as anatomic location which was categorized as unspecified site (25 cases), laboratory, radiological and treatment outcome data that may be of additional prognostic significance. These may be best appraised using a structured prospective study. Likewise, not all tissue gets to our institution due to wideness of the study area.

CONCLUSION

CRC is one of the leading causes of cancer death worldwide. It was initially thought to be rare in our environment but recent sub-Saharan African studies including the index one has shown a rising incidence in our setting. There is the need for widespread screening facilities and social behavioural change communication to drive

population-level shifts toward a healthier lifestyle.

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Nil

Conflicts of interest

There are no conflicts of interest.

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The Non-Melanoma Skin Cancers, A hospital-based Study; The Irrua Specialist Teaching Hospital Experience.

*Owobu CI, *Azeke AT, *Ideiyenmin V, *Owolabi DO, **Eitokpah A, ***Imasogie DE.

*Department of Anatomic Pathology, Irrua Specialist Teaching Hospital, Irrua, Edo State, Nigeria. **Department of Internal Medicine, University of Benin Teaching Hospital, Benin City, Edo State, Nigeria. ***Department of Anatomic and Forensic Pathology, University of Benin Teaching Hospital, Benin City, Nigeria

Abstract:

Introduction: Squamous cell carcinoma (SCC), and Basal cell carcinoma (BCC)) are collectively referred to as Non-Melanoma Skin Cancers (NMSC). They have a high morbidity rate with a low mortality rate. These may impact negatively on the burden of the health sector, hence data on these tumors are invaluable in research and planning. The aim of this study therefore is to determine the prevalence, age, and sex distribution of NMSC at the Irrua Specialist Teaching Hospital, (ISTH), Irrua, Edo State.

Methods: This was a retrospective study of all cases of NMSCs histologically diagnosed over a 9-year period at the Department of Anatomic Pathology, ISTH. Data was obtained from surgical pathology register, histology request form and archived tissue blocks. Data analysis was done using IBM SPSS version 23.

Results: The NMSCs were the most common (77%) malignant skin tumors. Their ages ranged from 20 to 77 years. The SCC doubles as the most common skin tumor (70.37%) and NMSC (90.48%) in this study. The SCC showed a slight male predilection while the limited cases of BCCs were only seen in females.

Conclusion: The base line data for NMSC in this environment has been elucidated, and it is our expectation that it serves a basis for comparison to other studies in future, and also aid in planning in relation to its burden at ISTH. Key Words: estimated Glomerular Filtration Rate, Occult Renal Disease, Serum Creatinine

INTRODUCTION:

Corresponding Author: Azeke AT. Department of Anatomic Pathology, Irrua Specialist Teaching Hospital, Irrua, Edo State, Nigeria. Email: akhator2001@yahoo.com

Malignant melanoma, squamous cell carcinoma (SCC), and basal cell carcinoma (BCC) are common primary malignant skin tumours.[1, 2] BCC and SCC together are referred to as non-melanoma skin cancers (NMSC).[3] The frequency of NMSC, is significantly higher than that of other skin cancers.[4]

According to reports, the age-standardized incidence rate of non-melanoma skin cancer in Nigeria was 1.7/100,000.[5] Brazil was found to have the highest age-standardized incidence rate in Central and South America, with 137 cases per 100,000 people.[6] In Costa Rica, Ecuador, Peru, Chile, and Argentina, the corresponding age-standardized incidence rates per 100,000 people were 28.5/29.6, 22.7/23.4, 13.5/13.9, 11.7/0.8, and 9.5/12.9.[6] Columbia had the lowest rate of 0/100,000. Turkey has Asia's highest age-standardized incidence rate, 13.7/11.9/100,000, according to data.[6] In Thailand, the Philippines, Japan, Kuwait, and China, the age-standardized incidence

rates per 100,000 people are 2/2, 1.6/1.5, 1.0/0.9, 0.8/0.8, and 0.7/0.8 respectively.[6] India was found to have the lowest incidence rate, with 0.2/0.3/100,000 people.[6]

On average, NMSC mortality rates are roughly 0.1% of their incidence rates, which is a low rate.[7, 8] Because of this, the NMSC (BCC and SCC) has a high morbidity rate, which adds significantly to the health sector's expenses.[8] It is anticipated that the information gathered from this study will be useful for documentation, research, and eventually regional and national planning. Finding out the prevalence, age, and sex distribution of NMSC at the Irrua Specialist Teaching Hospital, Irrua (ISTH), Edo State is the goal of this study.

MATERIALS AND METHOD: A descriptive retrospective study whose subjects were all cases of NMSC (BCC and SCC) diagnosed histologically between January 1st 2011 and December 31st 2019 in the Department of Anatomic Pathology, ISTH.

The surgical pathology records, histology request cards, duplicate copies of histology reports, archived paraffin embedded tissue blocks in the departmental archives, and stained slides with haematoxylin and eosin were the sources of information used in this investigation. Information on each patient's age, sex, type of specimen, hospital number, histology laboratory number, clinical presentation, and clinical diagnosis could be found through the surgical pathology register, histology request form and duplicate copies of the histology report.

The histology slides were obtained, examined under a light microscope, and the diagnosis was entered on a data spread sheet next to the name of the patient. In situations where slides were lacking or of significantly reduced quality, freshly prepared sections were created from paraffin-embedded tissue blocks that were taken from the Department of Anatomic Pathology, ISTH archives. The sections were then stained with haematoxylin and eosin.

The IBM Statistical Package for Social Sciences, version 23, was utilised to examine the data acquired from this investigation. The analysis of the frequency and corresponding rates in percentages for categorical factors (sex and histologic diagnosis of BCC and SCC) and the age range, mean age, standard deviation, interquartile range and peak ages for continuous variables (age) was done. All instances of incomplete demographic information, missing slides and blocks from the departmental archives met the exclusion criteria. The authors for this study were from Irrua Specialist Teaching Hospital, and the University of Benin Teaching Hospital.

RESULTS:

Twenty-seven (27) malignant skin lesions were observed during the study's review period, 77% (21 cases) of the total, were NMSC. Their ages ranged from 20 to 77 years, with an interquartile range of 40 years. The median age was 40 years while the modal age was 38 years.

The male to female ratio was 1.1:1. The fourth decade represented the study population's peak age and it accounted for 38% of cases as seen in Table 1. The peak ages in males and females of the study population is as shown in table 1.

In this study, SCC's were 19 cases and this represented 70.37% and 90.48% of malignant skin tumours and NMSC respectively. Of these, 52.4% (11 cases) occurred in males while 47.6% (8 cases) occurred in females as shown in table 2. This gave a male to female ratio of 1.38:1. With an age range of 20 to 77 years and a peak in the fourth decade, the mean age

for SCC was 42.00 years (SD = 13.12). Table 2 illustrates the observation of a peak age in the 4th decade in males and 5th decades in females. Figure 1 displays a photomicrograph of squamous cell carcinoma.

Two NMSC cases were due to basal cell carcinoma (BCC), which made up 7.41 percent of malignant skin tumours and 9.52 percent of NMSC, respectively. Table 2 shows that these 2 cases involved women. The median age was 41 years. Figure 2 displays a basal cell carcinoma photomicrograph.

Table 1 showing the Age group and sex distribution of the study population

	Sex		
Age Group	Male	Female	Total
20-29	2	0	2
30-39	5	3	8
40-49	1	4	5
50-59	2	1	3
60-69	0	1	1
70-79	1	1	2
Total	11	10	21

Table 2 showing the Age group and sex distribution of the study population

	Squamous cell carcinoma		Basal cell carcinoma		
Age Group	Male	Female	Male	Female	Total
20-29	2	0	0	0	2
30-39	5	2	0	1	8
40-49	1	4	0	0	5
50-59	2	1	0	0	3
60-69	0	1	0	0	1
70-79	1	0	0	1	2
Total	11	8	0	2	21

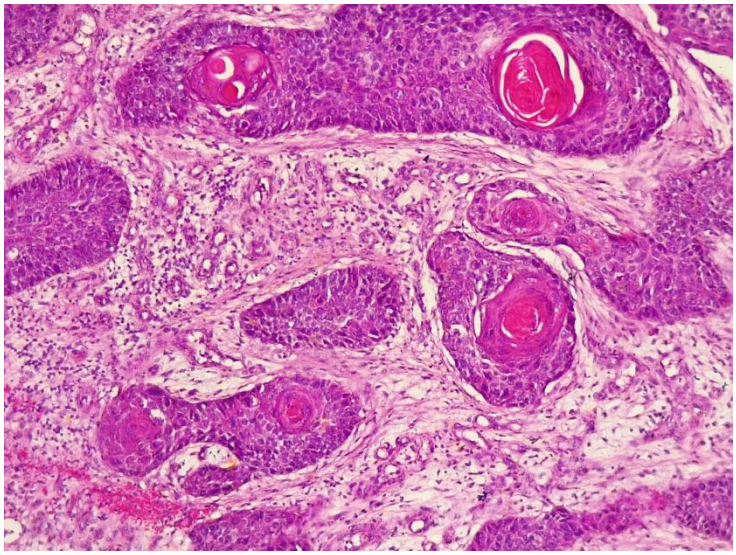

Figure 1: Squamous cell carcinoma, showing clusters of atypical epithelial cells forming keratin pearls. H and E stain. X 100 magnification.

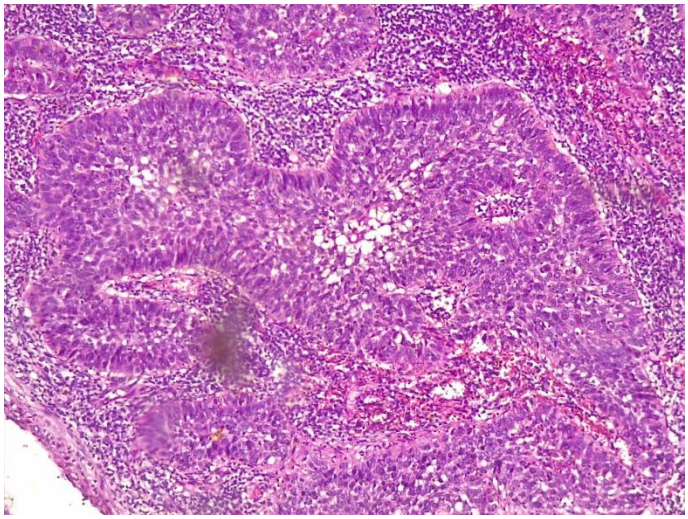

Figure 2: Basal cell carcinoma, showing nest of malignant basaloid epithelial cells with peripheral palisading. H and E stain. X 100 magnification.

DISCUSSION:

The NMSC (SCC and BCC) in this study accounted for approximately 4/5th (77.0%) of malignant skin tumours in this study. This is way higher than the findings of a previous study from Benin by Imasogie and Olu Eddo.[3] They reported that NMSC accounted for approximately 2/5th (36.90%) of malignant skin tumours in their study. Despite this, Squamous cell carcinoma accounted for a disproportionately high percentage of NMSC in comparison with BCC i.e. 90.48 % of SCC against 9.52% of BCC. This finding is comparatively similar to the findings of Imasogie and Olu-Eddo in Benin who also reported that SCC far outnumber BCC in frequency and corresponding percentages i.e. 82.6% of SCC as against 17.4% of SCC.[3] This study noted a slight male predilection of NMSC, a wide age range and a median age in the 5th decade, these are findings that are in agreement with a previous study from Benin.[3]

In this study, squamous cell carcinoma (SCC) accounted for 70.37% of malignant skin tumours. This is above the value of the upper limit of the reference range (13.6 to 51.3 percent) of malignant skin tumours reported from previous studies in Nigeria.[3, 9-14] The reason for this wide disparity is not readily discernable. This study noted a slight male preponderance in agreement with reports of previous studies in Caucasians and Nigerians.[9, 10, 15-17]

This study noted a peak in the incidence of SCC in the 4 decade which is consistent with the findings of previous studies that were carried out in Nigeria. [9, 10, 18-20] These studies have shown that SCC was most common in the 4 -6 decades.[9, 10, 18-20] These findings are contrary to what obtains in Caucasians where it has been documented that SCC is most common from the 7 decade.[8, 21]

In this study, basal cell carcinoma (BCC) accounted for 7.41 % of malignant skin tumours. This is consistent with the tumour being more common in the Southern part of Nigeria and comparatively similar to the findings of studies done in Ibadan (6.7%), Benin City (9.1%, 9.6% and 10%) and Lagos (10 %).[9-11, 13, 14] This is in contrary to the 22% reported by Datubo-Brown in Port Harcourt.[16] This may be attributed to a much relatively shorter study duration of 3 years when compared to a relatively longer duration in this study and also in studies with comparative values.[9-11, 13, 14] Contrary to our findings in this study, previous reports from studies done in Northern Nigeria had documented a lower frequency (2-4%) of BCC.[14, 18, 19] Australia has been reported to have the highest incidence of BCC worldwide with age the tumour in Caucasians with an outdoor occupation that exposes their skin to UV radiation from the sun is higher than those in Blacks, hence the reason for this disparity.[15, 22] The skin of Blacks is protected from UV radiation by the presence of melanin pigments in the epidermal layer of the skin.[8] A multicentre population based study in determining the age standardized incidence rates of BCC in Nigeria had been advocated in a previous study from Benin.[3] This we believe we add to the existing knowledge of this lesion on a national scale and allow for planning, research and ultimately planned patients care. The sex predilection in this study was in favour of the females, contrary to previous studies in the Saudis, Indians, Caucasians, and Nigerians which showed a male predilection.[1, 13, 15, 17, 23]

Conclusion

From the foregoing, the NMSC constitute a significant portion (77%) of malignant skin cancers in our own environment. The magnitude of SCC (90.48%) was by far

higher than that of BCC (9.52%). These tumours collectively had a wide age range (20–77 years) and a mean age in the 5th decade (40-49 years). There was no significant sexual predilection in the study population, and those with SCC on the one hand while on the other hand a female predilection was noted for BCC).

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