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Focus and Scope

The African Journal of Tropical Medicine and Biomedical Research is a multidisciplinary and international journal published by the College of Health Sciences, Delta State University of Abraka, Nigeria. It provides a forum for Authors working in Africa to share their research findings on all aspects of Tropical Medicine and Biomedical Sciences and to disseminate innovative, relevant and useful information on tropical medicine and biomedical sciences throughout the continent. The journal will publish original research articles, reviews, editorials, commentaries, short reports, case reports and letters to the editor. Articles are welcome in all branches of medicine and dentistry including basic sciences (Anatomy, Biochemistry, Physiology, Pharmacology, Psychology, Nursing etc) and clinical sciences (Internal Medicine, Surgery, Obstetrics and Gynaecology, Dental surgery, Child Health, Laboratory Sciences, Radiology, Community Medicine, etc). Articles are also welcome from social science researchers that document the intermediating and background social factors influencing health in countries of Africa. Priority will be given to publication of articles that describe the application of the principles of primary health care in the prevention and treatment of diseases.

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Editorial Commentary

The Desired Impact of Picture Archiving and Communication System (PACS) on Medical Research and Education: Its Shortcoming in A Centre in South South Nigeria

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INTRODUCTION

The ability to utilize the Picture Archiving and Communication System (PACS) to conduct research has been well documented in literature and has been used to conduct several profitable and notable researches. With this novel technology, researchers can easy retrieve data domiciled in PACS. The picture archiving and communication system (PACS) achieves this easy access to data by its working capacity of archiving, retrieving and routing or directing data to where they are needed. This is the expectation, but occasionally, things do not operate quite easily as it ought to. System failure occasioned by several intimidating factors could operate to hamper the usual smooth running of PACS.

Expectation and challenges

The components of a working PACS are assembled to acquire all images produced in the radiology department in a digital mode, thereby making it a filmless department. The innovative technology removes the old conventional way of producing images that are given to the patients in a paper jacket. The need for a dark-room, with tables carrying several trays filled with developing chemicals are subsequently discarded.

But occasionally, the smooth running of the system may fail, possibly due to electrical power outage or electrical power surges that could damage sensitive components in the machines. This negative challenge have been reported in the medical centre where PACS was installed. Apparently, no electrical stabilizers were installed along with the PACS. Due to this error electrical power fluctuations, and there were many instances, were transmitted to the sensitive component of the system, leading to damages.

Secondly, at the commencement of the utilization of the PACS at Delta State University Teaching Hospital, many dedicated consulting clinics with brand new computer sets where connected directly to the disseminating PACS office, images and reports were routed to these computer sets. At this period, consultation was relatively fast,

with patients literally viewing their images and reports online. The film clarity was good, such that patients could easily believe what reports they were given. Patients also had access to these images and reports outside the institution in the event of referrals and outside consultation. But with aging of the computer sets, and the economic situation did not allow for quick replacement, the online routing of images and reports declined drastically. With this development, the only available way of communicating results to the clinicians was via typical paper reports.

Thirdly, due to the stringent economic situation, attempts were made to repair damaged computers. However, this attempt failed because it was difficult to obtain genuine electrical parts of damaged computers. Thus, making it difficult to sustain the PACS in our centre.

Fourthly, the unwholesome incidence of the uni-directional migration of many of our skilled workers abroad for greener pastures has resulted in shortage of trained personnel at various levels of the work-force. A trend that was so severe there was less than 25% of the dedicated workforce available at certain time. This shortage of trained personnel led to increased workload on available staff as well as prolonged turnaround times in service delivery with delays in acquisition, processing and reporting images via the PACS. Furthermore, there was no reciprocal increment in the remuneration of these overworked staff to encourage and boost their morale.

All these challenges impacted negatively on the clinicians' interest to use the PACS to conduct teaching sessions with their students. Also, the possibility of utilization of the data for research was reduced due to the non-visibility of the PACS.[1]

Recommendation

Government funding of this technology is required especially in acquisition of dedicated electrical stabilizers, and replacement of damaged computers because of the desired importance of PACS in medical education and research.

Recruitment of new personnel to reduced work burden on the already depleted personnel is highly recommended.

Retraining of PACS personnel and clinicians is necessary to sustain the positive effects of this technology in medical education and research.

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Original articles

The Awareness of Cervical Cancer Prevention Strategies among Resident Doctors in Tertiary Centre in Benin City

Osazee K[1] and Obahiagbon O[2]

Abstract

Introduction: Cervical cancer is a disease of public health importance, being the fourth most common cancer among women worldwide and the most common cancer among women in developing countries. While developed countries practice a population-based cervical cancer screening program, developing countries like Nigeria practice an opportunistic screening mode. Therefore, health workers, including resident doctors, are expected to drive this model through opportunistic counselling and referral of their female patients and relatives.

This study was designed to assess the Awareness of resident doctors in UBTH regarding cervical cancer prevention strategies.

Materials and Method: This was a cross-sectional descriptive study from July 2022 to August 2023 among resident doctors involved in outpatient consultations at the University of Benin Teaching Hospital (UBTH).

Results: Overall, the knowledge of cervical cancer prevention strategies was good, with 62.5% of respondents demonstrating good knowledge. The attitude of the respondents towards cervical cancer prevention strategies was even better, with 86.4% of the respondents demonstrating an excellent attitude to these strategies. However, the practice of cervical cancer prevention strategies was generally poor. Most of the respondents (64.1%) had never referred a female patient for cervical cancer screening. Only 37.2% of the female participants had done a pap smear before, and most (68.8%) had done it just once. Among the male respondents, 75% of their female spouses had never done a pap smear.

Conclusion: The excellent knowledge and attitude about cervical cancer prevention strategies among resident doctors who participated in this study did not reflect on their practice of preventive measures.

Keywords: Cervical cancer, Human papillomavirus, Prevention strategies, Awareness

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INTRODUCTION

Cervical cancer is a disease of public health importance, being the fourth most common cancer among women worldwide[1] and the most common cancer among women in developing countries.[2,3] There has been a steady decline in the incidence of and mortality from cancer of the cervix in developed/high-income countries due to well-established screening programs, good human papillomavirus vaccine coverage and facilities/infrastructure for follow-up and prompt treatment of women with precancerous stages of the disease and cervical cancer.[4,5] This is not the case in low- and middle-income countries (LMICs) like Nigeria, with limited access to such preventive strategies. Therefore, most women in these countries present when cervical cancer is already in its advanced stages with associated high mortality rates.[1] In 2018, about 570,000 new cases and 311,000 deaths from cervical cancer were

estimated to have occurred globally, and almost 90% of these deaths occurred in LMICs.[1]

Nearly all cases of cervical cancer are caused by persistent high-risk (oncogenic) human papillomavirus (HPV) infection, with the viral DNA isolated in about 95% of cervical malignancies.[4,6,7] Over 200 species of this double-stranded DNA virus have been identified, but only about 40 are known to infect the lower genital tract.[3,6] High-risk serotypes 16 and 18 are the most common oncogenic serotypes, and they are implicated in about 65-75% of cervical cancers.[3] Other oncogenic subtypes include serotypes 31, 33, 35, 45, 52, 56, 58, amongst others. Serotypes 6 and 11 (low-risk HPV) are associated with genital warts.[3,4,6,7]

Human papillomavirus is sexually transmitted both by penetrative intercourse and skin-to-skin contact.[1] The peak time of acquiring this infection is shortly after coitarche in both males and females. The majority (up to 90%) of HPV infections are transient and resolve spontaneously within two years. The remaining 10% persist and give rise to preinvasive and malignant cervical lesions.[1,3] Factors associated with an increased risk of persistent HPV infection and cervical cancer include multiple sexual partners, early coitarche, tobacco smoking, immunosuppression, co-infection with other sexually transmitted infections like HIV and herpes simplex, prolonged oral contraceptive use and high parity.[1,3,7] The progression from infection to carcinogenesis takes 15 to 20 years in immunocompetent women and 5 to 10 years in the immunocompromised.[1,3] This provides a long window of opportunity for detecting the condition via different screening methods in its preinvasive or early malignant stages when a cure is achievable.[8]

The World Health Assembly in 2020 adopted a comprehensive approach to the control and prevention of cervical cancer utilizing primary, secondary and tertiary preventive strategies.[1] Primary prevention of cervical cancer involves vaccination of girls aged 9 – 14 years against HPV, preferably before they become sexually active[1,3,] while secondary prevention entails screening and treatment of preinvasive lesions in sexually active women from 25 – 30 years and above. Tertiary prevention involves early diagnosis and prompt treatment of invasive cervical cancer.[1]

It is expected that health workers and medical doctors will have a good level of knowledge about cervical cancer and its preventive strategies irrespective of their areas of specialization, which should result in a positive attitude and deliberate efforts towards its prevention. This is particularly important in developing countries where population-based screening programs are absent or not well established and where opportunistic screening is practised. Thus, health professionals would be expected to play a vital role in counselling and informing their female clientele about this condition, how to prevent it and going a step further to refer them to places where they can access these services. This study aimed to assess the knowledge, attitude, and practice of resident doctors in UBTH regarding cervical cancer prevention strategies.

MATERIALS AND METHODS

This cross-sectional descriptive study was carried out from June 2022 to August 2023 among resident doctors involved in outpatient consultations at the University of Benin Teaching Hospital (UBTH). "Resident doctors" refers to doctors undergoing specialist training in medical specialities. These doctors could play a vital role in the prevention of cervical cancer as they encounter female patients who may never have cause to visit the gynaecology/family planning clinic where routine screening is carried out.

Resident doctors involved in outpatient clinic consultations who had spent at least one year in residency training and consented to the study were included. Based on these criteria, residents from the surgery departments, internal medicine, paediatrics, and family medicine were selected for this study. Each department has a population of 40, 35, 25 and 20 residents, respectively, giving a total study population of 120. A total population sampling was done.

Resident doctors in the Department of Obstetrics and Gynaecology and Community Health were excluded from this study to avoid bias, as these departments are responsible for cervical cancer opportunistic screening in UBTH. Also excluded were residents not involved in outpatient clinic consultations, those less than a year in training and those who did not consent to the study.

A pretested self-administered structured questionnaire was utilized in data collection. The questionnaire was divided into sections A, B, C, and D. Section A assessed the sociodemographic characteristics of the respondents. In contrast, section B assessed respondents' knowledge of cervical cancer prevention strategies. Ten knowledge-based questions were asked, with a score of 1 for correctly answered questions and 0 for wrong or "unsure" responses, with a maximum score of 10 obtainable. Those with 50% correct responses and above were adjudged as having "good knowledge", while those with less than 50% correct responses were adjudged as having "poor knowledge". Section C assessed the attitude of the respondents towards cervical cancer prevention. Five questions were asked, and responses were put on a Likert scale. Those who agreed and strongly agreed were regarded as having a positive attitude to cervical cancer prevention. At the same time, those who strongly disagreed or were neutral were considered to have a negative attitude. Section D assessed the practice of cervical screening among the respondents.

Data was analyzed using the IBM SPSS software version 24, and results were presented in frequency tables, percentages and charts.

Ethical approval for the study was obtained from the University of Benin Teaching Hospital Research and Ethics Committee. All data collected were treated with utmost confidentiality and used for research purposes only.

RESULTS

SOCIODEMOGRAPHIC CHARACTERISTICS

One hundred three resident doctors participated in this study out of 120 residents from the selected specialities. The remaining 17 were excluded from the criteria stated in the methodology, giving a response rate of 86%. The mean age of participants was 36.6 years (SD ± 3.91), with the majority of the participants (81.5%) in the 4th decade of life i.e. 31 – 40 years (Table 1). There were more male than female participants (60 vs 43), and a more significant proportion were senior registrars (55.3%). Most participants (77.7%) had been in residency training for at least three years. Also, most of the participants were married (82.7%).

Table 1: Sociodemographic characteristics of respondents

VARIABLE	FREQUENCY n = 103	PERCENT %
Age (years)		
26 – 30	7	6.8
31 – 35	40	38.8
36 – 40	44	42.7
>40	12	11.7
Mean Age = 36.6 ± 3.91		
Sex		
Male	60	58.3
Female	43	41.7
the cadre of resident doctor		
Junior registrar	46	44.7
Senior registrar	57	55.3
Years in training		
1 -2	23	22.3
3 – 4	49	47.6
≥ 5	31	30.1
Specialty in-training		
Family medicine	18	17.5
Internal medicine	31	30.1
Surgery	34	33.0
Paediatrics	20	19.4
Marital status		
Single	17	16.5
Married	85	82.5
Separated	1	1.0
Religion		
Christianity	100	97.1
Islam	3	2.9

KNOWLEDGE OF CERVICAL CANCER PREVENTION STRATEGIES

The majority (95.1%) of the respondents were aware that cervical cancer has a long precancerous phase that is detectable by pap smear, as shown in Table 2. Most respondents were also aware of the risk factors for cervical cancer, and most answered all the questions concerning risk factors correctly (Table 2). The knowledge of vaccines available for cervical cancer was also high: 86.4% knew about the

Cervarix vaccine, while 45.6% knew about Gardasil. Furthermore, 60.2% of the respondents knew that HPV vaccines were available in the centre where they practised (UBTH). However, only 8.7% knew about Gardasil 9 (Table 2). Areas where the level of knowledge was also poor included the age group to be screened for cervical cancer, the screening interval and the HPV vaccine recommendation for males.

Overall, most participants (84.5%) demonstrated good knowledge about cervical cancer prevention strategies, while 15.5% had poor knowledge, as shown in Table 3.

Table 2a: Summation of Knowledge of Cervical Cancer Prevention Strategies

VARIABLE	**CORRECT RESPONSES FREQ(%)**	**INCORRECT RESPONSES FREQ(%)**
Risk factors for cervical cancer:		
Oncogenic HPV infection	98 (95.1)	5 (4.9)
All HPV infections	63 (61.2)	40 (38.8)
Early sexual exposure	91 (88.3)	12 (11.7)
Multiple sexual exposure	101 (98.1)	2 (1.9)
Cigarette smoking	74 (71.8)	29 (28.2)
Immunosuppression	87 (84.5)	16 (15.5)
Low social class	82 (79.6)	21 (20.4)
High parity	66 (64.1)	37 (35.6)
Immunosuppressive conditions	85 (82.5)	18 (17.5)
Cervical cancer has a long precancerous phase that is easily detectable by exfoliative cytology (pap smear).	98 (95.1)	5 (4.9)
Transmission of oncogenic HPV infection		
Vaginal sex	95 (92.2)	8 (7.8)
Anal sex	49 (47.6)	54 (52.4)
Oral sex	38 (36.9)	65 (63.1)
Blood transfusion	95 (92.2)	8 (7.8)
Average duration from HPV infection to invasive disease (cervical cancer)	29 (28.2)	74 (71.8)
Age group for cervical cancer screening	23 (22.3)	80 (77.7)

Table 2b: Summation of Knowledge of Cervical Cancer Prevention Strategies

VARIABLE	CORRECT RESPONSES FREQ(%)	INCORRECT RESPONSES FREQ(%)
Interval for cervical screening tests for women with no previous screening tests	34 (33.0)	69 (67.0)
HPV vaccines are recommended for:	26 (25.2)	77 (74.8)
HPV vaccines available		
Cervarix	89 (86.4)	14 (13.6)
Gardasil	47 (45.6)	56 (54.4)
Gardasil 9	9 (8.7)	94 (91.3)
Hiberix	96 (93.2)	7 (6.8)
HPV vaccines are available in UBTH	62 (60.2)	41 (39.8)

Table 3: Overall Knowledge of Cervical Cancer Prevention Strategies

LEVEL OF KNOWLEDGE	FREQUENCY n = 103	PERCENT %
Poor Knowledge	16	15.5
Good Knowledge	87	84.5

ATTITUDE TOWARDS CERVICAL CANCER PREVENTION

The participants demonstrate a positive attitude towards cervical cancer prevention, as shown in Tables 4 and 5. Overall, 86.4% had a positive attitude (Table 5).

Table 4: Attitude Towards Cervical Cancer Screening Strategies

VARIABLE	POSITIVE ATTITUDE FREQ(%)	NEGATIVE ATTITUDE FREQ(%)
Cervical cancer is a severe public health issue	86 (83.5)	17 (16.5)
A population-based cervical cancer screening program should be established in Nigeria	86 (83.5)	17 (16.5)
Cervical cancer prevention should be part of routine outpatient clinic conversations with women of reproductive age	90 (87.4)	13 (12.6)
Community-based cervical awareness campaigns will help reduce the burden of the disease in Nigeria	89 (86.4)	14 (13.60
HPV vaccination should be made accessible and added to the routine NPI immunization schedule	81 (78.6)	22 (21.4)

Table 5: Overall attitude towards cervical cancer prevention

VARIABLE	FREQUENCY n = 103	PERCENT %
NEGATIVE	14	13.6
POSITIVE	89	86.4

PRACTICE OF CERVICAL PREVENTION STRATEGIES

Most respondents (64.1%) had never referred or counselled a patient to have a pap smear. While half of them reported that they had not discussed cervical cancer screening with a patient in the preceding six months, 14.6% reported having never done so before. The most common reason for not having this conversation with patients was the busy nature of outpatient clinics. Among the female respondents, the majority (62.8%) had never had a pap smear; of the 16 respondents who had a previous pap smear done, 68.8% only had it done once. The common reasons given for not having a pap smear done were fear of detection of cervical cancer (27.6%), invasive nature of the test (24.1%) and unavailability of the service (17.2%). Among the male respondents, the majority (75%) reported that their female spouses had never done a pap smear.

Table 6a: Practice of cervical cancer prevention

VARIABLE	FREQUENCY	PERCENT %
Have you ever sent a patient for cervical cancer screening n = 103		
Yes	37	35.9
No	66	64.1
If yes, how many times? n = 37		
Once	1	1.0
2 - 5 times	19	18.4
6 - 10 times	7	6.8
More than ten times	10	9.7
When last did you discuss cervical cancer screening with a female patient n = 103		
One month ago,	21	20.4
2 - 6 months ago	16	15.5
Seven months - 1 year	16	15.5
More than one year	35	34.0
Never	15	14.6
Possible reasons for not discussing cervical cancer screening with female-female patients n = 96		
Busy outpatient clinics	34	35.4
No opportunity	29	30.2
No reason	21	21.9
Not within the scope of the specialty	6	6.3
Patients <18 years	5	5.2
I do not remember	1	1.0

Table 6b: Practice of cervical cancer prevention

VARIABLE	FREQUENCY	PERCENT %
Ever had a pap smear done n = 43		
Yes	16	37.2
No	27	62.8
If yes, how many times have you done it? n = 16		
Once	11	68.8
Twice	3	18.8
Three or more	2	12.5
Possible reasons for having never done a pap smear n = 29		
Fear of detection of cervical cancer	8	27.6
It's too invasive	7	24.1
Unavailability of service	5	17.2
Never considered it	3	10.3
Time constraints	1	3.4
Persistent postponement	1	3.4
No reason	1	3.4
Has your female spouse ever done a pap smear n = 60		
Yes	15	25.0
No	45	75.0
If yes, was it based on your counsel? n = 15		
Yes	10	66.7
No	5	33.3

Table 6c: Practice of cervical cancer prevention

VARIABLE	FREQUENCY	PERCENT %
Ever recommended cervical cancer screening for your partner/female friend n = 103		
Yes	59	57.3
No	44	42.7
Ever recommended cervical cancer screening for a relative n = 103		
Yes	52	50.5
No	51	49.5

DISCUSSION

Cervical cancer is the fourth most common cancer among women globally and the most common cancer among women in developing countries.[1-3,8] In Nigeria, it is the second most common cancer among women, breast cancer being the commonest.[9-11] Presently, there is no population-based screening program in Nigeria. Thus, opportunistic screening is practised, and it is expected that health workers, including medical doctors, should drive this process by educating patients about this condition and encouraging them to get screened for cervical cancer.

The knowledge of cervical cancer prevention strategies among resident doctors who participated in this study was good, as 84.5% responded correctly to 50% or more of the knowledge-based questions asked. Most of them (95.1%) were aware that cervical cancer has a long precancerous phase that is detectable by a pap smear, and they also knew about the vaccines available for its prevention, including the availability of vaccines in the hospital where this study was carried out. This level of knowledge was not surprising as these respondents were resident doctors with a high level of medical education. Esike *et al.,* in a similar study conducted among Nigerian resident doctors drawn from different training centres, reported even higher levels of knowledge.[8] In their study, 100% of the participants knew that cervical cancer had a precancerous stage and could be detected by a pap smear. This higher level of knowledge may have been recorded because their study was conducted among senior resident doctors with higher training and experience, unlike this study, which was among a mixture of senior and junior residents. Similarly, high levels of knowledge/Awareness of cervical cancer prevention strategies were reported among other health workers by Anyebe *et al.* [12], Addah *et al.* [13] and Awodele *et al.* [14] in Zaria, Port Harcourt, and Lagos, respectively, and by Kress *et al.* [15] in Ethiopia.

Despite the overall sound level of knowledge, some vital knowledge gaps were identified in this study. Only 22.3% of participants knew the recommended age group for cervical cancer screening, and only 33.0% knew the screening interval. Furthermore, only 25.2% of participants agreed that HPV vaccines can be

given to both males and females, while just 8.7% of participants were aware of the nonvalent HPV vaccine (Gardasil 9). These findings lend credence to the fact that resident doctors and, indeed, other health workers need more enlightenment about cervical cancer prevention strategies so that they can accurately counsel their patients and refer them for cervical cancer screening as appropriate.

The resident doctors' attitude to cervical cancer prevention in this study was positive. Most of them (>83.5%) agreed or strongly agreed that cervical cancer is a severe public health issue that should be prevented by the establishment of a population-based screening program, which has been proven to be effective in developed countries where this disease has almost been eradicated. A large proportion (78.6%) of the respondents also agreed or strongly agreed that HPV vaccination should be made accessible and added to routine immunization for children as this strategy has effectively controlled other deadly diseases like polio. Most of the respondents also submitted that cervical cancer prevention should be part of routine outpatient conversations with women of reproductive age and that community-based awareness campaigns should be carried out to increase Awareness of this preventable cancer. This cheerful disposition towards steps that can be taken to prevent cervical cancer was encouraging, considering that this was coming from doctors who are thought leaders in the health sector and as well as stakeholders in healthcare policy development. Awodele *et* al. also reported a positive attitude of Nurses towards cervical cancer prevention, where 89% of them thought it advisable to have a pap smear done.[14] Similar findings were reported by Zahedi *et al.* in a study among health workers in Haiti, where all the respondents agreed or strongly agreed that a cervical cancer screening program should be started in their community.[16]

Unfortunately, the excellent level of knowledge and positive attitude towards cervical cancer prevention did not translate to good practice among the resident doctors who participated in this study. Many (64.1%) had never referred or counselled a patient for a pap smear. In comparison, 14.6% of them reported that they had never had a conversation about cervical cancer prevention with a female patient. The reasons given for this level of practice included busy outpatient clinics (35.4%) and lack of opportunities to do so (30.2%), while 21.9% had no reason. Furthermore, an alarming 75% of male resident doctors reported that their female spouses had never done a pap smear. Similar findings were reported by Esike *et al.,* whose study was among resident doctors from diverse training centres in Nigeria, where 58% of respondents had never referred a female patient for cervical cancer screening, and 68% of the male respondents had never recommended cervical cancer screening to their female relations.[8] This suggests that more work needs to be done to encourage resident doctors who have contact with female patients who may never be present at the gynecologic clinic to include cervical cancer prevention in their clinic conversations and practice. This is particularly important in an environment where opportunistic screening is practised.

The uptake of pap smear among the female resident doctors in this study was poor at 37.3%, and of the 16 who had been screened before, 68.8% had only done it once. The primary reasons given for not taking the test included the fear of detecting cancer (27.6%) and the invasive nature of the test (24.1%). Esike *et al.* also reported a poor uptake of 22.7% among female resident doctors[8]. In studies conducted across the country which included other health workers, the

uptake has been reported to be even poorer: Anyebe *et al.* reported 15% in Zaria[12], Addah *et al.* – 12.8% in Port Harcourt[13], Anya *et* al. - 9% in Southeastern Nigeria[17] and Aboyeji *et al.* - 3% in Ilorin.[18] This trend is a cause for concern as female health workers are expected to be models in this regard. Poor uptake among these practitioners will likely negatively impact their ability to counsel and encourage other women to get screened.

CONCLUSION

The knowledge of cervical cancer prevention strategies among resident doctors undergoing training in UBTH is good, although this can be improved upon considering the knowledge gaps identified in this study. While the attitude of these doctors toward cervical cancer prevention strategies is also good, their excellent knowledge and attitude are not reflected in the practice of cervical cancer preventive strategies among them.

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Plasma electrolytes, osmolality and lipid profile in patients with acute stroke in a tertiary hospital in South-South, Nigeria.

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ABSTRACT

Introduction Stroke or cerebrovascular accident is a leading cause of morbidity and mortality worldwide. Electrolyte imbalances and dyslipidemia cause poor patients' treatment outcomes.

Aim of the study wasto evaluate Plasma electrolytes, osmolality and lipid profile in stroke patients.

Materials and Method: This was a descriptive cross-sectional study conducted between May 2022 to October 2022, on 144 stroke patients seen in the University of Benin Teaching Hospital. Serum electrolytes, Osmolality and lipid profile were assayed. Statistical analysis was done using SPSS version 22. Level of significance established at $p \leq 0.05$

Result: 69.5% of the subjects had ischemic stroke, 30.5% had hemorrhagic stroke. 45.1% of the subjects had hyponatremia and hypo-osmolality, 49% had hypokalaemia, 21.5% had metabolic acidosis and 6% hypochloraemia. Majority of the subjects (98%-99.3%) had normal lipid profile. No statistically significant difference between the electrolyte results of both ischaemic and hemorrhagic stroke.

Conclusion: Electrolyte derangements are common in patients with stroke. Hypokalaemia was the commonest observed, closely followed by hyponatremia and hypo-osmolality in this study. Electrolyte derangements in stroke patients should be promptly corrected and plasma levels monitored to reduce morbidity and mortality.

Key word: Acute Stroke, Plasma electrolytes, lipid profile

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INTRODUCTION

Stroke is a leading cause of adult disability and deaths worldwide, with an annual mortality rate of 5.5 million.[1] Prevalence seems to be on the increase, Nigeria not left out. Prevalence of stroke in Nigeria has been reported to be 1.4 per 1000, while the 30 day case fatality rate is said to be as high as 40%.[2] Some authors[3] reported a pooled crude incidence of 26 per 100,000 persons, while another author[4] reported incidence of 25 per 100,000.

In 2019 worldwide, 103 million cases of stroke was reported and 6.5 million deaths were accounted for by stroke. It was the second leading cause of death and disability[1,5] combined worldwide. Of the total death, 3.3 million deaths were due to Ischemic stroke.[5] One of the leading

causes of stroke in African countries is Hypertension.[6] Changes in lifestyles that support risk factors for stroke is on the increase.

The morbidity and mortality associated with stroke are due to some complications like Cerebral edema, infection, Deep Vein thrombosis and electrolyte derangements.

Disorders of serum electrolytes especially that of Sodium and Potassium have been reported to be the commonest electrolytes abnormalities found in stroke patients.[7] Electrolytes disturbances such as hyponatremia, hypernatremia resulting in increase in Brain Natriuretic Peptide and Atrial Natriuretic Peptide are common in acute phase of stroke.[7]

Studies[7,8] have also been done to determine the relationship of serum lipids and stroke; these studies reported dyslipidemia in stroke patients.

There seems to be paucity of information on electrolyte derangements, lipid profile and serum osmolality in stroke patients in Nigeria.

This study was aimed at evaluating the plasma electrolytes osmolality, lipid profile in stroke patients in Benin City.

MATERIALS AND METHODS

This descriptive cross-sectional study was conducted in the Neurology unit of the department of Internal Medicine in a tertiary care hospital, Benin City, from May 2022 to October 2022. A total of 144 patients aged 25-88 years with either ischaemic or hemorrhagic stroke, and diagnosed with either CT scan or MRI of the brain, every consecutive patient admitted in the ward was enrolled in the study. Data collected included demographic data, types of stroke (ischaemic or haemorrhagic), medical history of hypertension, diabetes mellitus was ascertained. This was collected using a structured questionaire. Plasma electrolytes, lipid profile, and Plasma osmolality were measured on the day of admission. Plasma electrolytes were measured using the Ion Selective Electrode Analyzer 4000. Plasma osmolality was measured using an Osmometer. Serum Total Cholesterol, Triglycerides, were measured using Enzymatic kit method.

Statistical Analysis: Statistical analysis was done using SPSS version 22. Student t test was used to compare means of variables. Level of significance was established at $P \leq 0.05$.

RESULT

A total of 144 subjects diagnosed with acute stroke were included in the study. They were aged between 21-94 years. One hundred.(69.5%) of the subjects had ischemic stroke, while 44 (30%) of them had hemorrhagic stroke (Table 1). Mean plasma sodium was 132.6±15.6mmol/L. Plasma Sodium level was normal in 77 (53.5%) of the subjects, while 65 (45.1%) had hyponatremia and 2 (1.4%) had hypernatremia (Table 2). Mean Plasma Potassium was 3.6 ± 0.6 mmol/L. Seventy one.(49%) of the subjects had normal Plasma Potassium, while 71 (49%) had Hypokalaemia and 2 (1.4%) had Hyperkalaemia (Table 2).

Mean Plasma Bicarbonate was 19.5±2.9 mmol/L. Plasma Bicarbonate was normal in 113 (78.4%) of the subjects, while 31 (21.6%) had low Bicarbonate levels (Table 2).

Mean Plasma Chloride was 100.6±7.5 mmol/L. Plasma Chloride was Normal in 138 (95.8%) of the subjects and low in 6 (4.2%) of the subjects.

Mean Plasma Osmolality was 280.5±23.4 mosm/kg. Seventy-seven (53.5%) had plasma osmolality within the normal reference interval,

while 65 (45.1.%) had hypoosmolality, and 2 (1.4%) had hyperosmolality.

Mean Serum Triglyceride was 92.1±43.5mg/dL. Plasma Triglyceride was normal in 143 (99.3%) of the subjects and high in 1 (0.7%) of the subjects (Table 2).

Mean Serum total Cholesterol was 154.7±70.7 mg/dL. Serum total cholesterol was normal in 141 (98%) of the sub subjects and high in 3 (2%) of the subjects (Table 3).

Mean Serum LDL Cholesterol was 97.2±60.0 mg/dL. LDL Cholesterol was normal in 141 (98%) of the subjects and high in 3 (2%) of the subjects (Table 2).

Mean Serum HDL was 38.6±18.3 mg/dL. HDL Cholesterol was normal in 143 (99.3%) of the subjects and low in 1 (0.7%) of the subjects (Table 2).

Mean Plasma Sodium was higher in Hemorrhagic stroke patients (139±11.5 mmol/L) than in ischemic stroke patients (132.9±7.2mmol/L). Difference was not statistically significant. P=0.166 (Table 3).

Mean Plasma Potassium in Haemorrhagic stroke was (3.4±0.2mol/L) and (3.4±0.8mmol/L) in ischemic stroke patients. No statistically significant difference in values observed. P=0.890 (Table 3).

Mean Plasma Bicarbonate was slightly higher (19.7±1.8mmol/L) in Haemorrhagic stroke patients compared with ischemic stroke patients (18.7±2.5mmol/L). Difference was not statistically significant (P=0.440) (Table 3).

Plasma Chloride was higher in subjects with Haemorrhagic stroke (107.2±11.9 mmol/L) compared with ischemic stroke subjects (97.9±6.1mmol/L). Difference was not statistically significant. P=0.131 (Table 3).

Dermographic parameters and types of stroke

TABLE 1:

Age (in years)	<65	67 (46.5%)
	≥65	77 (53.5%)
Sex	Male	80 (55.6%)
	Female	64 (44.4%)
Types of stroke		
	Ischemic – 100 (69.5%)	
	Hemorrhagic – 44 (30.5%)	

TABLE 2:

Plasma Electrolytes, Osmolality and Lipid Profile in the study population

Sodium	n	Mean
Normal (135-145mmol/L)	77 (53.5%)	132.6±15.6mmol/L
Hyponatremia (<135mmol/L)	65 (45.1%)	
Hypernatremia (>145mmol/L)	2 (1.4%)	
Potassium		
Normal (3.5-5mmol/L)	71(49%)	36.6±0.6mmol/L
Hypokalaemia <3.5mmol/L	71 (49%)	
Hyperkalaemia >5mmol/L	2 (1.4%)	
Bicarbonate		19.5±2.9mmol/L
Normal (20-30mmol/L)	113(78.4%)	
Low <20mmol/L	31(21.6%)	
Chloride		100.6±7.5mmol/L
Normal 96-108mmol/L	138(95.8%)	
Hypochloraemia <96mmol/L	6(4.2%)	
Osmolality		280.5±23.4 mOsm/kg
Normal 275-295mOsm/kg	77 (53.5%)	
Low <275mOsm/kg	65 (45.1%)	
High >295mOsm/kg	2 (1.4%)	
Triglycerides		
Normal <150mg/dL	143(99.3%)	92.1±43.5mg/dL

High >150mg/dl	1(0.7%)	
Total Cholesterol		
Normal <200mg/dl	141(98%)	154.7±70.7mg/dL
High ≥200mg/dl	3(2%)	
LDL Cholesterol		
Normal <130mg/dl	141(98%)	97.2±60.0mg/dL
High >130mg/dl	3(2%)	
HDL		
Normal 30-60mg/dl	143(99.3%)	38.6±18.3mg/dL
Low <30mg/dl	1(0.7%)	

TABLE 3:
Comparison of electrolytes in hemorrhagic and ischemic stroke

	Hemorrhagic stroke	Ischemic stroke	P value
Sodium (mmol/L)	139±11.5	132.9±7.2	0.166
Potassium (mmol/L)	3.4±0.2	3.4±0.8	0.990
Bicarbonate (mmol/L)	1 9.7±1.9	18.7±2.5	0.410
Chloride (mmol/L)	107.2±11.9	97.9±6.1	0.131

DISCUSSION

Out of the 144 subjects in this study, 77 representing 53.5% of them were in the age group 65 years and above. This implies that the incidence of stroke was higher in the older age group. Similar observations were made by Ajidahun et al[6] and Hassan et al[9] in their studies.

A larger percentage of the subjects had Ischaemic stroke, and a lower percentage had haemorrhagic stroke. Studies[7,10,11] in other parts of the world have also reported similar findings.

Ischaemic stroke appears to be commoner than Haemorrhagic stroke worldwide. This could be a reflection of socio-economic lifestyle. 45.1% of the subjects in our study had Hyponatremia. Several authors[7,9,12] have reported similar observations in their studies. Hyponatremia is frequent in Acute Stroke patients. Hyponatremia may be seen both in ischemic and hemorrhagic stroke[13] and is associated with worse outcomes and increased mortality.[13] Hyponatremia is usually hypoosmolal and may be due to syndrome of inappropriate Antidiuretic hormone secretion or Cerebral Salt Wasting Syndrome. This could be associated with high mortality rate. Khan et al[14]

reported in their study that it increases brain edema and subsequent neurological consequences. They reported that Hypernatremia is prevalent in ischemic stroke and is independently associated with in-hospital mortality and worse NIHSS scores at admission and discharge. Results in our study showed that hyponatraemia is more common in stroke patients in the area of study and hence, proper and adequate management protocol is to be instituted to prevent fatal outcomes.

Hypernatremia was observed in 1% of the study population. Hypokalaemia was also observed in 49% of the subjects in the study population. Wali[7] et al also reported hypokalaemia in their study in stroke patients in India. Gariballa et al[15] reported in their study that Hypokalaemia is common Post stroke and maybe be associated with a poor outcome. Hyperkalaemia was observed in 1.4% of the cases, hence may not be a common occurrence.

Majority of the patients had normal Plasma bicarbonate levels and a lower percent had low bicarbonate levels. Huang[16] reported in their study that low baseline bicarbonate levels and decreased bicarbonate levels during the ICU stay were associated with a high risk of 30-day mortality in Acute Ischemic Stroke. Metaolic acidosis can contribute to morbidity and mortality.

Majority of the subjects had normal plasma chloride with a few cases of hypochloremia. Bei[17] et al reported that hypochloremia was associated with a 2.4 fold increase in the risk of in-hospital mortality in their study.

Almost half of the separate population had hypoosmolality. This could be multifactorial, ranging from effects of syndrome of inappropriate ADH secretion, to fluid overload especially with hypotonic solution, amongst other causes. This could also be a contributory factor to hyponatremia observed the subjects.

Majority of the study population had normal lipid profile. Only 0.7% had hypertriglyceridemia, 2% hypercholesterolemia, 2% high serum LDL, 0.7% with low serum HDL. Some authors[8,18,19] reported dyslipidemia of varying degrees in their studies. Alamayehu[8] reported 51.1% cases of dyslipidemia in stroke patients in their study. Bharosay et al[18] reported increased risk of ischaemic stroke and poorer prognosis with increased serum levels of total cholesterol, triglycerides, low density lipoprotein, and low serum HDL. Rehman[19] also reported a high frequency of dyslipidemia in stroke patients in India. The observation of cases of dyslipidemia in our study may be influenced by socio-economic and dietary factors.

A comparison of Plasma electrolyte between Ischaemic and Hemorrhagic stroke patients showed that Mean plasma Sodium was higher in Hemorrhagic stroke than Ischaemic stroke, though difference was not statistically significant. Mean Plasma Potassium levels was virtually the same in both groups; Mean plasma chloride was higher in subjects with hemorrhagic stroke than ischaemic stroke, difference not statistically significant.

Mansoor et al[20] reported significantly higher sodium levels in hemorrhagic stroke patients compared with Ischemic stroke patients. Faramand and co authors[21,22] reported that increased sodium concentrations were associated with a higher incidence of stroke and worsening of neurological condition.

CONCLUSION

Electrolyte derangements are common in stroke patients. Hypokalemia is the commonest

observed in our study, followed closely by hyponatremia and hypoosmolality. Patients with Acute stroke should be screened immediately for electrolyte derangements. Early detection, proper monitoring and prompt correction of derangements in Serum electrolyte will reduce morbidity and mortality in stroke patients.

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Management of Ear Infections by Primary Healthcare Workers

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Abstract

Introduction: Ear infections are prevalent in children, and inadequate management of these infections by Primary Health Care Workers (PHCWs) contributes significantly to the burden of hearing loss. This study assessed PHCWs' knowledge and management practices of Childhood Ear Infections (CEI).

Materials and Method: The cross-sectional study used a semi-structured, self-administered questionnaire to elicit responses on knowledge and practice of CEI from 120 PHCWs working in urban and peri-urban areas in southwest Nigeria. Data were analyzed using descriptive and inferential statistics.

Result: The mean knowledge and practice scores were 27.2±4.7 and 9.7±2.9 respectively. Good and poor knowledge scores were seen in 14% and 4% of respondents respectively while 55% of respondents had poor practice scores. Knowledge was significantly associated with job cadre and the level of education was associated with CEI management practice.

Conclusion: PHCWs lack adequate knowledge of CEI, highlighting the need for continuous in-service training and mentorship in CEI management for all PHCWs.

Keywords: Childhood, Ear infection, Hearing loss, Primary Health Care, Health Workers

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INTRODUCTION

Ear infections occur in all age groups however, it is more common in children than adults. [1] Childhood ear infection (CEI) is the most frequently diagnosed illness among children in the United States (accounting for as high as 90%) [2] and in Uganda.[3,4] Ear infections affect 75 – 95% of the pediatric population,[5] most episodes occur within the first three years of life. The frequency of ear infections tends to peak between 12 to 18 months. [5] About 62% of children will have their first episode of middle ear infection by their first birthday, about 80 percent by the third birthday, and nearly 100 percent will have at least one episode by age five.[6] The burden of ear illnesses is highly prevalent in low- and middle-income countries (LMIC), [7] contributing significantly to the existing burden of health care.

The Primary Health Care (PHC) center is the first point of contact for healthcare in many LMIC communities and its services are often the entry point to health services for those in distress. 3 Primary healthcare workers (PHCWs) as health providers, therefore, play a huge role in the provision of basic health services for children, adults, and families. PHCWs are trained to recognize the risk factors as well as signs and symptoms of CEI in children. [8] The Standing Orders by the Federal Ministry of Health, Nigeria through the National Primary Healthcare Development Agency are guidelines for PHCWs, narrating health symptoms and describing how to

care for patients with different health conditions.[9] These Standing Orders include care for patients with CEI. PHCWs are also expected to recognize when the risk of harm is high enough to warrant referral to a higher level of healthcare provider. Poorly managed CEI may lead to complications such as hearing loss [10] with subsequent delayed acquisition of language, and impairment of cognition and emotional competence.[11] Other squeal of pediatric hearing loss include adverse effects on communicative skills, academic progress, and social success, with subsequent limitation of vocation and choices. [11] The earlier pediatric hearing loss occurs, the more significant adverse effect it exerts on a child's development.[12]

Children are the most vulnerable and dependent members of society, and their health is considered to be an overall measure of the health of society.[13] Since PHCWs are often the first point of contact with the healthcare system in LMICs the type of care they provide may form the core context for a child's development and a reflection of the health of the society. Thus, there is a need to ascertain the level of knowledge and practice of PHCWs in the management of CEI. This study aimed to determine the knowledge and practices relating to the management of CEI among PHCWs. The outcome can inform appropriate modifications to existing educational programs on ear health for PHCWs and policies regarding ear health safety.

MATERIALS AND METHODS

Study design, sampling, and data collection

This was a descriptive cross-sectional survey conducted in two purposively selected Local Government Areas (LGAs); Egbeda and Ibadan North LGAs in Ibadan, a cosmopolitan city in Southwest Nigeria. A total sampling of all the PHCWs (Nurses, Community Health Officers, Senior Community Extension Workers, and Junior Community Extension Workers) in both LGAs was done.

Data were collected from participants using an interviewer-administered structured questionnaire. The questionnaire included sections on socioeconomic status, socio-demographic characteristics of participants, knowledge, and practices relating to CEI. It also had 47 knowledge questions and 20 practice questions. Knowledge was categorized into causes, risk factors, signs and symptoms of CEI, the appearance of eardrums when diseased, and the consequences of poor management of CEI. Each question was scored with a mark and summed up to give a composite knowledge score which was categorized into good, average, and poor. Scores ≥33 were graded as good knowledge, 17 – 33 were graded as average knowledge, and scores ≤16 were graded as poor knowledge scores. Practice questions drawn out of the Standing Orders for Community Health Officers and Community Health Extension Workers with the inclusion of externally structured questions were used to test the management skill of CEI. Practice questions were also scored on a 20–point scale, scores <10 and >10 were categorized as poor and good practices respectively. An observational checklist was also used to collect data on the presence or absence of relevant ear health equipment such as otoscopes, ear syringes, headlights and mirrors, kidney bowls, and syringes in managing CEI in all the PHC facilities in the selected LGAs.

The data were analyzed using descriptive and inferential statistical tools. A chi-square test was done to establish associations between the independent (socio-demographic characteristics of the PHCWs) and dependent variables (knowledge and practices relating to CEI). Cross-tabulation of the dependent and independent

variables was also done to establish associations between variables. All statistical tests were conducted at a 2-sided significance level of 0.05.

The research adhered to the latest version of the Declaration of Helsinki throughout its implementation. Ethical approval for the study was granted by the joint University of Ibadan and University College Hospital Institutional Review Committee in Ibadan, Oyo state, Nigeria with approval number UI/EC/13/0327. Written informed consent was obtained from the Primary Health Care Workers after providing comprehensive information about the study.

RESULTS

A total of 120 primary health care workers responded to the survey with 69 PHCWs from Egbeda and 51 PHCWs from Ibadan North LGAs. There were more females 88 (73.7%) than males, and the mean age of the respondents was 40.94±7.71 years. Almost all 114 (95%) of the PHCWs had tertiary education as their highest level of education, 50.8% (61) were senior community health extension workers while the other half belonged to other cadres. Table 1 shows the socio-demographic characteristics of the respondents.

The majority 98 (81.7%) of the respondents had an average knowledge score, 4.2% (5) of respondents had poor knowledge, while only 14.2% (17) of respondents had a good knowledge score (Table 2). Most of the respondents missed significant knowledge questions relating to CEI, for example, 60% of the respondents disagreed that overcrowding could predispose children to CEI and 67.5% and 87.5% did not agree that bottle-feeding and exposure to passive smoking respectively, are risk factors for CEI. However, most of the respondents (83.3%) correctly identified vaccination as an important way of preventing CEI (see Questionnaire in Appendix II).

Overall, (66) 55% of the respondents had poor practice scores while (54) 45% had good practice scores (Table 3). Nurses and senior CHEWs had better practice scores compared to the CHOs and junior CHEWs. Similar to what was seen in the knowledge scores, key practice questions were missed by the respondents, for example, 82.5% of the PHCWs chose the administration of Artemether-Lumefantrine to a child with ear pain and discharge (see Questionnaire in Appendix II). Though the PHCWs agreed that the Standing Orders were well-designed to guide in the management of illness in children, (79) 65.8% of them had not received any training relating to ear health within the 24 months preceding the study. Apart from kidney bowls and syringes, all PHCs in the study sites lacked adequate ear health instruments to manage CEI (Table 4). The provision of training and equipment was suggested by the respondents as an important requirement for better management of CEI. Chi-square analysis revealed a positive association between the job cadre of respondents and the level of knowledge about CEI (Table 5), thus showing that the job cadre influenced the knowledge of CEI. Positive associations were seen between the management practices of CEI and both the educational level and job cadres of PHCWs (Table 6), suggesting that the level of education and job cadres of PHCWs influenced their management of CEI.

Table 1 Distribution of the socio-demographic characteristics of PHCWs

Variable	Category	Frequency (%)
Gender	Male	32 (26.7)
	Female	88 (73.7)
Age	20-30yrs	15 (12.5)
	31-40yrs	36 (30.0)
	41-50yrs	57 (47.5)
	51-60yrs	12 (10.0)
PHC Location	Egbeda	69(57.5)
	Ibadan North	51(42.5)
Educational level	Tertiary education	114(95.0)
	Secondary education	6(5.0)
Job role	Nurse	15(12.5)
	Community Health Officer	22(18.3)
	Senior Community Health Extension worker	61(50.8)
	Junior Community Health Extension worker	22(18.3)

Table 2 PHCWs Knowledge of childhood ear infections

Grade	Score	Frequency	Percent
Poor	≤ 16	5	4.2
Average	>16-33	98	81.7
Good	>33	17	14.2

Table 3 Practices of PHCWs as it relates to the management of childhood ear infections

Grade	Frequency	Percent
Good	66	55.0
Poor	54	45.0

Table 4 Checklist of available equipment for managing CEI

Equipment	Egbeda LG	Ibadan North LG
Otoscope	Absent	Absent
Pneumatic otoscope	Absent	Absent
Cotton applicators 14cm serrated	Absent	Absent
Headlight (spear bulb)	Absent	Absent
Head mirror	Absent	Absent
Ear syringe	Absent	Absent
Kidney bowls	Present	Present
Otoscope (spear bulb)	Absent	Absent
Disposable specula	Absent	Absent
Syringes	Present	Present

Table 5 Association between PHCW's education/ Job cadre and knowledge of CEI

Variable	Knowledge grade			Chi-square
Education				0.195
Secondary education	1(0.8%)	5(4.2%)	0(0%)	
Tertiary education	4(3.3%)	93(77.5%)	17(14.2%)	
	5(4.2%)	**98(81.7%)**	**17(14.2%)**	
Job Cadre				**0.020***
Nurse	0(0%)	13(10.8%)	2(1.7%)	
CHO	0(0%)	17(14.7%)	5(4.2%)	
Senior CHEW	0(0%)	52(43.3%)	9(7.5%)	
Junior CHEW	5(4.2%)	16(13.3%)	1(0.8%)	
	5(4.2%)	**98(81.7%)**	**17(14.2%)**	

***** indicates a significant relationship at a 5% margin of error (Yates correction of 0.5).

Table 6 Association between PHCW's education/ Job cadre and practice of CEI

Variable	Practice grade		Chi-square
Education			0.005*
Secondary education	6(5.0%)	(0.5%)	
Tertiary education	48(40.0%)	66(55.0%)	
	54(45.0%)	66(55.0%)	
Job Cadre			0.001*
Nurse	(0.5%)	15(12.5%)	
CHO	12(10.0%)	10(8.3%)	
Senior CHEW	22(18.3%)	39(32.5%)	
Junior CHEW	20(16.7%)	2(1.7%)	
	(0.5%)	15(12.5%)	

***** indicates a significant relationship at a 5% margin of error (Yates correction of 0.5).

DISCUSSION

The female gender was dominant among PHCWs, a trend that is seen in many PHC facilities in Nigeria,[14-16] Kenya,[17] and Nepal[18]. The majority of the respondents in this study had formal education, and a large proportion of these respondents had tertiary education; however, studies from other locations showed that the majority of PHCWs completed only secondary education..[19] The difference may be related to the localities where the study was conducted, the locales for this study were situated close to a major cosmopolitan city in Nigeria. The mean age recorded in this study showed that most of the PHCWs were older workers this peculiarity was recorded in other studies, suggesting that PHCWs are not highly mobile.[18,20]

There is no prior study detailing the knowledge of PHCWs on CEI, however, studies among caregivers in India[21] and Nigeria[22] showed low overall knowledge of otitis media. Most of the PHCWs in this study could identify some risk factors and symptoms of CEI, the better knowledge of the PHCWs compared to those of caregivers showed the impact of the training received by PHCWs. Nonetheless, this training appears inadequate with respect to CEI as shown in the overall knowledge score. This is may be due to a lack of training in primary ear and hearing care training (PEHC) by many PHCWs in LMICs.[23] There is a need to improve knowledge about risk factors for CEI among PHCWs.[24] The responses and knowledge scores of the study participants suggests the need to prioritize provision of additional courses targeted at improving and refreshing the knowledge of PHCWs on CEI; the trained PHCWs can then pass this knowledge across to parents and caregivers.

The importance of standard operating procedures for all cadres of health workers was demonstrated in the knowledge of immunization practices. Several reports have shown that over 80% of health workers have poor knowledge of national policy on safe immunization practices,[20,25,26] but the majority of PHCWs in this study were knowledgeable on the importance of

immunization in the prevention of CEI. More than 80% of children under the age of three suffer from CEI, with an average treatment cost of $5 billion annually,[27,28] yet vaccination has been shown to benefit children who are prone to recurrent CEI.[29]

While the majority of the PHCWs had an average score on knowledge parameters, the majority also had poor practice scores relating to CEI. This poor practice may be related only to CEI as it has been shown that some PHCWs have good practices on drug provision for general childhood ailments.[30,31] The practices of junior PHCWs (community health officers, and junior community health extension workers) in the management of CEI were poor. There was also a difference in the level of practice between the various cadres of PHCWs. The lower cadre of PHCWs could not deliver better CEI management services like those of the higher cadres probably due to differences in the level of training and experience compared to the senior cadres. This hypothesis explaining the differences between job cadre and management capabilities is corroborated by other reports which showed that higher education produces better performance among health workers, and more educated community health workers deliver better services.[32] Higher education levels tend to boost general knowledge among PCHWs, which in turn improves their performance, whereas a lower education level is linked to poorer healthcare service delivery.[33] However, the education level of PHCWs did not impact their knowledge scores of CEI. A possible cause for this observation could be related to the age of the respondents. The majority of the PHCWs were in the older age category and thus had attained their highest educational level several years earlier. Insufficient training for PHCWs is a significant contributor to the knowledge and practice gap, and accounts for the average to poor grades obtained in the study. Lack of training or insufficient training is a proven problem in PHC practices[15] with healthcare workers reporting inadequate training.[34] Thus, despite the level of education of the respondents it is probable that the lack of regular on-the-job training contributed to the lack of correlation between the level of education and the knowledge scores. Unfortunately, this lack of training for PHCWs appears not to be an isolated incident.[34] PCHWs with additional or refresher training are more likely to achieve high-performance levels as continuous training helps PCHWs perform more effectively.[35] This has been demonstrated in several studies where on-the-job training improved PCHWs' skills and knowledge and enabled better job performance.[36-38] Thus, provision of periodic refresher courses for PHCWs is vital for enhanced service delivery in the management of CEI. Provision of financial motivation and incentives in addition to supplemental training and appropriate equipment provision will also encourage PHCWs to improve the delivery of primary Ear and Hearing Healthcare in LMICs.[15,34]

The poor practice scores of CEI observed among the PHCWs denote key deficiencies in the management of childhood illnesses. This is not an isolated trend as similar reports have been documented.[34] PHCWs were not familiar with the Standing Orders guiding their operations as revealed by the poor practice scores. These Standing Orders serve as a foundation for effective training, monitoring, and assessment of all primary healthcare services to improve healthcare delivery quality,[39] therefore, non-adherence to the standing orders poses health risks to the members of the society. The necessary equipment for the management of CEI in a primary health care center was inadequate and did not meet the recommendations specified by

the WHO Primary Ear and Hearing Care manual.[40] Lack of this equipment can adversely affect the services provided by PHCWs in managing CEI; it may also contribute to the poor management practices of CEI. A previous survey of health workers revealed complaints of lack of equipment, lack of motivation, and inadequate training and supervision in health facilities. [34] This suggests that periodic assessments and monitoring of PHCs are necessary to ensure the adequacy of necessary equipment for CEI management[15]

The study was limited by the relatively small sample size (though reflective of all PHCWs in the study sites), thus limiting the power for comparisons. The cross-sectional nature of the study also made it impossible to incorporate all personnel especially those on vacation at the time of the study.

CONCLUSION

The level of knowledge and management of CEI among PHCWs is less than optimal. There is a need for regular in-service training on the management of CEI for PHCWs, especially the lower cadre officers. Adequate resources should be deployed on health, education, and social services including provision of appropriate medical equipment for PHCWs, to facilitate better service delivery and sustainability.

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Declaration of Conflicting Interest

The Authors declare that there is no conflict of interest.

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Inhibition of *Naja nigricollis* Venom Phospholipase A2 by Ethylacetate Extract of *Solanum dasyphyllum* Schum and Thonn leaf: An *In-vitro* and *In-silico* Approach

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Abstract

Introduction: Snakebite envenomation is an acute medical emergency, particularly in the tropics, and clinical treatment is through the administration of antivenom. However, given the limitations of conventional antivenoms, the plant kingdom is being explored for possible antivenom compounds. The aim of this study was to evaluate the phospholipase A_2 inhibitory potential of ethylacetate extract of *Solanum dasyphyllum* and to isolate the compound responsible for the antivenom activity.

Materials and Method: The leaves of *S. dasyphyllum* were extracted, phytochemical constituents were screened and phospholipase A_2 enzyme inhibition study was carried using standard methods. The ethylacetate extract was subjected to various chromatographic techniques to isolate the antivenom compound, and the structure was determined using HNMR and CNMR spectra. The proposed structure of the isolated compound was used for molecular docking study with cobra venom phospholipase A_2.

Results: The result of phospholipase A_2 enzyme inhibition shows that different concentrations of ethylacetate extract of *S. Dasyphyllum* significantly inhibited the activity of phospholipase A_2 in *N. nigricollis* venom. Chromatographic investigations of the extract lead to the isolation of methyl linolenate, and a strong interaction with the enzyme active site and a binding energy of -6.60 kca/mol was recorded when docked with cobra phospholipase A_2 enzyme, thereby making it a potential inhibitor of the enzyme.

Conclusion: Conclusively, ethylacetate extract of *S. dasyphyllum* demonstrated a significant inhibition of phospholipids A_2 enzyme and this finding suggests that methyl linolenate may be a potential inhibitor of phospholipase A_2 and could possibly lead to the development of a drug to treat snakebites.

Keywords: *Solanum dasyphyllum*, envenomation, molecular docking, chromatography, NMR, Inhibition.

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INTRODUCTION

According to the World Health Organization, snakebites are a neglected public health problem, especially in tropical countries, where millions of people suffer from snakebite envenomation [(1)]. It is estimated that over 435,000 snakebites occur annually in Africa, while Nigeria reportedly accounts for a fifth of the total West African snakebite burden [(2)]. Snake venom is a mixture of pharmacologically active substances such as acetylcholinesterase, L-amino acid oxidase, phosphodiesterases, phospholipase A_2, etc., which have potent, lethal and debilitating effectson biological system [(3)]. Phospholipase A_2

are esterolytic enzymes found in snake venoms that typically catalyze the breakdown of glycerophospholipids, the main component of biological cell membranes, into lysophospholipids and fatty acids, including arachidonic acid, the precursor of inflammatory cascade, leading to a range of adverse pharmacological effects by altering the physical properties of cell membranes and activating downstream signal transduction pathways [4].

Venom is used to immobilize and digest prey as well as for defensive purposes [5]. However, venomous snakebite is an acute medical emergency characterized by local tissue damage and systemic toxicity such as bleeding disorders, hypotension, severe paralysis, etc. [6,7]. There are over 3000 species of snakes known to science, 30% of which are poisonous and considered dangerous to humans [8]. In Nigeria, *Elapidae* and *Viperidae* are the two snake families that cause the majority of recorded morbidity and mortality in humans. The family *Elapidae* includes the cobras, whose venom are mainly neurotoxic and cytotoxic, while *Viperidae*, such as carpet vipers and saw scale vipers, are mainly hemotoxic [9]. Antivenom immunotherapy is the specific treatment against snakebites, but is associated with various side effects such as serum sickness and pyrogen reactions [10, 11]. Therefore, it is important to explore the plant kingdom for an alternative treatment that involves the use of various venom inhibitors that could replace the action of antivenom.

Solanum dasyphyllum, a semi-woody perennial medicinal plant, belongs to *Solanaceae* family [12]. It has been reported to possess antioxidant, antispasmodic and neuromodulatory activities [13, 14]. In southwestern Nigeria, *S. dasyphyllum* is used ethnomedically to treat snakebite envenomation; however, the effectiveness of the plant as anti-snake venom has not been scientifically studied. In the present study, the isolated compound from the ethyl acetate extract of *S. dasyphyllum* was investigated for possible inhibition of *N. nigricollis* venom phospholipase A_2 enzyme using in vitro and in silico methods.

MATERIAL AND METHODS

Solanum dasyphyllum leaves were collected from Odeomu town (Latitude: 7°32'0\"North; Longitude: 4°24\'0\"East) in Ayedaade local area, Osun State. They were identified and authenticated at the Department of Botany Herbarium, Obafemi Awolowo University, Ile-Ife, Osun State and a voucher specimen was issued with number IFE-17489. The leaves were air dried in the shade for a week and pulverized by manual grinding. 300 g of the powder was then soaked in 3000 mL of ethylacetate for 72 hours with intermittent stirring. Under reduced pressure, the filtrate was evaporated to dryness to give a dark green crude extract.

The ethylacetate extract of *S. dasyphyllum* was evaluated for the presence of alkaloids, tannins, saponin, carbohydrate, flavonoids, terpenes, steroids and cardiac glycosides according to the method described by Sofowora (1993).

Lyophilized *N. nigricollis* venom was obtained from the Department of Pharmacognosy and Drug Development, Ahmadu Bello University, Zaria, Nigeria. Before use, the venom was reconstituted in phosphate buffer, pH 7.2, centrifuged at 2000rpm for 10 minutes and the supernatant was used for further studies. The venom was preserved at 4^0C.

Phospholipase A_2 was determined according to the titrimetric method of Adamich et al [20] with slight modification. A lecithin emulsion was prepared by dissolving 4 g of lecithin in 30 mL of 1 M NaCl and 10 mL of 0.1 M $CaCl_2$; the mixture was made up to 200 mL with distilled water. The

reaction mixture containing 15 mL of lecithin emulsion and 1 mL (1 mg/mg) of the reconstituted venom was adjusted to pH 8.0 with 0.02 M NaOH. The volume of 0.02 M NaOH required maintaining pH at 8.0 by titration for 4 minutes was recorded. A decrease of 1 pH unit corresponds to a fatty acid release of 133 µmol. Enzyme activity was expressed in µmol of fatty acid released per minute. For the inhibition study, the extract was pre-incubated with venom at 37 °C for 45 min.

Calculation:

[NaOH] = ml NaOH used Test - ml NaOH used Blank

Units/mg enzyme =
(Molarity of NaOH) × [NaOH] ×1000
(4)× (mg enzyme in the reaction mixture)

1000 = conversion from millimoles to micromoles.

4= Time of assay

Silica gel (100 g) was wet packed into a glass column using 100% chloroform. A portion of the ethylacetate extract (2 g) in fine powder form (pre absorbed with silica in chloroform) was loaded onto the packed column. The eluents (fractions) were collected in 5 mL each while the column was filled with 100% chloroform, chloroform/methanol mixtures (90:10; 70:30; 60:40; 50:50; 40:60; 30:70; 10:90) and methanol (100%). The fractions were analyzed on analytical TLC and similar R_f values from the column were pooled to give Nine (9) fractions designated E_1 to E_9. The fractions E_1 to E_9 were subjected to phospholipase A_2 enzyme inhibition study, the fraction with the best inhibition activity (E_2) was further subjected to preparative thin layer chromatography (TLC) according to the conventional one-dimensional ascending method using a TLC plate, followed by gel filtration with Sephadex LH-20 with 100% methanol as elution solvent, which resulted in the production of a white crystalline substance with the name E_{2i} (26 mg). The isolated compound was subjected to 1H-NMR and 13C-NMR analysis by Agilent Technologies (Jackson_NMR vnmrs 500 spectrometer). The sample was dissolved in the deuterated solvent, filtered and placed in a 5 mm NMR tube. Chemical shifts were recorded in parts per million (ppm).

Molecular docking protocols are often used to predict binding affinities for a range of ligands. The computational docking study was carried out to predict the most favorable binding position of the isolated compound within the binding pocket of the phospholipase A_2 enzyme isolated from Cobra venom. To obtain accurate results, all docking was performed with default parameters. Molecular docking was performed on the three-dimensional structures of Cobra phospholipase (PDB: 1A3F, resolution = 2.65 Å) obtained from the protein database (http://www.rcsb.org/pdb/home/home.do) and the 2D structure of the isolated compound, drawn using ChemDraw.

Intermediate steps, such as pdbqt files for protein and ligand preparation and grid box creation, were performed using the graphical user interface program AutoDock Tools (ADT). ADT assigned polar hydrogen, uniform atom Kollman charges, solvation parameters, and fragment volumes to the protein. AutoDock saved the prepared file in PDBQT format. AutoGrid was used to create the grid map using a grid box. During the docking process, both the protein and the ligands are considered rigid. The results with a positional root mean square deviation (RMSD) of less than 1.0 Å were summarized and represented by the most favorable binding free energy result. The pose with the lowest binding energy was analyzed

by Discovery Studio

RESULTS

The result of the phytochemical screening as shown in Table 1 revealed that presence of Alkaloids, Flavonoids, Tannins, Steroids, Terpenoids and Carbohydrate; Cardiac glycoside was not detected.

The in-vitro enzyme inhibition study of Phospholipase A_2 enzyme activity was carried in triplicates and mean ± standard deviation was calculated. The different concentrations of ethylacetate extract were able to significantly inhibit the activity of phospholipase A_2 enzyme in the treated groups compared to the control group, as shown in Figure 1. However, 200 and 400 µg/ml showed the best inhibitory effect (88.2%), followed by 600, 800 and 1000 µg/ml (76.5%).

The effect of different fractions of ethylacetate leaf extract of *S. dasyphyllum* on phospholipase A_2 activity of *N. nigricollis* venom is presented in Figure 2 where fraction 2 exhibited the least activity, followed by fraction 4. The details of the isolate obtained after series of chromatographic techniques is presented in table 2, table 3, figure 3 and figure 4. 3D structure of proposed isolated compound Methyl linolenate isolated from *S. dasyphyllum* leaf extract serve as ligand used for molecular docking study as presented in Fig 5, 6 and 7. The binding free energy values observed for Methyl linolenate docked with Phospholipase A_2, − 6.60 kcal/mol.

Table 1: **Phytochemical Constituents of Ethylacetate Leaf Extract of Solanum dasyphyllum**

Phytochemicals	**Observation**
Alkaloids	
Dragendorff's	+
Mayer's reagent	+
Flavonoids	
Shinda's test	+
Ferric chloride	+
Tannins	
Ferric chloride	+
Bromine water	–
Steroid	+
Terpenoids	+
Carbonhydrate	
Molish test	+
Cardiac Glycoside	
Keller-kilian	

Key: + = Present - = Absent

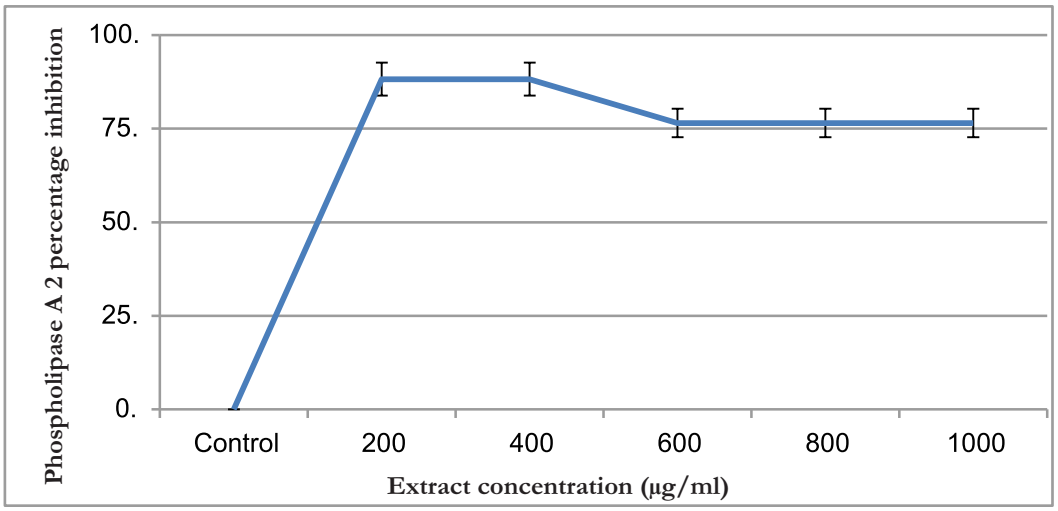

Figure 1: Effect of different concentrations of Ethylacetate leaf extract of *Solanum dasyphyllum* on phospholipase A_2 activity of *Naja nigricollis* venom.

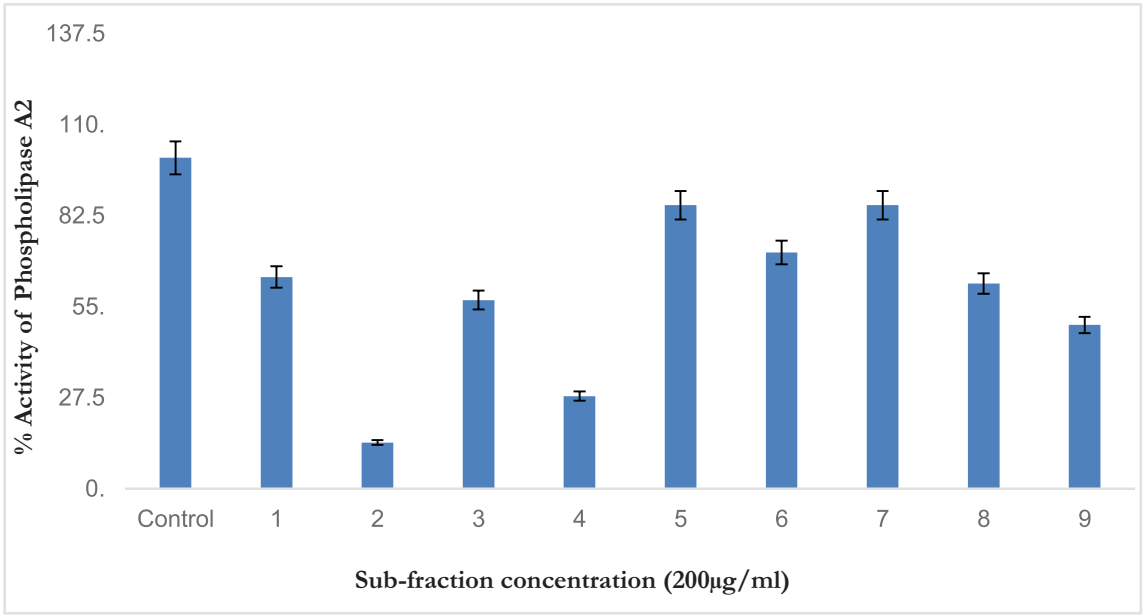

Figure 2: Effect of Different fractions of Ethylacetate Leaf Extract of *S. dasyphyllum* on Phospholipase A_2 Activity of *N. nigricollis* Venom.

Table 2: Physical properties of the isolated compound ($E2_i$)

Colour of isolate	Colour of spot	Solvent system	*Rf* value	Solvent
Crystal white	light purple	Butanol/Acetic acid/Water (5:4:1)	0.77	Chloroform

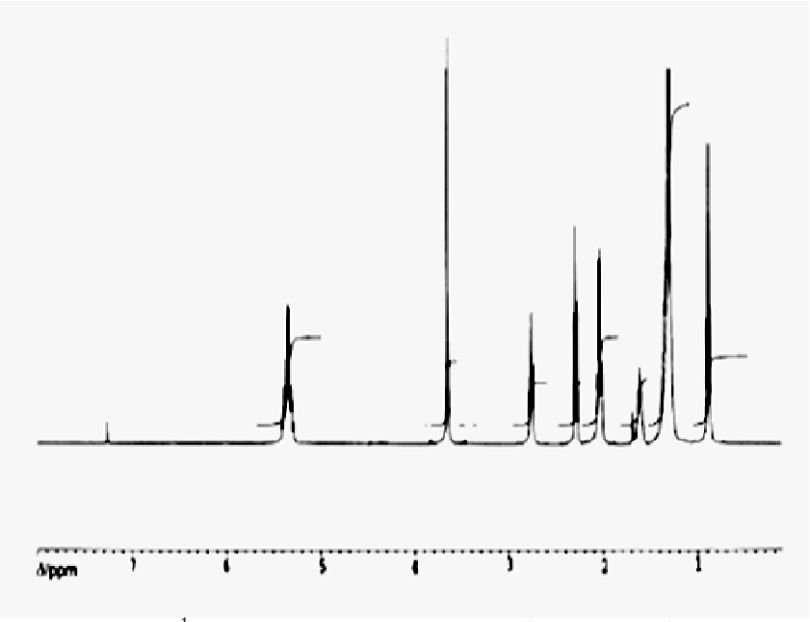

Figure 3: ^{1}H-NMR spectra of isolated compound ($E2_i$).

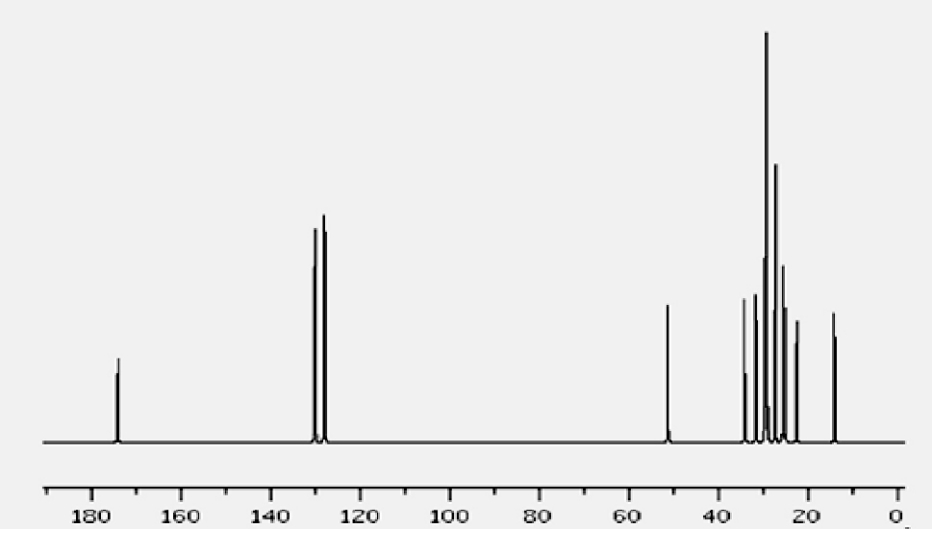

Figure 4: ^{13}C-NMR Spectrum of Isolated Compound (E_{2i})

Table 3: ^{1}H-NMR and ^{13}C-NMR Chemical Shift of the Isolated Compound

Position	^{13}C chemical shift	^{1}H chemical shift
1	14.02	0.86
2	22.63	1.24
3	31.75	1.2
4	29.11	1.25
5	27.21	1.96
6	130.4	5.47
7	128.4	5.48
8	25.81	2.25
9	128.4	5.49
10	130.4	5.50
11	27.2	2.63
12	29.1	1.26
13	29.4	1.28
14	29.4	1.42
15	29.4	1.43
16	24.84	1.55
17	33.88	1.20
18	173.4	-
19	52.21	3.63

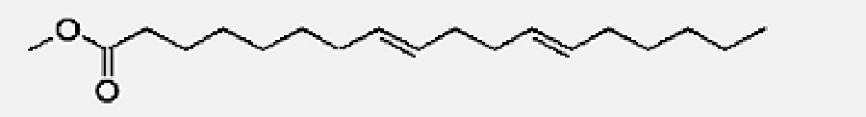

Figure 5: Proposed structure of isolated compound ($E2_i$): Methyl linolenate

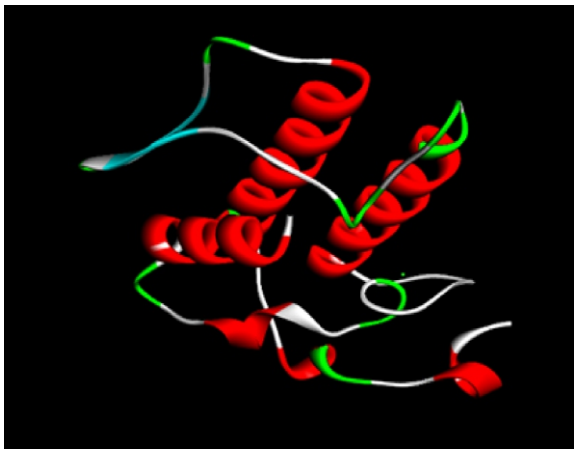

Figure 6: 3-D structure of Phospholipase A_2 (Protein data bank)

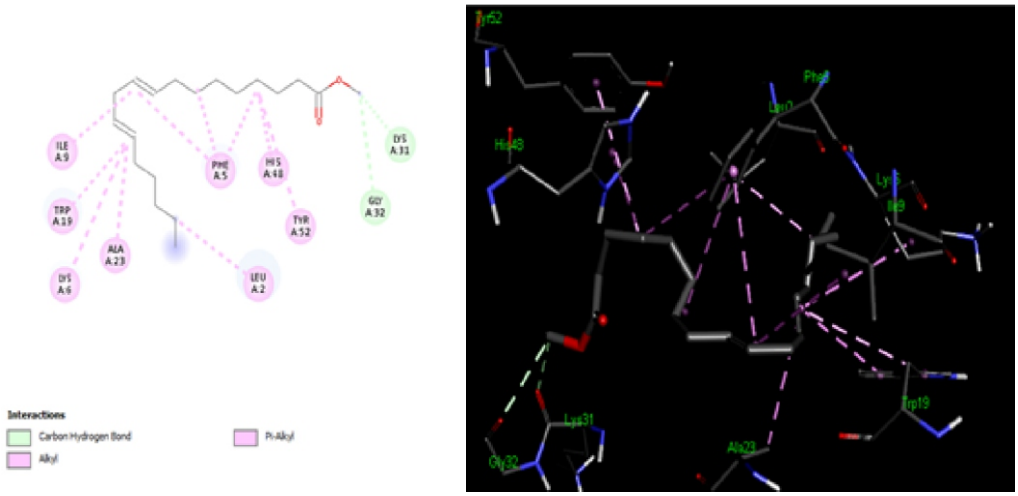

Figure 7: Outline of the molecular docking process. (A) The two-dimensional structure of Phospholipase A_2- Methyl linolenate complex with intermolecular interaction; (B) 3-dimensional conformation of Methyl linolenate docked into the active site of the Phospholipase A_2 enzyme.

Table 4: Molecular docking studies of Methyl linolenate isolated from ethylacetate extract of *Solanum dasyphyllum* on venom Phospholipase A_2 enzyme

S/No	Protein	Binding energy (Kcal/mol)	No of H-bond	Inhibition Constant: Ki (uM)	Amino acids involved in H-bond interaction	Amino acids involved in Hydrophobic bond interaction
1	Phospholipase A_2	-6.60	2	14.14	LYS A:31; GLY A:32	ILE A:9; TRP A:19; LYS A:6; ALA A:23; LEU A:2; PHE A:5; HIS A: 48; TYR A:52

DISCUSSION

The use of herbal remedies in the treatment of various diseases is increasing at a rapid pace worldwide; the low toxicity and easy accessibility contribute significantly to this global acceptance [15]. Various researchers have studied the bioactivity of the plant *S. dasyphyllum*; However, the active ingredient responsible for some of these biological activities is not precisely known. The venom of *N. nigricollis* contains proteases, phospholipase A_2, phosphodiesterase, acetylcholinesterase and hyaluronidase enzymes, also known as major enzyme toxins (METs). The phytochemical screening of the ethylacetate leaves extract of *S. dasyphyllum* revealed the presence of alkaloids, tannins, flavonoids, terpenoids, steroids and carbohydrates, but it was devoid of cardiac glycosides. These result correlated with those previously reported by Sodeinde et al. [18] and Manal et al [22], who worked

on *S. dasyphyllum* and *S. incanum L*, another species of the Solanaceae family. Mors et al. [23] reported that phenolic compounds, saponins, flavonoids and tannins can bind to proteins and can directly act on venom constituents. Similarly, Lans et al. [21] reported that plant alkaloids are effective against snake bites. Aristolochic acid, 8-methyloxy-6-nitophenanthro, 12-methoxy-4-methylvoachalotine and atropine are all isolated alkaloids compounds that inhibit the lethal effect of snake venom [24]. Although the quantitative estimate of phytochemicals in the extract was not evaluated, the inhibition of the enzyme suggested that the leaf extract may contain phytochemicals that are likely to bind to the enzyme, thus preventing it from binding to its substrate, leading to its inhibition.

The results of the inhibition study of phospholipase A_2 enzyme activity by different concentrations of ethylacetate leaves extract of *S. dasyphyllum* showed that the extract is potential Phosplipase A_2 inhibitor. This was similar to the results of Akindele et al. [16] where they reported that the ethyl acetate fraction of *M. oleifera* was a potential source of effective compounds against pathologies caused by the venom of *N. katiensis* [16].Furthermore, Ajiboye et al. [12] reported that the ethyl acetate fraction of the leaves of *Solanum macrocarpon* L., a plant belonging to the nightshade family, has an inhibitory effect on cholinergic enzyme activities as well as radical scavenging activity [12].

Chromatographic separation of the ethyl acetate extract resulted in the isolation of the compound methyl linolenate, whose properties, NMR spectra and chemical structure are shown in Table 3, Figures 3, 4 and 5. The compound was confirmed to be a fatty acid ester with the molecular formula $C_{19}H_{32}O_2$ and a molecular weight of 292.5 g/mol.

Molecular docking techniques, a tool used for structure-based drug design strategies to develop novel drugs against the inhibition of therapeutic targets, and several researchers have reported that a negative and low binding energy value indicates strong binding efficiency [17]. In this study, molecular docking investigation was carried out to evaluate the likelihood of inhibition of cobra venom phospholipase A_2 by methyl linolenate, a compound isolated from the ethyl acetate fractions of methanolic extract of *S. dasyphyllum*.Therefore, the docking of the isolated compound drawn with the aid of chemdraw was successfully carried out with cobra phospholipase A_2 obtained from protein data bank as shown in figure 5,6 and 7. The docking of methyl linolenate to the target enzyme was examined with regard to interacting amino acids, atoms involved in hydrogen bonding, predicted binding energy and inhibition constant (Ki) as shown in Table 4. The docking studies revealed the involvement of H-bonds between amino acid residues in the prominent binding site associated with other non-covalent interactions such as alkyl, pi-alkyl, pi-sigma interactions and vander Waals forces. The binding energy of methyl linolenate to the enzyme phospholipase A_2 is -6.60 kcal/mol. This suggests that methyl linolenate may inhibit phospholipase A_2 in snake venom, thereby attenuating the effects of snake venom in a biological system.

CONCLUSION

The present study revealed that the ethylacetate leaf extract of *S. dasyphyllum* contains bioactive components that can inhibit phospholipase A_2 enzyme in*N. nigricollis* venom. Therefore, methyl linolenate isolated from *S. dasyphylum* is worth both in vitro and in-vivo evaluation to assess and optimize its therapeutic efficacy.

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Socio-economic and Clinical Correlates amongst Hypertensive Patients utilizing Complementary and Alternative Medicines (CAM) in A Tertiary Health Institution in Niger Delta, Nigeria.

Afamefuna FU[1], Yowin DG[2], Anyanwu EB[3]

Abstract

Introduction: World over, patronage of CAM products is on the increase, even when more potent conventional therapies with less side effects are continually being researched and produced. This study aimed at determining the socio-economic and clinical correlates of hypertensive patients utilizing CAM products in a tertiary health institution in Delta State.

Materials and Methods: A total of 572 participants diagnosed with essential hypertension that met the study criteria were studied. A half of the participants (286) were on conventional treatment only (Group A) while the other half (286) were on conventional treatment and CAM (Group B). Types of CAM products used, reasons for utilization, sources of CAM product knowledge and Family support for use were studied.

Results: Age group, marital status, higher levels of education, social class group, monthly level of income, body mass index, family history of hypertension and duration of hypertension were significantly associated with CAM utilization.

Conclusion: Family influence, higher body mass index as well as the duration of hypertension are strong predictors of utilization of CAM products amongst hypertensive patients.

Key words: Complementary and alternative medicine, Hypertension

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INTRODUCTION

Complementary and Alternative Medicine (CAM) as a group of diverse medical and healthcare systems, practices and products have been in use for several decades, the report of its use have been hinged more on cultural inclinations.[1] One of the compelling reason for this is the fact that until very recently, this aspect of care was not taught in medical schools.[2(1)] Consequently, many clinicians are either unaware of this group of therapy and their practice or they do not understand the rationale for the health-seeking behaviour warranting their utilization. Whatever the explanation, the patronage of CAM globally, is on the increase. In Africa and globally the prevalence of CAM utilization has been shown to range between 20 - 80%.[2]

It is true that socio-demographic and clinical characteristics of patients constitute some of the determinants for CAM use, but it is difficult to completely ascertain what has driven this high level of patronage of unconventional health products and practices known as CAM even when we now have more potent conventional therapies with fewer side effects.[3]

Several factors such as gender, beliefs and medication costs have been shown by various researchers [4 – 7] to be determinants for CAM utilization.

Despite the fact that the use of CAM is increasing, there is paucity of scientific evidence to support their efficacy or elucidate on their potential for adverse effects and drug interactions.[8] Therefore, both physicians and patients may lack knowledge of the efficacy and potential risks of CAM remedies.

Aims and Objectives

The Aim of the Study: is to assess the socio-economic and clinical correlates of CAM utilization amongst hypertensive patients in a tertiary hospital setting in the Niger Delta region.

Specific objectives are to determine the relationships of CAM utilization with socio-economic status, age beliefs and family influences amongst hypertensive participants.

MATERIALS AND METHODS

This is a comparative cross-sectional survey of all patients with hypertension attending the Family Medicine Clinic of the Delta State Teaching Hospital (DELSUTH) Oghara. The hospital is a 180-bed tertiary center with facilities for inpatient and outpatient care. It is located at Oghara the headquarter of Ethiope West Local Government Area of Delta State.

Inclusion Criteria were Adults of 18 years and above, that are diagnosed clinically with essential hypertension for at least three months and are on conventional medical treatment for at least three months. The willingness to participate in the study with an ability to give informed consent was also considered important inclusion criterion.

Exclusion Criteria: Those not included were; Pregnant patients with hypertension, those having acute or debilitating disease or diagnosed with secondary Hypertension. All who declined participation in the study were excluded too.

The instrument was an interviewer-administered questionnaire consisting of 3 parts.

The first part consisted of socio-demographic data. Social class was graded according to the British classification into A (higher managerial administrative and professional), B (intermediate managerial administrative and professional), C (supervisory, clerical and junior managerial administrative and professional, and skilled manual workers), D (semi-skilled and unskilled manual workers) and E (pensioners, casual and lowest grade workers, and unemployed).[9] The level of income of subjects was determined using the Nigerian National Minimum wage act approved by the Nigerian National Assembly.[3] According to the act, low-level income earners ranged from salary grade levels 01 to 07 (<₦60,000 basic), middle-level income earners ranged from salary grade level 08 to 15 (≥₦60,000 – ₦165,000 basic), and high-level income earners ranged from salary grade level 16 to 17 (≥₦165,000 basic).

The second part consisted of hypertension-related data. Anthropometric indices (weight in Kilogrammes [Kg], height in meters [m], and body mass index in Kg/m^2) were taken and recorded. Obesity was defined as body mass index $\geq 30 Kg/m^2$. Blood pressure at initial presentation at the clinic (as recorded in the case notes), and current blood pressure (using standard method) were documented. Blood pressure control was defined based on the JNC8 criteria of blood pressure level of ≤140/90mmHg in patients 18 to 59 years of age without major co-morbidities and in patients 60

years or older who have diabetes, chronic kidney disease or both conditions, and blood pressure level of ≤150/90mmHg in patients 60 years or older who do not have diabetes or chronic kidney disease.[10]

The third part modified from a standard questionnaire format on the use of CAM by cancer patients in Nigeria.

The data obtained was sorted, coded and entered into the spread-sheet of the Statistical Package for Social Sciences (SPSS 22). Analysis of frequency was done and presented using frequency tables, proportions and charts. Bivariate analysis was done using Chi square (X^2), Z-score and Student T-test. Statistical significance was set at p-value < 0.05.

Ethical approval was obtained from the Ethic Board of the DELSUTH Oghara.

RESULTS

Table 1 shows the socio-demographic characteristics of the study population. 572 participants diagnosed with essential hypertension were studied. A half of the participants (286) were on conventional treatment only (Group A) while the other half (286) were on conventional treatment and CAM (Group B). The mean ages of the participants were 61.8±13.3 and 59.1±12.0 in Group A and Group B respectively which was comparable. Most of the participants in both groups were females (328[57.3%]), married (404[70.6%]), Almost all the participants were of the Christian extraction. (525[91.8%]) Over half of the participants were low level income earners (375[65.6%]), and belong to lower social class (406[71.0%]), while less than half, had post-secondary/tertiary education (212[37.1%]). There were comparability (p>0.05) in the age group (18-39years and 60-79years), sex, marital status (single and divorced/separated), highest level of education (primary, post-primary/ secondary and post-secondary/ tertiary), social class group (social class A, C and D), monthly level of income (₦60,000-165,000) and religion of the participants in Group A and Group B respectively.

Table 1: Socio-demographic characteristics of the study population

Variables	Group A (N=286) n (%)	Group B (N=286) n (%)	z-score	p-value
Age Group (years):				
18-39	13(4.5)	9(3.1)	0.87	0.384*
40-59	111(38.8)	146(51.0)	2.94	0.003
60-79	127(44.4)	111(38.8)	1.36	0.174*
≥80	35(12.2)	20(7.0)	2.13	0.033
Mean age	61.8±13.3	59.1±12.0	1.98ṫ	0.293*
Sex:				
Male	125(43.7)	119(41.6)	0.51	0.610*
Female	161(56.3)	167(58.4)	0.51	0.610*
Marital Status:				
Married	189(66.1)	215(75.2)	2.39	0.017
Single	6(2.1)	1(0.3)	1.90	0.057*
Widow/Widower	80(28.0)	49(17.1)	3.10	0.002
Divorced/Separated	11(3.8)	21(7.3)	1.82	0.069*
Highest Level of Education:				
No formal education	58(20.3)	26(9.1)	3.78	< 0.0001
Primary	76(26.6)	82(28.7)	0.56	0.575*
Post-primary/Secondary	57(19.9)	61(21.3)	0.41	0.682*
Post-secondary/Tertiary	95(33.2)	117(40.9)	1.90	0.057*
Social Class Group:				
Social class A	10(3.5)	9(3.1)	0.23	0.818*
Social class B	25(8.7)	45(15.7)	2.55	0.011
Social class C	37(12.9)	40(14.0)	0.37	0.711*
Social class D	131(45.8)	133(46.5)	0.17	0.865*
Social class E	83(29.0)	59(20.6)	2.32	0.020
Monthly Level of Income (naira):				
Below 60,000	204(71.3)	171(59.8)	2.90	0.004
60,000 – 165,000	60(21.0)	77(26.9)	1.67	0.095*
Above 165,000	22(7.7)	38(13.3)	2.18	0.029
Religion:				
Traditional	4(1.4)	3(1.0)	0.38	0.704*
Christian	268(93.7)	257(89.9)	1.67	0.095*
Islam	4(1.4)	8(2.8)	1.17	0.242*
None	10(3.5)	18(6.3)	1.55	0.121*

ṫ = t-test statistic

Figure 1 shows the sources of CAM knowledge among participants. The most common source of knowledge about CAM was family members (110[38.5%]); followed by friends (100[35.0%]), migrant advertisers (57[19.9%]), mass media (30[10.5%]), religious group (21[7.3%]), other patients (11[3.8%]), health personnel (6[2.1%]), providers/dealers (2[0.7%]) and CAM practitioner (1[0.3%]) in descending order respectively.

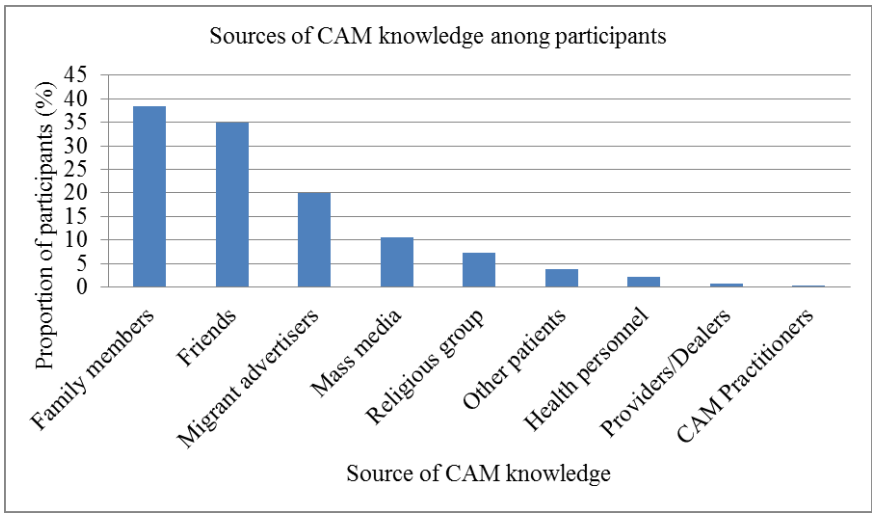

Figure 1: A Bar Chart showing Sources of CAM knowledge among participants

Figure 2 shows the types of CAM utilized among participants. The most common type of CAM utilized was biological products (277[96.9%]); followed by physical therapy (19[6.6%]), others (17[5.9%]), spiritual therapy (13[4.5%]) and alternate systems (4[1.4%]) in descending order respectively. Others comprised of bloodletting, local scarification, urine therapy and detoxification therapy.

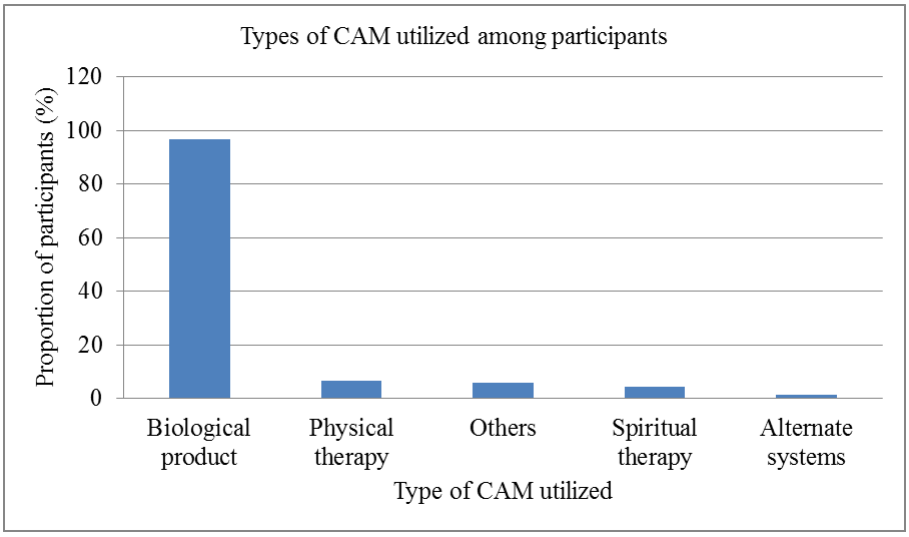

Figure 2: Bar Chart showing Types of CAM utilized among participants

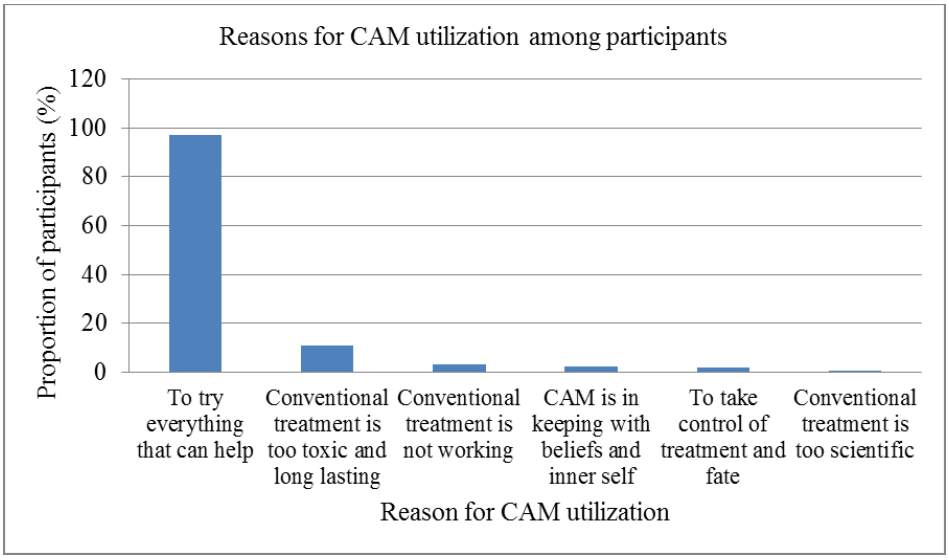

Figure 3: Bar Chart indicating Reasons for CAM utilization among participants

Table 2 shows the factors influencing CAM utilization among participants. Age group, marital status, highest level of education, social class group, monthly level of income, body mass index, family history of hypertension and duration of hypertension were significantly associated with CAM utilization ($p<0.05$). Sex, religious group, duration of current conventional treatment, application of lifestyle measures, type of therapy and adherence to conventional treatment were not significantly associated with CAM utilization ($p>0.05$). Participants who were within the middle age bracket (146[56.8%]), married (215[53.2%]), in social class D (133[50.4%]), diagnosed of hypertension for 1-5years duration (141[50.2%]), middle level income earners (77[56.2%]), obese (123[56.7%]) and had post-secondary/tertiary education (117[55.2%]) and family history of hypertension (135[55.6%]) were most likely to utilize CAM.

Table 2: Factors influencing CAM utilization among participants

Variables	Number Interviewed	Current CAM Use		Chi-square
		Yes n (%)	No n(%)	
Age Group (years):				
18-39	22	9(40.9%)	13(59.1%)	X^2=8.77; df=2
40-59	257	146(56.8%)	111(43.2%)	p=0.012*
60-79	238	111(46.6%)	127(53.4%)	
≥80	55	20(36.4%)	35(63.6%)	
Sex:				
Male	244	119(48.8%)	125(51.2%)	X^2=0.26; df=1
Female	328	167(50.9%)	161(49.1%)	p=0.612
Marital Status:				
Married	404	215(53.2%)	189(46.8%)	X^2=15.82; df=3
Single	7	1(14.3%)	6(85.7%)	p=0.001*
Widow/Widower	129	49(38.0%)	80(62.0%)	
Divorced/Separated	32	21(65.6%)	11(34.4%)	
Highest Level of Education:				
No formal education	84	26(31.0%)	58(69.0%)	X^2=14.84; df=3
Primary	158	82(51.9%)	76(48.1%)	p=0.002*
Post-primary/Secondary	118	61(51.7%)	57(48.3%)	
Post-secondary/Tertiary	212	117(55.2%)	95(44.8%)	
Social Class Group:				
Social class A	19	9(47.4%)	10(52.6%)	X^2=9.96; df=4
Social class B	70	45(64.3%)	25(35.7%)	p=0.041*
Social class C	77	40(51.9%)	37(48.1%)	
Social class D	264	133(50.4%)	131(49.6%)	
Social class E	142	59(41.5%)	83(58.5%)	
Monthly Level of Income (naira):				
Below 60,000	375	171(45.6%)	204(54.4%)	X^2=9.28; df=2
60,000-165,000	137	77(56.2%)	60(43.8%)	p=0.010*
Above 165,000	60	38(63.3%)	22(36.7%)	
Religious Group:				
Traditional	7	3(42.9%)	4(57.1%)	X^2=3.99; df=3
Christian	525	257(49.0%)	268(51.0%)	p=0.262
Islam	12	8(66.7%)	4(33.3%)	
None	28	18(64.3%)	10(35.7%)	
Body Mass Index (Kg/m^2):				
<18.5	9	3(33.3%)	6(66.7%)	X^2=11.39; df=3
18.5-24.9	162	65(40.1%)	97(59.9%)	p=0.010*
25.0-29.9	184	95(51.6%)	89(48.4%)	
≥30	217	123(56.7%)	94(43.3%)	

Family History of Hypertension:				
Yes	243	135(55.6%)	108(44.4%)	X^2=5.22; df=1
No	329	151(45.9%)	178(54.1%)	p=0.022
Duration of Hypertension (year):				
<1	93	28(30.1%)	65(69.9%)	X^2=31.88; df=8
1-5	281	141(50.2%)	140(49.8%)	p=<0.0001*
6-10	89	59(66.3%)	30(33.7%)	
11-15	56	29(51.8%)	27(48.2%)	
16-20	21	11(52.4%)	10(47.6%)	
21-25	9	8(88.9%)	1(11.1%)	
26-30	14	5(35.7%)	9(64.3%)	
31-35	6	4(66.7%)	2(33.3%)	
36-40	3	1(33.3%)	2(66.7%)	
Duration of Current Conventional Treatment (year):				
<1	229	98(42.8%)	131(57.2%)	X^2=9.12; df=4
1-5	294	158(53.7%)	136(46.3%)	p=0.058
6-10	35	22(62.9%)	13(37.1%)	
11-15	10	6(60.0%)	4(40.0%)	
16-20	4	2(50.0%)	2(50.0%)	
Use of Lifestyle Measures:				
Yes	120	69(57.5%)	51(42.5%)	X^2=3.42; df=1
No	452	217(48.0%)	235(52.0%)	p=0.065
Type of Therapy:				
Monotherapy	207	103(49.8%)	104(50.2%)	X^2=0.01; df=1
Combination therapy	365	183(50.1%)	182(49.9%)	p=0.931
Adherence to Conventional Treatment:				
Yes	305	155(50.8%)	150(49.2%)	X^2=0.18; df=1
No	267	131(49.1%)	136(50.9%)	p=0.675

Table 3 shows the determinants of CAM utilization among participants. Body mass index and duration of hypertension were found to be the independent predictors of CAM utilization ($p<0.05$).

Table 3: Determinants of CAM utilization among participants

Variables	Adjusted odds ratio (AOR)	95% C.I	p-value
Age	1.10	0.77-1.57	0.616
Marital status	1.10	0.92-1.31	0.307
Highest level of education	0.91	0.76-1.10	0.333
Social class	1.08	0.88-1.33	0.463
Monthly level of income	0.86	0.63-1.17	0.328
Body mass index	0.78	0.63-0.96	0.019*
Duration of hypertension	0.88	0.77-0.99	0.037*
Family history of hypertension	1.19	0.83-1.71	0.351

DISCUSSION

There were various sources for the knowledge of CAM products as a form of treatment observed amongst the participants. Family members and migrant advertisers were the most common sources of CAM knowledge among the participants (Figure 1), this observation that is consistent with findings from previous studies on sources of information for CAM utilization.[5, 6, 11 – 13] This observation is not surprising in Nigeria where people display and sell their CAM products and practices within the community (e.g. from house to house, in public buses and coaches, on the streets, markets, schools and even health centres) despite the existence of government regulatory agency.[14,15]

The most common type of CAM utilized among the participants was biological products (Fig. 2). In addition, garlic (*Allium sativum*) was the most common CAM product utilized among the participants. This observation is consistent with the findings in other global studies as well as in Nigeria among patients with hypertension.[4, 5, 6, 8, 13] One common belief expressed by participant in previous work is that natural (biological) products are safe because of their "naturalness".[2] In some other studies[16, 17], addition of garlic with allicin as the active ingredient has been shown to reduce cardiovascular events by lowering plasma cholesterol, blood pressure and inhibiting platelet aggregation.[16, 17] This may explain the popularity of biological products and garlic as the most commonly utilized CAM type and product respectively.

The most common reasons for CAM utilization among participants were to try everything that could help and that conventional treatment was too toxic and long lasting (Figure 3). This finding is in line with the most common reasons reported in previous studies among hypertensive and

family practice patients.[5, 11] These reasons may explain the relevance of CAM to hypertensive patients who may have become overwhelmed with the continuous intake of medicine without "cure". This misconception of "cure" was demonstrated by Oke and Bamidele (2004). They reported in a survey that about 21% of their respondents were of the opinion that they would achieve a permanent cure of hypertension only from CAM practitioners.[18]

In this study, socio-demographic characteristics associated with CAM utilization were age group, marital status, level of education, social class group and monthly level of income while the clinical characteristics were body mass index, family history of hypertension and duration of hypertension (Table 3). The participants in the middle age brackets, majority of which were obese and were in the middle income level as well as having family history of hypertension were found to utilize CAM products the most. This finding is consistent with the observations in previous works.[1, 3, 4, 11] The health seeking behavior the middle age brackets and probable influence of spouses on the health seeking choices of an ill partner may have been responsible for the association.

The association between higher BMI and CAM utilization seen in this study, is in keeping with findings in other studies.[8, 19] This may be related to the regular advertisement of the efficacy of some herbal products and nutritional supplements with regards to weight reduction which readily meets the desires of those finding other methods of weight reduction. Moreover, the majority of obese utilize CAM products for the benefit of improved physical wellbeing which could have included weight reduction.

In majority of the respondents, the aim of trying anything that can be of help was a strong reason for CAM utilization (fig. 3). It is important to note that very often, many people with chronic conditions like hypertension that utilize CAM products, do so concurrently with their conventional treatment.[1–4] This concurrent use of conventional and CAM therapies is risky not only because of the potential for unwanted side effects and serious adverse effects that could arise from drug interactions as a result of combination of these therapies but also the reduction in efficacy.[20] Another possible reason strengthening this concomitant use may be attributable to published work on biological products such as Garlic and other herbs like ginger and Aloe Vera that have been reported to have significant influence on concurrently administered cardiovascular drugs including antihypertensive medications thereby reducing their efficacy.[23] Nonetheless drawing this thin line in other CAM products is crucial.

CONCLUSION:

Our study demonstrates that, family influence, higher body mass index as well as the duration of hypertension are strong predictors of utilization of CAM products amongst hypertensive patients.

Recommendations;

1. Physicians and other healthcare professionals should be willing to proactively engage patients regarding their current or intended use of CAM especially in those with long standing history of hypertension and obese clients. Also significant family member(s) taken into consideration when counselling our clients during clinical encounters on the ills of concurrent use of CAM therapies.
2. There should be improved legislation and sustained effort by the relevant government agency for the regulation and control of CAM products and

practices in Nigeria.

Limitations;

This hospital based research finding has only looked at a small aspect of the population and may not reflect the exact situation of the general population of hypertensive patients utilizing CAM products. However it does draw attention to the reality that some factors influence a concomitant utilization.

Conflicting interests:

There is no conflicting interest in this work

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Knowledge and Uptake of Covid-19 Vaccine Amongst Students of Tertiary Institutions in Oghara, Delta State, Nigeria

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Abstract

Introduction: Coronavirus disease is a global health emergency that began in China, in 2019. It resulted in several morbidity and mortality worldwide. The introduction of Covid-19 vaccine in Nigeria was hampered by wide spread vaccine hesitancy due to factors like misinformation, rapid rollout, safety concerns, potential adverse effects, and conspiracy theories. The objective of this study was to assess the knowledge and uptake of Covid-19 vaccine among students of tertiary institutions in Oghara, Delta State, Nigeria.

Materials and methods: A descriptive cross-sectional study design was employed to collect data from 354 participants in three tertiary institutions in Oghara using multistage sampling technique. Data analysis was done using IBM-SPSS version-26 software. Both descriptive and inferential statistics were done and level of significance set at $P<0.05$.

Results: Most respondents were between ages 21-25 (53.2%) with females constituting 55.6%. Seventy-one percent of respondents had good knowledge of Covid-19 vaccine. Only 27% had been vaccinated while 73% are unvaccinated. Among those unvaccinated, 57.7% were not willing to be vaccinated. Good knowledge of Covid-19 vaccine ($P=0.048$) and having previous exposure to information, education and communication about Covid-19 vaccine ($P=0.024$) were found to have a statistically significant association with the uptake of Covid-19 vaccine.

Conclusion: Majority of students of tertiary institutions in Oghara have good knowledge of COVID-19 vaccine however the uptake was poor. More effort should be invested in providing accurate information about the vaccines while mitigating misinformation.

Keywords: Acceptability, COVID-19 vaccine, Knowledge, Uptake

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INTRODUCTION

In December 2019 in Wuhan, a city in the Hubei province of China, a cluster of fast spreading viral pneumonia was observed among citizens, although initially called Wuhan pneumonia by local health workers;[1] this highly contagious disease (COVID-19) caused by severe acute respiratory syndrome corona virus-2 (SARS-CoV-2 virus) quickly spread world-wide and was declared a global pandemic by the world health organization (WHO) on March 11, 2020.[2]

The majority of COVID-19 infections results in mild-to-moderate symptoms and recovers without the need for special treatment; but a substantial number of cases lead to severe illness which may ultimately lead to death.[3]

With no scientifically proven treatments or medicines found; governments across the world

imposed border control measures, travel bans, public health campaigns, social distancing, mask mandates, and quarantine in a bid to stop the spread of the virus that has caused a massive economic downturn[4].

As at 28th January 2022, there have been 364,191,494 confirmed cases, 5,631,457 deaths globally reported by the World Health Organization (WHO).[5] This has been a significant concern to public health and has greatly affected all aspects of people's lives all over the world. On February 27, 2020, Nigeria announced the confirmation of its first case, which was an Italian national who tested positive at the Virology Laboratory of Lagos University Teaching Hospital.[6] Subsequently, all 36 states and the Federal Capital Territory, Abuja were affected; and by September 25, 2022, Nigeria had recorded 265,105 confirmed cases, 257,594 patient discharges and 3,155 deaths. However, Delta state confirmed its first case on the 7th of April, 2020 and by February 2022 it has recorded 5,727 confirmed cases, 5,170 discharges and 112 deaths.[7]

The long-term pandemic's effects on public health are still being felt by communities throughout the world. Lockdowns and travel restrictions imposed to stop the spread of COVID-19 have severely hindered economic activity that has led to low economic output and loss of jobs for almost half of the world's workforce; roughly affecting 3 billion people as well as lower household incomes and increase healthcare costs.[8]

To help restrict the spread and eliminate the likelihood of future incidents, preventive measures in the form of vaccines is crucial and the need for a safe and effective vaccine has intensified in every region of the world[9]. Vaccines are biological preparations that provide active acquired immunity to a particular infectious disease. They do so by stimulating an immune response (producing antibodies) to an antigen, a molecule found on a pathogen.[10]

Several vaccines, including those from Oxford-AstraZeneca, Pfizer-Biontech, Moderna/ NIAID, Johnson and Johnson, etc., have been made available for use in various nations. The first worldwide mass vaccination campaign started in December 2020 and was first limited to individuals deemed to be at high risk, such as elderly people and healthcare professionals.[11]

The rapid development and deployment of COVID-19 vaccines is the result of not only unprecedented levels of international collaboration but also of decades-long massive public investment in research, development, and manufacturing capacity.[12] It is particularly significant when framed against previous estimates of the probability of the approval process for a vaccine entering clinical trials of as little as 12% to 33% after some 7 to 9 years of development.[13]

Despite the availability of vaccines, vaccine compliance remains variable and inconsistent, and vaccine hesitancy is considered a vital obstacle to instituting preventive measures to combat infectious diseases.[14]

Covid-19 vaccine hesitancy and uptake refusal are global, and several factors have been propounded as reasons for population response to the vaccine use. These include misinformation, rapidity of its rollout, government perceived insincerity in some quarters, concerns of safety, potential adverse effects and conspiracy theories, including an alleged link to the 5G network and vaccine impact on fertility and pregnancy.[15]Vaccine hesitancy was also linked to age, low educational attainment, female sex, black race, single or divorced status,

and unemployment.[16]

Among tertiary students the risk of contracting the virus and spreading it to others is high due to student's activities, behaviors, socializing and unwillingness to adhere to COVID-19 preventive measures. Asymptomatic infections typically affect young students (less than 20 years old), who can then infect others, particularly those in high-risk groups.[17]

Although a number of studies have attempted to investigate the knowledge and uptake of the COVID-19 vaccine among various group of the population, evidence is scarce among tertiary students in Oghara, Delta state, Nigeria. Due to populated class settings and communal living, tertiary institutions may contribute to the rapid spread of Covid-19. Also, it is assumed that students of higher learning are agents of change and would have a better influence on their families, friends, and society. Thus, assessing the knowledge and uptake of the Covid-19 vaccine amongst these students would help informed decisions towards reducing the spread of the disease. It is therefore against this background, that the study was conducted to assess knowledge and uptake of Covid -19 vaccine among students of tertiary institutions in Oghara, Delta State, Nigeria.

MATERIALS AND METHODS

The study was conducted among tertiary institutions in Oghara, Delta state, Nigeria. Oghara is located in Ethiope West Local Government Area of Delta State, Nigeria. It is home to the Urhobo ethnic group of Delta State. The 2006 final census results put the population of Ethiope west at 202,712 persons.[18] However, the population of the area is estimated to be over 300,000 persons in 2020 using the national growth rate of 3 percent.[19] Oghara is home to 3 tertiary (health and educational), institutions namely: Delta State University Teaching Hospital (DELSUTH), Delta State Polytechnic (DESPO) and Western Delta University (WDU).The clinical students (nursing and medical) of Delta State University (DELSU), Abraka are sent to DELSUTH for their clinical training and posting.

A descriptive cross-sectional study design was employed to collect data from students of tertiary institutions in Oghara, Delta state between the periods of July – September 2022.
All consenting adult students of tertiary institutions in Oghara who were physically present were included in the study. Students of tertiary institutions who were below 18years of age and in the first year of study were excluded from this study.

A multistage Sampling technique was employed in this study. In the first stage, two faculties were selected by simple random sampling by balloting from the list of faculties in each of the three tertiary institutions in Oghara. In the second stage, two departments were selected from the list of departments in each of the selected faculties using simple random sampling by balloting. In the third stage, one class was selected by simple random sampling (balloting) from the list of classes in each selected department. Every eligible participant in the selected class was interviewed consecutively until the assigned sample size was completed.

The minimum sample size for this study was calculated using Fischer's formula.[20] Based on prevalence of knowledge of Covid -19 vaccine of 73.5% from a previous study,[21] an error margin of 5% and a standard normal deviation of 1.96 at 95% confidence level, the determined minimum sample size was 323. Considering a non-response rate of 10%, the sample size for this study was

increased to 354. However, 422 questionnaires were distributed (190 in DELSU, 117 in WDU and 115 in DESPO) for the study and 354 were retrieved and analysed giving a response rate of 84.0%.

Data collection was done using a pre-tested semi-structured self-administered questionnaire as the primary research instrument consisting of a series of questions to gather the relevant information from respondents.The questionnaire comprised of four sections namely: socio-demographic characteristics of respondents, knowledge of covid-19 vaccines, acceptability and uptake of covid-19 vaccine and factors influencing uptake of covid -19 vaccines respectively. The questionnaire was validated to ensure face and content validity by experts who reviewed the contents of the instrument. To ensure reliability, the instrument was pretested among 20 students in a non-participating tertiary institution in Delta State, which provided necessary feedback to refine the questions, ensure clarity and avoid ambiguity. The test-retest method was used and the resulting data yielded a correlation coefficient of 0.9 indicating high reliability.

Data collected was sorted and analyzed using IBM-SPSS (Statistical Product and Service Solution) version 26. Both descriptive and inferential statistics was done and results presented using frequency tables, cross tabulations and charts. Continuous variables were summarized using mean, median and standard deviation and categorical variables were summarized using frequencies and percentages. Chi-square was used to test for significant association between independent and dependent variables, with level of significance set at $p<0.05$.

Ethical approval (HREC/PAN/2023/018/0465) for this study was obtained from the Health Research Ethics Committee of Delta State University Teaching Hospital (DELSUTH). Permission was also granted by the heads of the respective institutions. Informed consent was obtained from each participant prior to data collection. Participation was voluntary, and respondents were assured of the confidentiality and anonymity of their responses.

RESULTS

Socio-Demographics Characteristics

This study reveal that the mean age of respondents was 22.34 ± 3.38 and most respondents were between the ages of 21-25 (58.2%) with females constituting 55.6%. The respondents were distributed across various departments, with the highest representation from Medicine (39.5%) and the lowest from Engineering (5.9%). Majority of the respondents were Christians (81.6%); Urhobo was the dominant tribe with 34.2% and a greater proportion of respondents (52.8%) were students of Delta state university (table1).

Knowledge of Respondents Regarding Covid -19 vaccines:

Majority of respondents (71.0%) had good knowledge of Covid 19 Vaccine while 29.0% had poor knowledge (figure 1). Most respondents (66.6%) agree that the vaccine helps build immunity while 69.7%% disagree that Covid-19 vaccine can prevent the disease. Social media (83.8%) was the most common source of information about the vaccine followed by television/radio (70.0%). The least common source of information about covid-19 vaccine was newspapers/newsletter (21.4%). However, NCDC website (42.9%) was the third most common source of information regarding covid-19 vaccine. Majority of respondents know about the Pfizer (70.0%) and Mordena (69.5 %%)

vaccines. While 53.5% of respondents know about Johnson & Johnson, 50.0% know about AstraZeneca vaccine. Seventy nine point nine percent of respondents are aware that COVID-19 vaccine requires at least 2 doses and 47.4% know that it is given intramuscularly. While 70.3% of participants are aware that the vaccine may have side effects, 90.4% recognize the side effects may be pain at the site of injection and fever respectively (table 2).

Uptake and Acceptability of Covid-19 Vaccine among Respondents

Only 27% of respondents (n=94) have taken the Covid-19 vaccine while majority (n=260; 73%) were unvaccinated (figure 2). Among those unvaccinated, only 42.3% were willing to get vaccinated while most of them (57.7%) were not willing to get covid-19 vaccination (table 3).The most common reason for unwillingness to get covid -19 vaccination was side effects of the vaccine (35%). However, 20.1% of respondents who were unvaccinated believe there is a conspiracy behind the vaccine; which was the reason for their unwillingness to be vaccinated (figure 3).

Factors Associated with Acceptance and Uptake of Covid 19 Vaccine

This study revealed that covid-19 vaccine was slightly more acceptable to respondents with good knowledge (27.4%) of the vaccine compared to those with poor knowledge (24.8%) of the vaccine; thus the uptake was more among respondents with good knowledge (27.4%) of the vaccine compared to those with poor knowledge (24.8%). The association between knowledge (P= 0.048) and uptake of covid-19 vaccine was statistically significant (table 4). Similarly, respondents who had received any form of Information, Education, and Communication (IEC) regarding the importance of the covid-19 vaccine had a higher uptake (31.25%) compared to those who have not receive any form of IEC (19.9%). The association between receiving IEC (P=0.024) and uptake of the vaccine was also statistically significant (table 5)

Table 1a: Socio-demographic characteristics

Variable	Categories	Frequency (n=354)	Percentage
Age (years)	18 – 20	76	21.5
	21 -25	206	58.2
	26 – 30	46	13.0
	> 30	26	7.3
	mean age (SD)	22.34	(3.38)
Sex	Male	157	44.4
	Female	197	55.6
Marital status	Single	318	89.8
	Married	36	10.1
Institution	DELSU	187	52.8
	WDU	96	27.1
	DESPO	71	20.1
Religion	Christianity	289	81.6
	Muslim	37	10.5
	Traditional	28	7.9
Tribe	Urhobo	121	34.2
	Isoko	28	7.9
	Itsekiri	33	9.3
	Ijaw	30	8.5
	Ika	39	11
	Ukwani	35	9.9
	Delta Ibo	26	7.3
	*Others	42	11.9

*others – Yoruba, Igbo, Hausa, Edo, Esan etc

Table 1b: Socio-demographic characteristics cont'd

Variable	Categories	Frequency (n=354)	Percentage
Department	Medicine	140	39.5
	Nursing	58	16.4
	Law	33	9.3
	Accounting	33	9.3
	Engineering	21	5.9
	Computer science	25	13.0
	**Others(management, arts)	44	12.4
Residence	on campus	273	77.1
	off campus	81	22.8

**others – management, arts etc

Table 2 Assessing Respondents Knowledge of Covid 19 Vaccine

Variable	Categories	Yes (%)	No (%)	Not sure (%)	Total responses
Function of Vaccine	Prevents Disease	33(13.1)	175(69.7	43(17.1)	251
	Helps the body build immunity	167(66.5)	41(16.3)	43(17.1)	251
Source of Information	television/Radio	150(70.0)	40(18.7)	24(11.2)	214
	Social Media	181(83.8)	30(13.9)	5(2.3)	216
	Newspapers/Newsletter	50(21.4)	184(78.6)		234
	Friends/Family members	59(21.5	200(73.0)	15(5.5)	274
	Healthcare Personnel	91(33.8)	122(45.4)	56(20.8)	269

	NCDC website	75(42.9)	100(57.1)		175
Types of Vaccine	Mordena	105(69.5)	15(9.6)	31(19.9)	156
	Johnson & Johnson	88(53.0)	64(38.6)	14(8.4)	166
	AstraZeneca	92(50.5)	72(39.6)	18(9.9)	182
	Pfizer	113(70.0)	14(8.6)	35(21.6)	162
Dose of Vaccine	One	122(74.8)	41(25.2)		163
	At least two	163(79.9)	41(20.1)		204
Route of administration	Intramuscular	117(47.4)	77(31.2)	53(22.1)	247
Side Effects		166(70.3)	49(20.8)	21(8.9)	236
Specific Side Effects	Pain at site of injection	150(90.4)	14(8.4)	2(1.2)	166
	Body weakness	100(60.2)	20(12.0)	46(27.7)	166
	Fever	150(90.4)	11(6.6)	5(3.0)	166
	Dizziness	45(27.1)	70(42.2)	51(30.7)	166
	Headache	120(72.3)	30(18.1)	16(9.6)	166

Table 3 Willingness to Receive Covid-19 Vaccine among Unvaccinated Respondents

Variables	Category	Frequency	Percent
Willingness to receive covid-19 vaccination (n=260)	Yes	110	42.3
	No	150	57.7

Table 4 Association between Knowledge and Uptake of Covid-19 Vaccine

		Have you been vaccinated?			
Variable	**Categories**	**Yes (%)**	**No (%)**	**Total**	**Test Statistics**
Knowledge of covid-19 vaccine	**Poor Knowledge**	23(19.6)	94(80.34)	117	$X^2 = 3.915$ P = 0.048 df = 1
	Good Knowledge	71(29.9)	166(70.0)	237	
	Total	94	260	354	

Table 5: Association between Reception of IEC and Uptake of the Vaccine

		Have you been vaccinated?			
Variable	**Categories**	**Yes (%)**	**No (%)**	**Total**	**Test Statistics**
Have you received any IEC regarding the importance of covid 19 vaccines?	Yes	65 (31.25)	143 (68.75)	208	$X^2 = 5.134$ P = 0.024 df = 1
	No	29 (19.9)	117 (80.1)	146	
	Total	94	260	354	

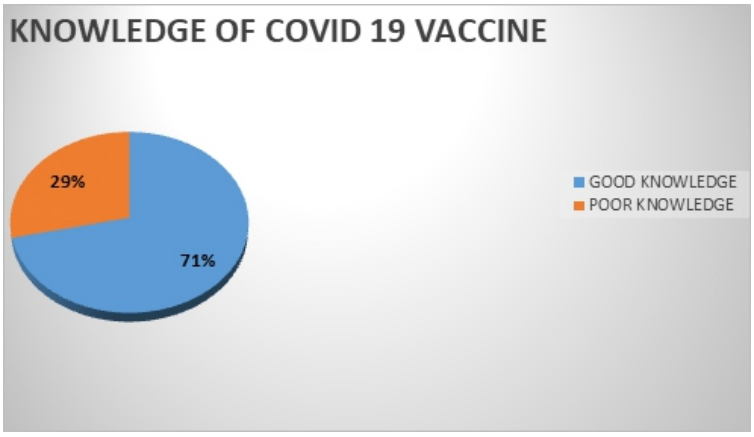

Figure 1: Knowledge of Covid-19 vaccine among respondents

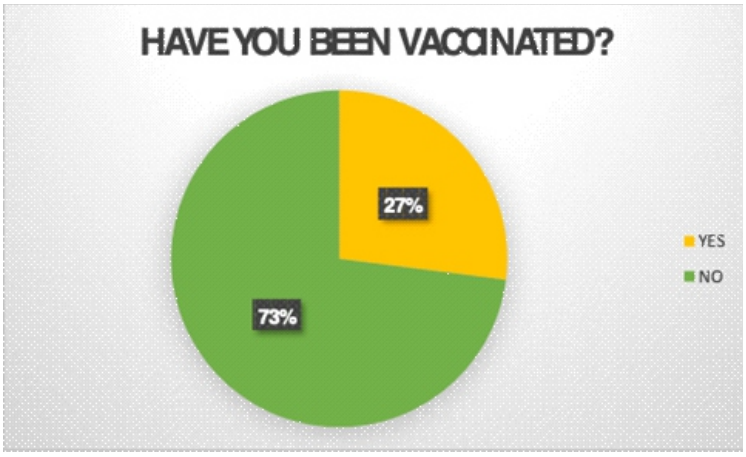

Figure 2: Uptake of Covid-19 Vaccine

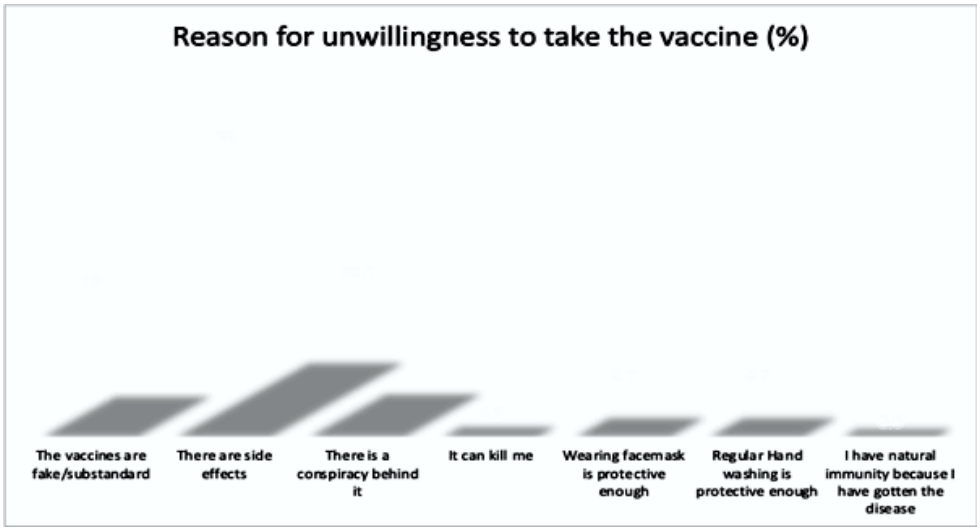

Figure 3: Reasons for unwillingness to take Covid-19 Vaccine among Unvaccinated Respondents

DISCUSSION

This study revealed that the most respondents were between the ages of 21-25years with females constituting more than half of the respondents. This observation is contrary to a previous study in Lagos were about half of the respondents were less than 21 years and majority were males.[21] This could be due to differences in the geographical locations of the studies.

The observation that majority of respondents in this study have good knowledge about covid-19 vaccine is comparable to the findings of previous studies conducted in Nigeria.[1,22] This study also revealed that social media (84%) television/radio (70%) and NCDC web site (43%) were the major sources of information regarding covid-19 vaccine among the respondents. This finding is in agreement with previous studies done in Nigeria

where social media was reported as the primary source of information.[1,23] It is also in consonance with the findings of a study done among university students in Turkey where social media was reported as one of the major sources of information on influenza pandemic.[24] The implication of this finding is that social media can be exploited as a veritable channel for health promotion. This observation supports the trend that majority of young adults get vital information from social media because it easy to access and also because events can be broadcasted in real time.

Contrary to expectation, most respondents know about the Pfizer and Mordena vaccines more than the other vaccines. This finding was in spite of the fact that AstraZeneca vaccine was more popular and available in our locality. This observation could be due to the fact that Pfizer was the first vaccine to be approved for use and it aroused the most controversies mainly on social media.[10] Majority of respondents were aware that covid-19 vaccine requires at least 2 doses. This finding is comparable to the findings of a study conducted in Jordan which showed that two-thirds of participants knew that the covid-19 vaccine should be issued in 2 doses.[25]

The uptake of the covid-19 vaccine observed in this study was poor. Similar findings had also been reported in previous studies.[26,27] This study revealed that fear of side effects and belief in conspiracy theory were the major reasons for unwillingness to take covid-19 vaccine. This finding is in agreement with a similar study done in India.[27] However, it is in contrast with similar studies conducted in Nigeria in which vaccine efficacy and vaccine safety were reported as the main reason for vaccine hesitancy respectively.[1,26] This study observed a statistically significant association between knowledge of covid-19 vaccine and uptake of the vaccine. Similar finding was reported among undergraduates in a tertiary institution in Lagos, and other selected universities in Nigeria.[21,28] This finding implies that knowledge about the vaccine is crucial to mitigating vaccine hesitancy. Although it has been reported that knowledge alone is insufficient to change attitudes and behaviors significantly.[29] In a study to assess vaccination hesitancy and conspiracy belief in United Kingdom during covid-19 pandemic, it was reported that despite high levels of knowledge, vaccine hesitancy persisted due to underlying mistrust and misconceptions.[29] This underscores the need for comprehensive interventions that address both knowledge gaps and attitudinal barriers through strategic health communication and engagement. Furthermore, this study also observed a statistically significant association between those who received information, education, and communication (IEC) on covid-19 and uptake of the vaccine. This observation corroborates previous studies in United Kingdom and United Arab Emirate where lack of information was reported a major reason for not receiving the covid-19 vaccine.[30,31] This finding further highlights the need for strategic health communication as a way of promoting covid-19 vaccination.

This study should however, be interpreted with caution since it focused only on students of tertiary institutions in Oghara; hence cannot be generalized to students in all tertiary institutions in Nigeria.

CONCLUSION

Majority of students of tertiary institutions in Oghara Delta state had good knowledge about covid-19 vaccine with social media been the major source of information. However, Uptake of the vaccine was poor with fear of the side effects being the major cause of vaccine hesitancy. The association between knowledge of the vaccine,

receiving IEC regarding the vaccine and uptake of the vaccine was found to be statistically significant. It is therefore recommended that social media and other veritable sources of communication should be employed by medical professionals; governmental and non-governmental organizations to educate, dispel fear and misconception, and provide correct information regarding covid-19 vaccines. Students should be provided with the right sources of information and encouraged to adopt responsible health behavior and preventive measures like covid-19 vaccination.

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A Computed Tomographic Study on The Morphological Variants of The Uncinate Process in A Selected Nigerian Population

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Abstract

Introduction: The variants of the uncinate process (UP) influence the patency of the osteomeatal complex. They impair the paranasal sinus drainage hence, predispose to chronic rhinosinusitis. They also make endoscopic sinus surgery challenging and increase the risk of iatrogenic complications. This study investigated the different anatomical forms of the UP using computed tomography.

Materials and Methods: Non-contrast cranial Computed Tomographic images of adult patients were obtained from digital archives of a Teaching Hospital (Radiology department) in Nigeria (Delta State) after ethical clearance. The site of superior attachment, orientation, deviation, atelectasis and aeration of the UP were evaluated. The data were reported in frequencies and further compared using the Chi-square test. A p-value of <0.05 implied statistical significance.

Results: The UP commonly inserted superiorly onto the lamina papyraecea (208,61.9%) followed by the middle turbinate (81,24.1%) and the skull base (47,14%). Horizontally oriented UP was more common (197,58.6%) compared to vertical UP (139,41.4%). The prevalence of the uncinate tip deviation was 38.7% (130) medially and 10.7% (36) laterally, with significant sex differences ($p<0.05$). The uncinate bulla was present in 9.5% (32).

Conclusion: This study enlightens on the existing forms of the UP among patients evaluated, thus the need for their identification prior to functional endoscopic sinus surgery to minimize iatrogenic complications.

Keywords: uncinate process, ethmoid, pneumatization, attachment, deviation, orientation

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INTRODUCTION

The uncinate process (UP) is a crescent-shaped projection from the ethmoid bone situated along the lateral border of the nasal cavity.[1] It is bordered by the inferior nasal concha and lacrimal bone inferiorly and anteriorly respectively.[2-4] Posteriorly, the UP possesses a free margin. The osteomeatal complex (OMC), a pathway that drains the antrum of Highmore, anterior ethmoidal plus frontal sinuses, is delineated by the middle concha, ethmoidal infundibulum, ethmoid bulla, uncinate process, hiatus semilunaris, maxillary sinus ostium and the frontonasal recess. [3,4] The UP forms the inferior boundary of the semilunar hiatus and the medial limit of the ethmoid infundibulum.[2-4]

The superior attachment of UP (SAUP) is variable influencing the channel for draining the frontal sinus and affecting the size of its ostium and beak.[1,2] The UP is bound to the lamina papyracea on the medial orbital wall. Subsequently, the frontal sinus drains medial to the UP and directly via the middle nasal meatus.[2]

An enlarged Agger Nasi cell can potentially displace the UP medially causing it to attach onto the middle concha/ turbinate. In this scenario, frontal sinus secretions are directed on the lateral side of the UP via the ethmoidal infundibulum into the middle meatus.[2,3] This drainage conduit is also observed in rare instances where the UP superiorly attaches on to the roof of ethmoid at the cranial base. [2,4] Infundibular disease is more commonly seen when the SAUP allows the frontal sinus air cell recess to open through the infundibulum than straight into the middle nasal meatus.[4]

The UP could be oriented either horizontally or vertically. [4] A vertically oriented UP has the capacity for expansion or deformation while a horizontally oriented one may coexist with a great ethmoid bulla or contralaterally deviated nasal septum. [3,4] The uncinate's upper end could deviate relative to the position of middle nasal meatus, resembling a second middle turbinate. [5] The lateral divergence of the tip constricts the semilunar hiatus and the infundibulum, reducing the gap amid the UP and the orbital papyraceous lamina. Consequently, caution should be exercised during uncinectomy to prevent orbital injury. [4] A medially deviated uncinate tip has been significantly linked to anterior ethmoidal sinusitis resulting from middle meatus obstruction.[5]

The ethmoidal process may be aerated forming an uncinate bulla. [6-8] This variation can impact the extent of OMC patency potentially leading to pansinusitis. [7,6] An atelectatic UP is adherent to the medial orbital wall inferiorly, and is typically associated with a hypoplastic antrum of Highmore or hypoplastic ethmoidal bulla. [7] Identifying this variant preoperatively is essential to prevent accidental injury to orbital contents like the optic nerve during uncinectomy in the course of functional endoscopic sinus surgery (FESS). [7,9]

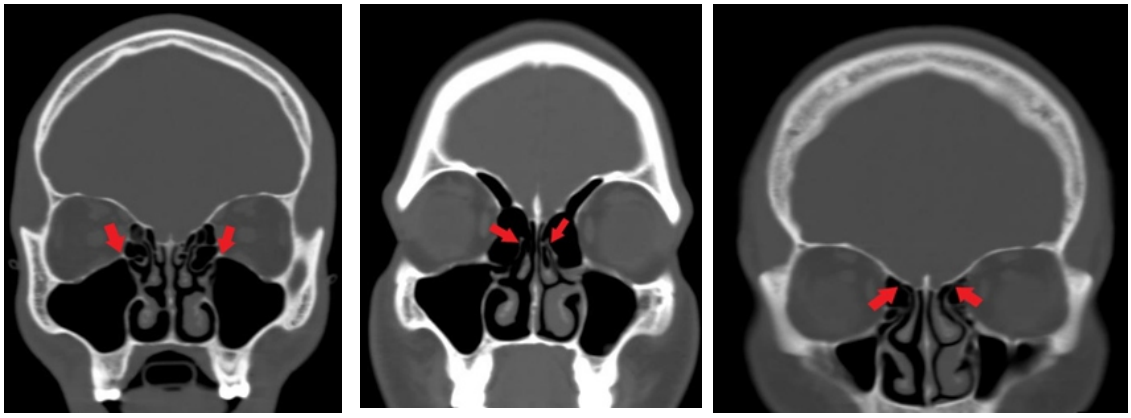
The uncinate's diverse morphological forms can potentially cause OMC obstruction and impede sinus drainage, predisposing to chronic rhinosinusitis which often necessitates FESS. [6] In the literature, structural modifications of the UP exhibit variations among different population groups. [2,5-7] These discrepancies are largely influenced by genetics, racial, locational and ecological factors. [5,7] Recognizing these variants is crucial for achieving better surgical approach to the sinus outflow and minimizing intraoperative complications. [1, 6-9] Consequently, this study focused on utilizing computed tomographic (CT) images to ascertain the distribution of the structural variants of the UP within the adult population in Nigeria.

MATERIALS AND METHODS

This was an observational cross-sectional analysis of retrospective nature, which was undertaken within the Radiology Section of Delta State University Teaching Hospital (DELSUTH) located in Oghara, Nigeria. After reviewing the study's protocol, the hospital's ethical committee granted approval before commencement of this investigation (EREC/PAN/2020/030/0371). Non-contrast brain CT scans captured in a time-frame of 5 years (June 1, 2015 to July 1, 2020) and stored in digital radiological databank were used. These scans were acquired to investigate suspicious diverse pathologies including space occupying lesions, chronic headache, stroke and emboli. Scans of 336 subjects; 137 females and 199 males, aged 20 years and beyond were selected. Patients below this age were not considered due to immaturity of the sinuses which typically reach their adult size by 20 years. [10,11] Poor quality scans with visible artifacts, inadequate exposure, and obscured field of view were also not included. Additionally, images displaying apparent pathological abnormalities,

congenital anomalies or proof of earlier surgery were omitted.

Identification of the UP was conducted on coronal slices. The superior attachment of the UP (SAUP) either on ethmoid lamella (lamina papyracea), middle turbinate, or cranial base was assessed (Figure 1). The uncinate's orientation or alignment either vertically or horizontally besides the deviation of its tip either medially or laterally were evaluated. The uncinate bulla was defined by any extent of pneumatization (Figure 2). Furthermore, any UP adhering onto the inferomedial orbital wall and associated with either a hypoplastic ethmoidal bulla or maxillary sinus was considered as an atelectatic UP. [7,9]



A B C

Figure 1. (Original) Reformatted Coronal CT images of the skull (bone window) depicting the superior attachment of the uncinate process A. On lamina papyraecea B. On middle turbinate C. On skull base

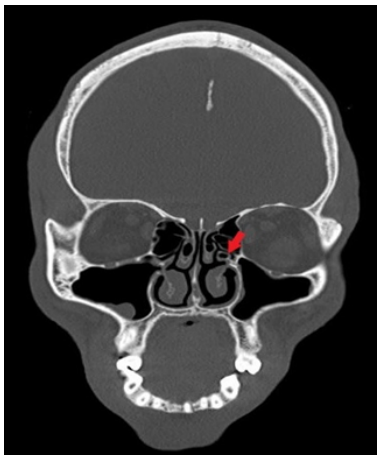


Figure 2 (Original) Reformatted Coronal CT images of the skull (bone window) showing pneumatization of the left uncinate process

The IBM Corporation's Statistical Package for Social Sciences (SPSS) version 23, located in Armonk, New York, USA was employed in the analysis of data. Data were organized by gender and the distribution of the variants represented as percentages. To assess disparities in the frequencies based on side and gender, the Pearson's Chi-square test was applied. A P-value less than 0.05 was regarded as statistically significant.

RESULTS

The prevalent placement of the SAUP was typically on ethmoid lamella, observed bilaterally in 208 (61.9%) (Figure 1A). Subsequently, the SAUP was found on the middle concha/turbinate bilaterally (81, 24.1%) and lastly on the skull base (47, 14%) (Figures 1B and 1C). No significant differences based on gender were observed among these three types of SAUP (P>0.05) (Table 1). Conversely, all the three insertions demonstrated statistically significant dissimilarities between sides (P=0.001 each). Table 2 presents the occurrence of the variant SAUP in different studies.

Table 1. Gender differences in the superior attachment of the UP

Attachment Site	Average (%)	Males (%)	Females (%)	P value
Lamina papyraecea	208 (61.9)	117 (58.8)	91 (66.4)	0.032
Middle turbinate	81 (24.1)	54 (27.1)	27 (19.7)	0.216
Skull base	47 (14)	28 (14.1)	19 (13.9)	0.856

Table 2. The prevalence of variant superior attachment of the UP in different studies (Original)

Author	Country	Lamina papyraecea	Skull base (%)	Middle Turbinate
Arun et al. [1]	India	67.5	18.5	9.5
Oghenero et al. [2]	Nigeria	83	2.2	14
Tuli et al. [8]	India	79.8	16.7	3.6
Kansu, et al. [12]	Turkey	19.8	12	9
Current study	*Nigeria*	*61.9*	*14*	*24.1*

The UP demonstrated equal prevalence in bilateral orientation occurring either vertically or horizontally. Prevailing presence of the horizontally oriented UP (197, 58.6%) followed by vertical orientation (41.4% ,139) were noted. Both indicated noteworthy variations between sides (P=0.001 each) but lacked association with gender (*P*=0.286, 0.230) (Table 3). The uncinate's tip was medially deviated and laterally deviated bilaterally in 130 (38.7%) and 36 (10.7%) patients respectively. These deviations were significantly associated with gender (*P*=0.005, 0.003) and side (*P*=0.001) (Table 3).

Table 3. Orientation of the UP and deviation of the UP tip (Original)

Variant		**Frequencies**			
		N	%	N	%
Orientation of UP		***Vertical***		**Horizontal**	
	Male	77	38.7	122	61.3
	Female	62	45.3	75	54.7
	Total	139	41.4	*197*	58.6
	p value	***0.286***		***0.230***	
Deviation of UP		***Lateral***		**Medial**	
	Male	*13*	*6.5*	*96*	48.2
	Female	*23*	*16.8*	34	24.8
	Total	*36*	*10.7*	130	38.7
	p value	***0.003***		***0.005***	

The frequency of the pneumatized uncinate was 9.5% (32), occurring unilaterally in all the cases. Besides, it did not exhibit any notable differences between sides (p=0.363) or in either gender (*P*=0.413 and 0.473) (Table 4 and Figure 2). Its occurrence differs across various populations as indicated in Table 5. There were no instances of atelectatic UP observed in any of the examined images.

Table 4. Prevalence of uncinate bulla (Original)

Variant		Right		Left		Total	
		N	*%*	*N*	*%*	*N*	*%*
UP Bulla	Male	9	4.5	7	3.5	16	8
	Female	9	6.6	7	5.1	16	11.7
	Total	18	5.4	14	4.2	32	9.5
	p value	*0.413*		*0.473*			

Table 5. Prevalence of the pneumatized UP in different studies (Original)

Author	Country	Pneumatized UP (%)
Fadda et al. [5]	Italy	2.8
Sheikh et al. [6]	India	15.5
Dasar and Gokce, [7]	Turkey	13.8
Gungor and Okur [9]	Turkey	11.6
Tuli et al. [8]	India	4
Kaya et al. [14]	Turkey	4.1
Shpilberg et al. [16]	America	13.5
Abesi et al. [18]	Iran	7.5
Current study	*Nigeria*	*9.5*

DISCUSSION

The superior insertion of the uncinate was on the lamina papyraecea (61.9%), middle turbinate (24.1%) and cranial base (14%) in that descending order of frequencies. These varied from reports by a previous Nigerian study by Oghenero et al. [2] who evaluated CT scans of adults in Osun State. Furthermore, our findings were different from those documented in Turkey and India (Table 2).[1,8,12] Contradicting the accounts provided by Tuli et al., [8] our study found no association between SAUP and gender. However, all the three superior insertions exhibited notable differences between sides which were significant. It is therefore important to recognize the site of uncinate insertion on each side to avoid

aggressive traction and torque which may inadvertently damage the ethmoid roof. [1,12] The SAUP was identical on either sides in all (100%) images assessed, contrary to the observations presented by Kansu [12] who found identical insertion in 46.3%.

We highlight a prevailing occurrence of the horizontally oriented UP bilaterally (58.6%) within our studied demographic. This slightly exceeded the figure earlier reported by Lingaiah et al. [4] in India. Due to its frequent association with great ethmoid bulla or contralaterally deviated nasal septum, a horizontal uncinate should raise the suspicion of the simultaneous presence of the additional two variants which should be identified. [3,13] The prevalence of vertically oriented UP (41.4%) was marginally less than the frequency documented in India. [4] Its recognition is crucial because it is more susceptible to deformation. [2,4]

The UP tip exhibited bilateral medial deviation in 38.7% surpassing the documented figures of 22.8% in Italy and 8.4% in Turkey. [5,14] Alternatively, Mahajan et al. [15] reported a greater prevalence of 52% primarily with bilateral occurrence (58%) among Indians. The bilateral ethmoid processes were deviated laterally in 10.7% exceeding the documented figure of 5.7% in Turkey. [14]In contrast, our prevalence was lesser than the earlier reported rates. [5,15] These differences may stem from variations in race and dissimilarities in the methodologies adopted; either endoscopic or radiological [15] Understanding the uncinate's deviation is essential, as it may be linked to compromised sinus ventilation and present challenges during FESS [4,5,15]

The existence of the uncinate bulla in (9.5%) surpassed the rates in Italy (2.8%) [5]. Our frequency was within the documented ranges in the Indian (4%-15.5%) and Turkish (4.1%-13.8%) populations. [6-8,14] Higher frequencies have been noted in the Americans (13.5%) and Arabs (7.5%) as indicated in Table 5. [16,18] The discrepancies may stem from differing definitions employed in the various studies. We considered any extent of pneumatization or aeration of the UP. However, Bolger et al. [17] reported some pneumatization in 4% and defined an uncinate bulla to be that which is extensively pneumatized. Bolger et al. [17] recognized the occurrence of pneumatized uncinate unilaterally (2%) and bilaterally (0.5%). In Iran, Abesi et al. [18] noted a 29.82% bilateral occurrence while unilateral existence was higher on the left (67.5%) in comparison to the right (32.5%). Counter to these findings, all pneumatized UP herein occurred unilaterally (9.5%) with no preference for either side (P=0.363). These disparities could be linked to race, regional location, and population size. An atelectatic UP was absent and this is aligns with earlier studies that recorded it to be rare, with low frequencies of 0.5-2.5% in Turkey and India. [7,9] Its presence predisposes to the unintentional injury to orbital structures during uncinectomy in FESS. [9]

The population disparities in UP variants might be caused by regional, genetic, environmental and racial factors on the UP morphology. The observed association between UP deviation and gender aligns with the observations by Tuli et al. [8] hence, implying that sex genes and hormones play a significant role in these variants. The significant variations between sides in the morphological UP variants may be linked to the separate intrauterine development of bilaterally existing structures. [3,19]

CONCLUSION

The present study sheds light on the occurrence of the variant structural forms of the UP in adult residents of Delta State, Nigeria. This highlights the importance of preoperative identification to mitigate surgical complications.

Strengths of study

Computed tomographic scans used were suitable since this modality precisely illustrates the skull bones and the intricate organization of the sinonasal region.

Limitation of study

The study omitted CT images featuring sinonasal pathology, preventing a determination of these variants' contribution to chronic rhinosinusitis. The relatively restricted sample size resulted from the retrospective design of this study and the use of CT images from a single center.

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Review articles

The Pharmacological Profile, Therapeutic Importance and Limitations with the Use of Oxycodone: A Review

Umukoro, EK[1], Elijah OB[1], Igben VJO[1], Moke EG[2]

Abstract

Introduction: Pain is perhaps the commonest symptom for which patients seek medical care and represents a major socioeconomical burden on healthcare systems globally. Despite a great deal of research into pain and analgesic strategies, the effective management of pain remains challenging. Oxycodone is an old drug but still holds significant therapeutic utility today. Its use has however been fraught with challenges such as abuse. Furthermore, the precise mechanism of action/receptors through which it acts is still the subject of some controversy.

Materials and Methods: A literature search on PubMed and google scholar was performed using the terms 'opioid crisis' 'pain pathway', 'types of nociception', 'opioid receptors' 'peripheral and central sensitisation', 'descending modulation pathway', 'pain management'. Studies, review articles and editorials published in English from 1st Jan 2000 to 1st Dec 2023 were included in this study.

Results: The depth of the problem of the opioid crisis and the effects in different continents has prevented the global utilization of oxycodone; the pharmacological profile of oxycodone which is an old drug with current clinical relevance was also reviewed. Significantly, there exists a gap in existing knowledge of the mechanism of action and precise receptors through which oxycodone acts.

Conclusion: The pain pathway is a complex process with multiple interdependent processes and under modulations from neuronal, endocrine, and inflammatory systems. Oxycodone exploits the pain pathway in producing analgesia but presents a real and present danger of addiction and dependence.

Keywords: Oxycodone**;** pain pathway; opioid crisis; opioid receptors

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INTRODUCTION

Oxycodone, also known as "hillbilly heroin" is an opioid alkaloid that is one of the most commonly used opioid analgesics in the treatment of different forms of pain, especially acute post-operative pain and is comparable to morphine in terms of efficacy. The opioid crisis gave the drug more notoriety than fame; but being an old drug, the basic pharmacology of oxycodone is often overlooked in the field of research and as such, what is known about its mechanism of action is subject to some controversy. (Kalso, 2005) Drug discovery has developed in leaps and bounds since the discovery of oxycodone and contemporary techniques and facilities need to be applied to old drugs to confirm or discover their full pharmacological profile.

Oxycodone is also a common substance of abuse and as such is a controlled substance in most countries of the world. The opioid epidemic remains a significant pressing issue and will not resolve easily. Numerous factors, including the

inappropriate prescription of opioids, lack of understanding of the potential adverse effects of long-term therapy, opioid misuse, abuse, and dependence, have contributed to the current crisis. Alarmingly, the overwhelming majority of opioid abusers begin their addiction with prescription medications, primarily for chronic pain.

METHODOLOGY

We performed a literature search on PubMed and Google Scholar using the terms 'opioid crisis' 'pain pathway', 'types of nociception', 'opioid receptors' 'peripheral and central sensitisation', 'descending modulation pathway', 'pain management'. We included any studies, review articles and editorials published in English between 2000 to 2022. Due to the relatively large number of articles published on the subject, review articles that were published in well-established journals in the field were prioritised.

DISCUSSION

History

Oxycodone was synthesized from thebaine in 1916 and achieved clinical application in 1917. It was used in many parts of Europe mainly for acute pain, alone or in combination with acetaminophen and phenacetin (Kalso, 2005)

Oxycodone is also one of the most abused drugs worldwide. Since its release in 1917, it has proven to be a drug with significant risk of dependence and fatal toxicity if misused. In 2007, oxycontin (one of the brands of oxycodone) manufacturers, Purdue Frederic Company Inc., (an affiliate of Purdue Pharma), pled guilty to misleading regulators and prescribers about the risks of addiction abuse potential of this drug. The law suit arose due to the increase in incidence of oxycodone related deaths when there was an increase in prescription and supply of oxycodone and other related law suits have been filed since then. (Van Zee, 2009; Webster, 2012) There are presently more deaths due to prescription opioids than due to cocaine, heroin and psycho-stimulants combined and this appears to be aided by a high street demand for opioids, with street value for a single oxycodone tablet estimated to be about £25 (Pilgrim *et al.*, 2015) Most of the prescribers of oxycodone in the USA are located in Florida and there has been a steady increase in its prescription and supply in that region. Oxycodone related deaths in the region between 2007 and 2010 increased by 62.5% while during this same time frame, there was a decrease in deaths attributed to other painkillers such as methadone (1.1% decrease) and hydrocodone (30.7% decrease). These were the findings upon autopsy and toxicological screens to determine the cause of death in accidental deaths. Findings were compared to data from previous years and from other regions in the USA. (Ogle *et al.*, 2015) In 2015 alone, 52,000 people died of drug overdoses, with over 30,000 of those people dying from opioid drugs. A recent community forum led by the Cleveland Clinic contrasted this yearly death rate with the loss of 58,000 American lives in 4 years of the Vietnam War. (Vadivelu, 2018)

Non-medical prescription opioid use is particularly problematic in rural areas example of which are some American areas encompassing poverty stricken, educationally less developed and geographically mountainous Appalachian Kentucky, Virginia and West Virginia and this is where oxycodone derives its other name "hillbilly heroin". (Young *et al.*, 2010; Tunnell, 2016)

Classification of Opioids

Opiates are the non-peptide synthetic morphine-like drugs whilst the term opioid is more generic,

including all substances that have effects similar to morphine and can be classified into four:

- Endogenous opioid peptides (e.g. endorphin,dynorphin and enkephalin)
- Opioid alkaloids such as morphine purified from the poppy, *Papaver somniferum*
- Semi synthetic opioids such as heroin which have modifications to the basic morphine structure in this case, diacetylation.
- Synthetic derivatives with structure unrelated to morphine

  Examples are: The phenylpiperidine series e.g. Fentanyl
  The Methadone series e.g. Methadone
  The Benzomorphan series e.g. Pentazocine
  Semi-synthetic thebaine derivatives e.g. oxycodone. (Adapted from McDonald and Lambert, 2008)

Sources of Oxycodone

Phenantrenes and Benzyl-isoquinolines make up the two alkaloid chemical classes of Opium. Thebaine, a phenantrene alkaloid, is present in 90% of the opium derived from *Papaver bracteatum* which is morphine-free. It is also present to a lesser extent (0.2-0.8%) in *Papaver somniferum* which contains morphine. While thebaine is the precursor of oxycodone, it is very toxic and lacks analgesic properties. (McDonald and Lambert, 2008)

Structure of Oxycodone

The oxycodone molecule consists of four rings (two planar and two aliphatic). Its basic chemical formula is 6-deoxy-7, 8- dihydro- 14-3-O-methyl-6-oxomorphine and differs from morphine by a dehydroxylated 6th carbon atom. (Figure 1).

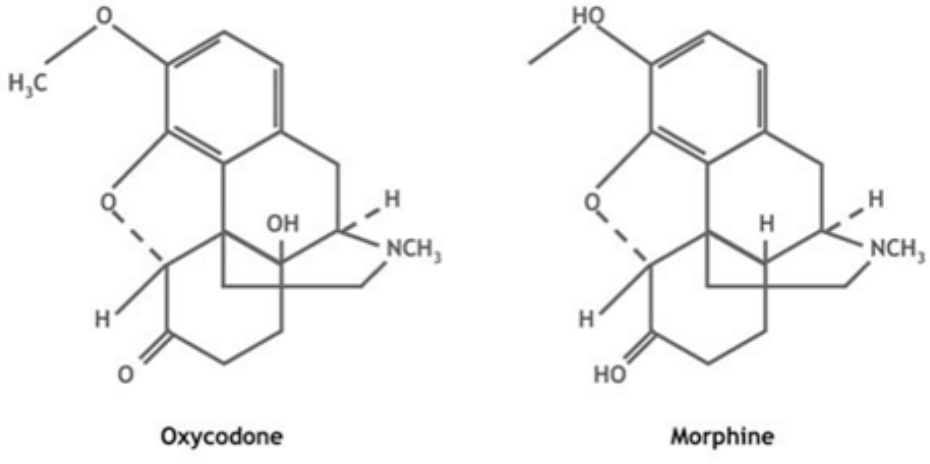

Figure 1: Chemical structural comparison of oxycodone and morphine (Ordonez *et al.,* 2007)

Pharmacokinetics of Oxycodone

Oxycodone is available in several different preparations for oral immediate, oral extended/ controlled release and intravenous use. Onset of action with pain relief is rapid, as the effect occurs as early as 15 minutes, and peaks at approximately one hour following oral administration. Peak Oxycodone plasma concentrations were noted at between 1.4 hours and 3 hours after administration depending on the type of preparation.

Oxycodone has an apparently higher bioavailability than morphine due to the 3-methoxy substituent that prevents significant first pass metabolism. This is reported at between 42% and 87 %. (Riley *et al.,* 2008)

Oxycodone is 45% protein bound, predominantly to albumin and is extensively distributed into tissues including skeletal muscle, liver, intestinal tract, lungs, spleen and brain. The apparent volume of distribution of oxycodone is 2.4 ± 0.8 L/Kg following intravenous administration. Oxycodone has relatively low lipid solubility and thus is not suitable for sublingual administration. (Lugo *et al.*, 2005)

The major metabolic pathway of oxycodone in man is by N-demethylation which leads to the formation of noroxycodone. Oxycodone and occasionally noroxycodone is further metabolized to noroxymorphone and oxymorphone most likely by O-demethylation. Oxymorphone and norxymorphone are active metabolites (), but as their plasma concentrations are significantly lower than that of the parent compound, oxycodone, they probably do not contribute markedly to the analgesic effects. Less than 10% of oxycodone also gets broken down to oxycodol via 6-keto reduction. (Lofddal *et al.*, 2013)

N-demethylation is carried out by CYP3A4/5 while O-demethylation is carried out by CYP2D6. The genetic polymorphisms of CYP2D6 causes inter individual and interethnic variability in the rate of metabolism giving rise to poor, intermediate, extensive and ultra-rapid metabolizers. (Kokki *et al.,* 2012)

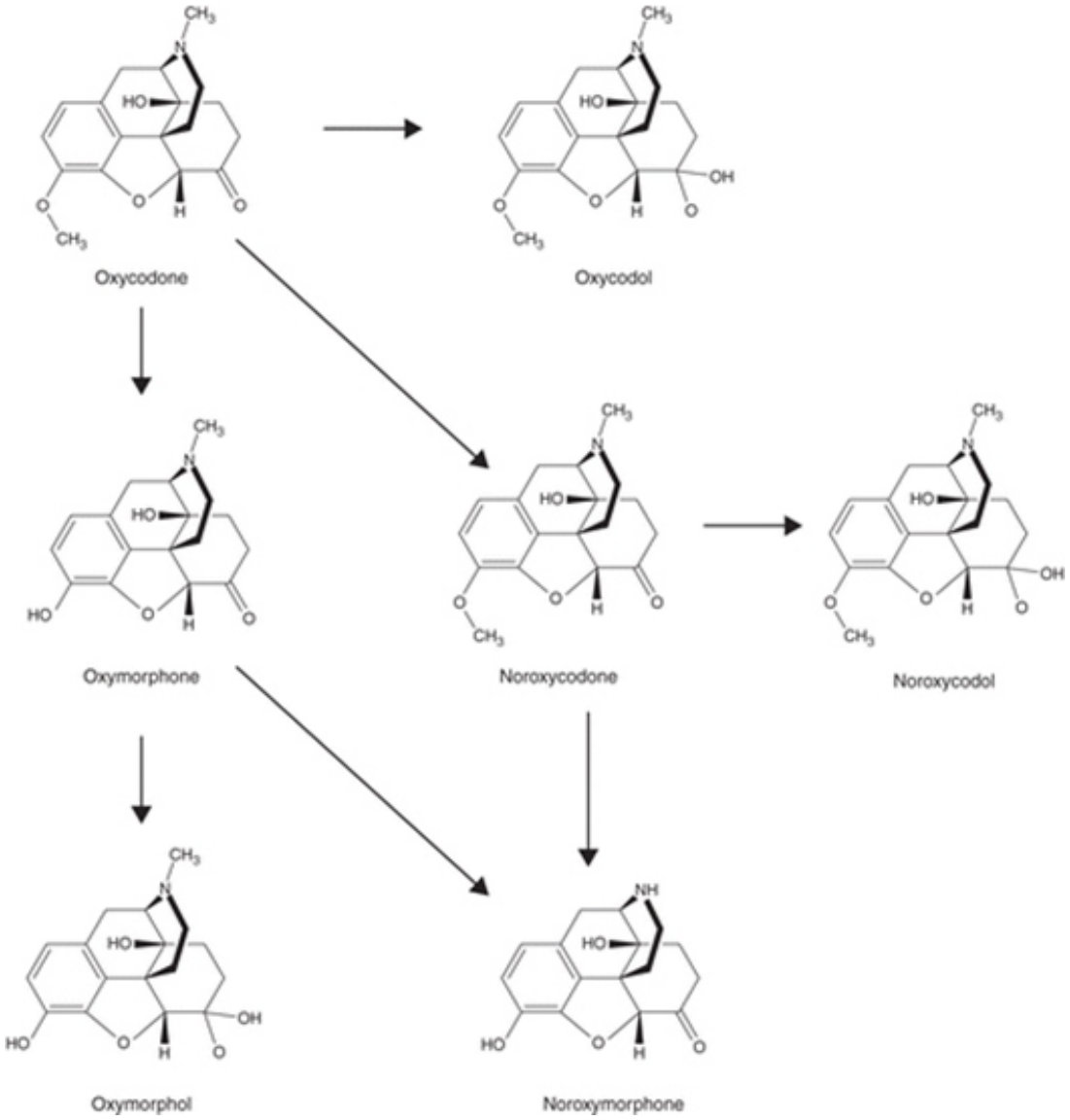

Figure 2: Metabolism of Oxycodone (Kokki et al., 2012)

Pharmacodynamics of Oxycodone

Although the major opioid receptors are G-protein coupled and as such similar in structure and function, binding affinity profiles and intrinsic efficacy exhibited with different ligands clearly distinguish them.

Types of opioid receptors

The opioid receptor family includes Mu opioid receptors (MOR), Delta opioid receptors (DOR),

Kappa opioid receptors (KOR) and ORL receptors. They are encoded by Oprm1, Oprd1, Oprk1 and pronociceptin/preproorphanin FQ genes respectively but all have approximately 60% amino acid sequence homology with each other. A number of subtypes are also known to exist such as MOR_1, MOR_2, $DOR_{1,}$ $DOR_{2,}$ $KOR_{1,}$ $KOR_{2,}$ and KOR_3 and were suggested on the basis of *invitro* and *invivo* pharmacological studies. Some techniques have been and are being employed to define the structure and mechanisms of the opioid receptors including agonist directed signalling at the different receptors and fluorescence recovery after photobleaching (FRAP). (Lomberk *et al.*, 2008)
The prototype agonist at MOR is morphine while that of KOR is ketocyclazocine. These agonists were used to define their respective receptors. The delta receptor was defined by comparing the activity of endogenous opioid peptides and opiate ligands across various systems while nociceptin/orphanin is the ligand at the ORL receptor. Their location and function appears to vary as do their ligands. In fact, ORL receptor plays a role in antinociception. (MacDonald and Lambert, 2011; Baiula *et al.*, 2015)

All receptors appear to have a high affinity for the opioid receptor antagonist, Naloxone. Further studies have also suggested MOR_1 subtype antagonist, naloxonazine. (Chaijale, *et al.*,

Opioid receptor signalling and behaviour
All four opioid receptors are coupled to heterotrimeric (Gαβ) inhibitory G proteins $G_i/G_{(0)}$ as seen in . Following ligand binding, the G protein dissociates into subunits and initiates a cascade of events ending in interaction with inward rectifying potassium channels (kir3) and inhibition of adenylyl cyclase activity with a decrease in cyclic adenosine monophosphate (cAMP) and protein kinase A (PKA) while there is an increase in mitogen activated protein kinase (MAPK) phosphorylation. There is also a reduction in voltage activated opening of calcium ion channels. Interaction with these ion channels causes cellular hyperpolarization and inhibition of tonic neural activity. (Costantino *et al.,* 2012; Al Hasani and Bruchas, 2011) Studies have shown that all opioid receptor subtypes may come together to form homomeric or heteromeric complexes. () These complexes appear to show a unique pharmacological profile distinct from that of individual receptors. There is also evidence that complexes may also be formed between some opiate receptors and cannabinoid or α2 adrenergic receptors or even proteins such as β arrestin 2 at the level of desensitization. (Costantino *et al.,* 2012)

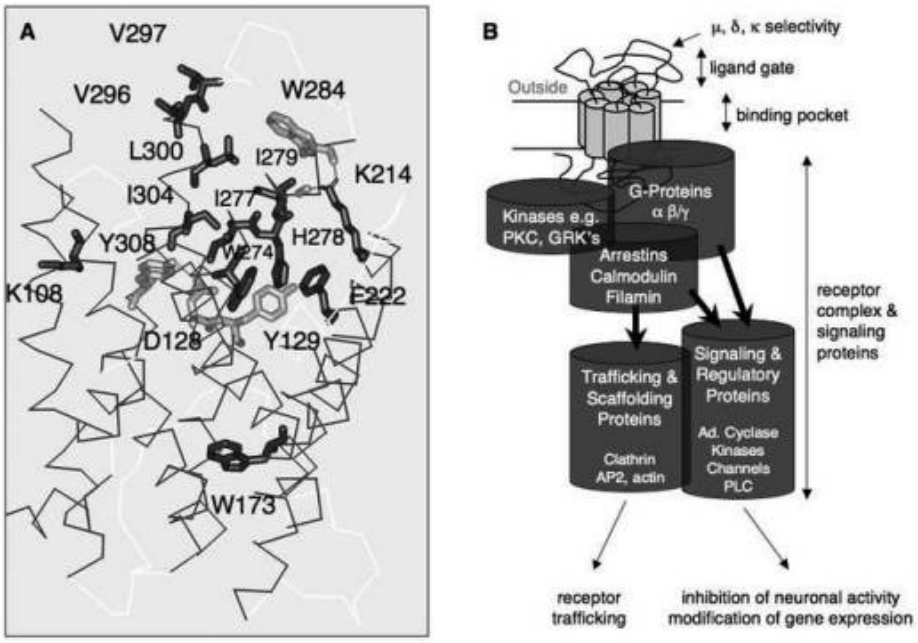

Figure 3: Prototype structure and signalling pattern of opioid receptors (Kieffer and Evans, 2010)

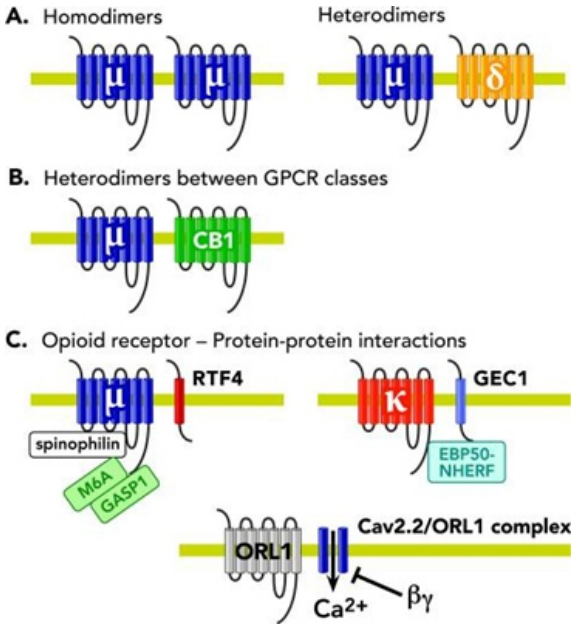

Figure 4: Opioid receptor dimerization/ complex formation (Al Hasani and Bruchas, 2011)

Effects of Oxycodone and the Controversy Surrounding its Mechanism of Action

The beneficial and adverse effects of oxycodone in part, contribute to the controversy surrounding its mechanism of action. Some authors suggest that based on the mechanism of its effects, oxycodone is primarily a KOR agonist with only a little affinity for the MOR, (Ordonez *et al., 2007)* while others join the school of thought that oxycodone is an MOR agonist primarily.

Pain

The most vital effect of the opioid family is on pain control and as such they are the mainstay of treatment for moderate to severe postoperative pain as well as other types of pain. Pain is defined as an unpleasant sensory or emotional experience associated with actual or potential tissue damage. (Terman and Bonica, 2003) Pain may also be classified as physiological or pathological. Physiological pain occurs in the absence of actual tissue or nerve damage, serving as a warning sign for impending injury. Examples include muscle cramp and abdominal colic. In pathological pain, tissue or nerve damage occurs. (Liu and Kelliher, 2022)

Pain can be acute or persistent and it is in the latter that opioids find the most significance. Persistent pain is classified into nociceptive pain (such as post-operative or chronic inflammatory pain) or neuropathic pain which is a dysfunction of the nervous system causing pain perception in the absence of tissue injury (such as phantom limb pain and post-stroke pain). While nociceptive pain readily responds to opioids, neuropathic pain does not. Nociceptors are pain receptors that are located in the dorsal root ganglia and trigeminal ganglia. They receive sensory information from the peripheral tissues and transmit these signals to the higher centres via the peripheral and central branches respectively. The source of sensory information is usually from release of neurotransmitters following tissue damage. There are two types of nociceptors: peptidergic nociceptors which express neuropeptides and terminate in the most superficial laminae of the dorsal horn targeting lamina I projection neurons and interneurons of outer lamina II; and non peptidergic nociceptors which target interneurons of inner lamina II. These are important in nociception and complex interactions between excitatory and inhibitory parts of the pain pathway occur. (Zhang et al., 2013) Tissue injury evoked hyperalgesia evolves in two distinctive forms. First is primary hyperalgesia which is characterised by enhanced nociceptor excitability within the damaged zone and caused by accumulation of pro inflammatory mediators. Secondary hyperalgesia develops more slowly around the zone of injury and is due to central sensitization which is neuronal sensitization at the spinal cord level. Secondary hyperalgesia gives rise to referred pain in visceral inflammation. (Treede and Mageri, 2003) Both these forms of hyperalgesia involve ascending and descending tracts. () The ascending tracts contain second order neurons which ascend to higher centres via the contralateral spinothalamic and spinoreticular tracts, which are located in the anterolateral white matter of the spinal cord and terminate in the primary and secondary somatosensory cortices, the insula and the anterior cingulate cortex and the prefrontal cortex. Information travelling along this tract gets processed in the thalamus. (Liu and Kelliher, 2022) The descending pathways are responsible for modulating pain and are inhibitory. They involve the peri aqueductal gray (PAG) which receives input from the thalamus, hypothalamus and cortex and also collaterals from the spinothalamic tract. MOR is found mainly pre-synaptically in the periaqueductal gray and in the superficial dorsal horn of the spinal cord. They are also located in external plexiform layer of the olfactory bulb, the nucleus accumbens in several

layers of the cerebral cortex and in some of the nuclei of the amygdala as well as the nucleus of the solitary tract. (Liu and Kelliher, 2022; McDonald and Lambert, 2005) The PAG neurons excite cells in the Nucleus Raphe Magnus (NRM) that in turn projects down to the spinal cord to inhibit pain transmission by the dorsal horn cells. NRM cell bodies synapse on cells in lamina II and III and stimulation of this region produces a powerful analgesia by activation of inhibitory interneurons. (Steeds, 2009) KOR localizes to the limbic and other diencephalic areas, brain stem and spinal cord and has been implicated in spinal, supra-spinal and peripheral analgesia. The DOR are found primarily in the brain and participate in supra-spinal and spinal analgesia. (Lomberk *et al.,* 2008)

Under physiological conditions, opioid receptors are transported from primary afferent neuronal cell bodies to central/spinal terminals. Cell bodies of the DRG neurons express mRNA and proteins of opioid receptors which are also subsequently transported to the small medium and large diameter peripheral nerve terminals. Tissue injury induces this process even more so. These opioid receptors mediate anti-hyperalgesia by opioid agonist binding. (Stein and Lang, 2009)

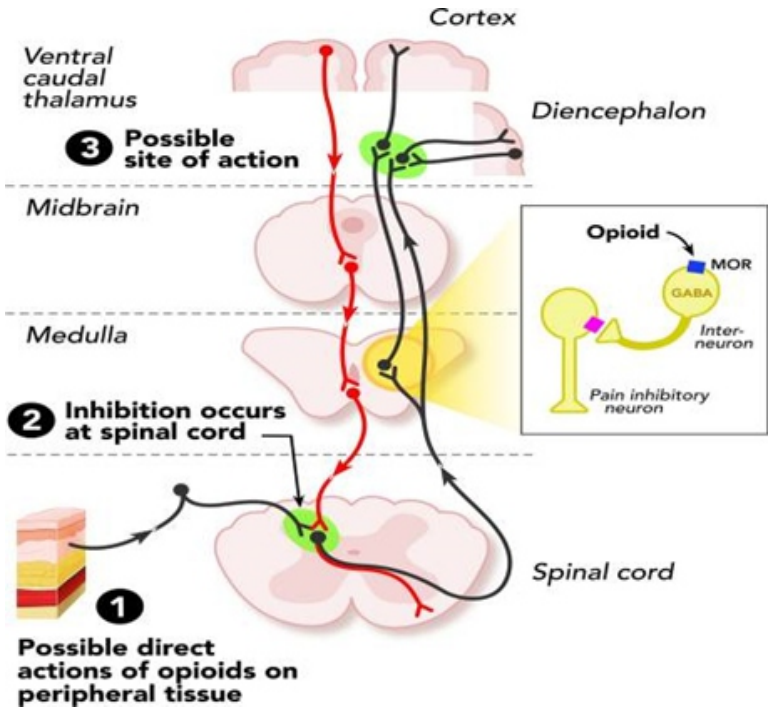

Figure 5: **The pain pathway and the role of opioids (Al Hasani and Bruchas, 2011)**

Mechanism of action

The mechanism of action of oxycodone in analgesia is still controversial. In one study, experimental rats with chronic constriction injury of the sciatic nerve and streptozotocin induced diabetes were given either morphine or oxycodone intravenously or subcutaneously. Behavioural studies confirmed analgesic effects

of oxycodone and morphine on test animals. The effects of oxycodone however, were abolished by the selective KOR antagonist nor-binaltorphimine (norBNI), while those of morphine were not. This was also supported by radioligand binding which found preferential binding of oxycodone to KOR specifically $KOR_{2\beta}$ over MOR in the CNS. (Riley *et al*., 2007) Similar study by Nielson et al., in 2007 appear to confirm this. Following chronic constriction injury (CCI) of the sciatic nerve in rats, the antinociceptive effects of intrathecal (i.t.) oxycodone, but not intrathecal morphine, were abolished by nor-BNI. They therefore concluded that oxycodone is active at KOR in contrast to morphine. KOR has also been implicated in aetiology of visceral pain in animal models as mice lacking KOR are found to be more susceptible to visceral inflammation and hence visceral pain. Furthermore following abdominal inflammation, KOR signalling, mRNA and protein expression are up regulated suggesting that agonists with significant enough activity at KOR can cause sufficient analgesia in pathologic conditions but not in health. (Hughes *et al.,* 2013) The effect of oxycodone and morphine on visceral pain was studied in human subjects who received multimodal pain stimulation to the oesophagus in order to elicit pain. It was observed that oxycodone was superior to morphine in improving pain threshold, though this could not be categorically attributed to KOR. (Riley *et al.,* 2007) A further study on efficacy of oxycodone and morphine in chronic pancreatitis concluded that oxycodone was a more effective mode of pain management than morphine. (Staahl *et al*., 2007) Together, these studies provide presumably sufficient evidence that oxycodone is a KOR agonist at the very least.

If the data that oxycodone acts by stimulating KOR primarily appears compelling, the evidence that it is a MOR agonist is even more so. In fact, most of the effects of oxycodone have been suggested as being caused by MOR stimulation. However, Kokki *et al.,* (2012) opines that oxycodone is a MOR agonist but with comparatively significant lower binding affinity than morphine. It also has affinity for the KOR and DOR but comparatively lower than that for the MOR. Nozaki and Kamei (2007) agreed with this suggestion at least in part by experiments on normal mice and mice with streptozocin induced diabetes mellitus. Different groups of both sets of mice were pre-treated with norBNI (KOR selective antagonist), β-funaltrexamine and naloxonazine (selective MOR antagonist); then administered oxycodone. Behavioural analyses were then carried out to assess the effects of all the drugs on pain threshold. It was found that the analgesic effects of oxycodone were abolished completely by naloxonazine, attenuated to a lesser extent by β-funaltrexamine and partially but significantly by norBNI. It was therefore concluded that oxycodone produces its antinociceptive effects primarily through MOR_1, and to a lesser extent through KOR and other MOR subtypes.

Constipation, a common side effect of oxycodone characterised by inhibition of propulsion in the GIT, appears to be a direct consequence of MOR activation. Ahmedzai *et al.,* (2012) clinically proved this by carrying out a study on patients with moderate to severe cancer pain. Patients were switched from other opioids to either oxycodone alone or a combination of oxycodone and naloxone. The patients switched to the combination therapy experienced clinically relevant and statistically significant improvement in constipation compared to those on oxycodone alone. Furthermore, Delgado-Aros *et al*., (2003) compared the effects of selective KOR agonist Asimadoline and a placebo on visceral sensation and gastrointestinal motor functions in humans

and concluded that it did not cause inhibition of gastrointestinal reflexes thus reducing the possibility that effects noted by Ahmedzai *et al.,* (2012) could have been caused by naloxone antagonism at KOR. *Invitro* pharmacological techniques have also been used to compare the mechanism of inhibition in circular muscle and longitudinal muscle. Phe-Cys-Tyr-D-Trp-Arg-Thr-Pen-Thr-NH_2 (CTAP), naltrindole, norBNI, DAMGO [Tyr-D-Ala-Gly-(*N*–Me)Phe-Gly-ol] and DADLE [d-Ala^2, d-Leu^5]-enkephalin acetate amongst others, which are all antagonists and agonists at MOR, DOR or KOR were used to define the mechanism of inhibition and the conclusion was that MOR and not KOR mediated the inhibition of contraction in longitudinal muscle. (Gray *et al.,* 2005*)*

The role of MOR in onset of physical dependence was studied using knockout mice with MOR gene deletions and strengthens the case for MOR stimulation as the mechanism of action of oxycodone. They displayed no expression of naloxone induced withdrawal symptoms. (Narita, 2001) Stimulation of the reward pathway results in craving which is the psychological component of dependence and this is mediated by MOR located in the mesocorticolimbic pathway originating in the ventral tegmental area (VTA) and projecting to the nucleus accumbens, amygdala and prefrontal cortex. Oxycodone appears to induce dopamine release indirectly by decreasing GABA-inhibition via MOR located in the VTa which releases dopamine. This release of dopamine causes euphoria and reinforcement of drug-seeking behaviours. Stimulation of KOR however, appears to inhibit striatal dopamine release. (Narita, 2001; Ballantyne and La Forge, 2007) Euphoria, nausea, vomiting, pupillary constriction and respiratory depression which are long known to be caused by stimulation of MOR are more commonly associated with Oxycodone use. (Eldalal et al., 2020)

All together, these studies suggest a preponderance of evidence for oxycodone as a MOR agonist; however, when contrasted with evidence for oxycodone as a KOR agonist which appears compelling by itself, it highlights the controversy on the subject and justifies the need for further research in the area. Oxycodone remains a drug poorly or incompletely studied, universally abused yet clinically relevant and as such extensive research of its mechanism of action is necessary to better improve its benefit profile.

Oxycodone as a substance of abuse

Oxycodone is approved by the US Food and Drug Administration (FDA) as a schedule II narcotic analgesic though it is not commonly prescribed in Nigeria. Consequently, the opioid crisis in Nigeria was more centred around codeine and tramadol. (Dumbili, 2023) Each year however, prescription opioid abuse and misuse results in approximately 13,800 deaths and 250,000 emergency department visits as reported in. Over 85,000 admissions to addiction treatment facilities for prescription opioid abuse occur annually. Prescription opioid abusers incur more healthcare costs than non abusers, and fraud associated with prescription opioids is estimated to cost public and private payers

about $75 billion per year. It is estimated that nearly a third of people who abuse drugs started with prescription opioid medicines. This has severely limited the use of oxycodone in healthcare. (Vadivelu et al., 2018)

CONCLUSION

In conclusion, oxycodone is a potent analgesic that works primarily by stimulating opioid receptors. The particular receptors stimulated is still of some dispute as modern technology is yet to be applied to research the mechanism of action of the drug. Furthermore, the use of these drugs has over time been severely limited by the high abuse potential as oxycodone played a major role in the opioid crises. It will also be beneficial to research the specific receptors oxycodone stimulates in bringing about its effects as well as the relative abundance of different opioid receptors in different tissue.

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Acute Kidney Injury in The Critically ill Patient: A Review of Epidemiological Studies in Low-middle Income Countries

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Abstract

Introduction

Acute kidney injury (AKI) refers to the sudden reduction in the kidney's ability to carry out its functions. AKI poses a major health burden in both low and middle income countries (LMIC) resulting in increased morbidity and mortality. It is a common complication in critically ill patients and has the potential of progressing to CKD.The objective of this article is to review the existing epidemiological studies on AKI in ICUs in LMIC.

Methods

Pubmed, Google Scholar, Web of Science and the Scientific Electronic Library online (SciELO) were searched for published reports, including article reviews on AKI in critically ill patients in LMIC. Search items included key words such as "acute kidney injury", 'critically ill patient", 'intensive care unit', 'epidemiology' low and middle income countries, 'developing countries'. The Search occurred between September to November 2022.Articles published from 2010 to 2022 were included in the search. The results reported according to PRISMA 2020 guidelines.

Results

Sixteen studies done in 13 LMIC were identified, with these studies analyzing data from 14835 patients from 51 ICUs within these countries from 2010 to 2022. Out of the studies reviewed, Six were from African countries and ten from non-African countries with male sex preponderance. The mean age of patients in the various studies ranged from 36 to 78 years with similar comorbidities reported such as hypertension, diabetes mellitus, stroke and heart failure. The overall incidence of AKI in ICU ranged from 29% to 58.5%. RIFLE criteria was used to define AKI in 4 of the reported studies with same number using AKIN criteria and lastly, KDIGO used in 8 studies. While most of the studies used just serum creatinine to define AKI, the study done by Passoni et al included urine output as well. Mortality rate was between 25.7% to 68%. Risk factors for AKI in critically ill patients reported from most of the studies reviewed include increasing age, male sex, sepsis, increasing length of ICU stay, hypovolemia and vasopressor use. Also, comorbidities such as hypertension (14%-46%) and diabetes mellitus (13%-45.9%) was common among patients. The length of ICU stay varied from 2 to 45 days with longer duration of stay noticed for patients with AKI for those reported.

Conclusion

it is reasonable to conclude that the high incidence of AKI and its contributory factors are persistent in LMICs with the associated poor outcomes.

Key words: acute kidney injury", 'critically ill patient", 'intensive care unit', 'epidemiology' low and middle income countries, 'developing countries'

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INTRODUCTION

Acute kidney injury (AKI) refers to the sudden drop in the kidney functional capacity following anatomical or physiological abnormalities or both.[1–3]Low Middle income Countries (LMICs) are countries in which the Gross National Income (GNI) per capita is less than four thousand two hundred and fifty five dollars; with the country Nigeria being a typical example.[4,5] LMICs are also known as developing countries AKI poses a major health burden in LMICs resulting in increased morbidity and mortality.[6] AKI is a common complication in critically ill patients and has the potential of progressing to CKD. Risk factors for AKI in critically ill patients include increasing age, male sex, hypovolaemia, nephrotoxic medications and presence of cormobidities.[6]

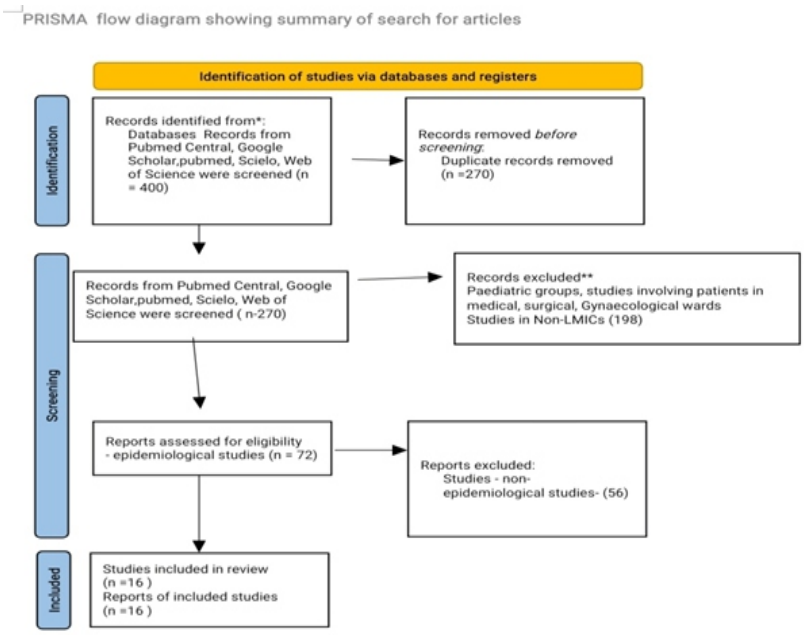
Epidemiological studies of AKI in ICU has showed variable results across different countries which could be due to factors such as the population studied (general, hospitalized, specific-patient sub-groups e.g surgical, ICU), differences in definition criteria used for the study, socio-demographic and economic status of populations studied.[7-9] AKI being more in older patients in high income countries may be due to advancement in medical care and interventional procedures; availability of well-equipped healthcare facilities and long lifespan. This is unlike low middle income countries where AKI in ICU patients is more in young adults which may be due to reduced lifespan, higher occurrence of infectious diseases and poor infrastructural development.[10-14] The objective of this article is to review the existing epidemiological studies on AKI in ICUs in LMICs to possibly provide insights into the modifiable factors that would improve disease outcome.

METHODS

Search Strategy and Selection Criteria

Pubmed, Google Scholar, Web of Science, WHO Global Health Library databases and the Scientific Electronic Library online (SciELO) were searched for published reports on AKI in critically ill patients in Low- and Middle-income Countries. The Search items included 'acute kidney injury'', 'acute renal failure', 'critically ill patient'', 'intensive care unit', 'epidemiology' low and middle income countries, 'developing countries', global south countries. The Search occurred between September to November 2022.Articles published from 2010 to 2022 were included in the search.

The abstracts of all selected studies including the complete articles were reviewed for inclusion. Observational and cohort studies (retrospective or prospective) involving critically ill adults patients in LMICs were eligible for inclusion. Selected papers were from both English speaking and non-English speaking countries. However, papers from non-English speaking countries were available online in the English version Unpublished articles, reviews, case reports and Studies involving paediatric age groups, or patients on the open wards (medical, surgical or gynaecological and maternity ward) or outpatients were excluded. A further review of articles was done to ensure appropriateness and for subsequent data extraction. The results reported according to PRISMA 2020 guidelines



RESULTS

Sixteen studies done in 13 LMIC were identified, with these studies analyzing data from 14835 patients from 51 ICUs within these countries from 2010 to 2022. Out of the studies reviewed, six were from African countries and ten from non-African countries with male sex preponderance. The mean age of patients in the various studies ranged from 36[14] to 78 years[6,13] with similar comorbidities reported such as hypertension, diabetes mellitus, stroke and heart failure.[6,8,11,14,16] The overall incidence of AKI in ICU ranged from 29%[14] to 58.5%[15]. RIFLE criteria was used to define AKI in four of the studies, Acute Kidney Injury Network (AKI) criteria in four and Kidney Disease Improving: Global Outcomes (KDIGO) criteria used in eight studies. While most of the studies used just serum creatinine to define AKI, the study done by Passoni et al included urine output as well.

Risk factors for AKI in critically ill patients reported from most of the studies reviewed include increasing age, male sex, sepsis, increasing length of ICU stay, hypovolaemia and vasopressor use. Comorbidities such as hypertension (14%-46%) and diabetes mellitus (13%-45.9%) was common among patients. The length of ICU stay varied from 2 to 45 days with longer duration of stay noticed for patients with AKI for those reported. Mortality rate was between 25.7%[8] to 68%[11]. Table 1 provides detailed information on studies reviewed.

Table 1. Summary 0f Information About the Epidemiology of Aki in Critically Ill Patients in LMIC In Reviewed Articles

						Population Characteristics			Epidemiological Data				Length of ICU stay		
Author/ Year	Place	Study type	No. of Px	AKI Def. Criteria	Mean age (yrs)	Male (%)	Female(%)	Comor-bidities	Risk factors for AKI	Incidence (%)	RRT for AKI (%)	Mortality (%)	With AKI	Without AKI	Outcome
Park et al.[8] 2010	Korea	R	378	RIFLE	62.6	62.7	37.3	DM, HTN	Older age, male sex, pul.dx, malignancy	41.3		AKI-25.7	17.2+-17.2		Survivor 70%
Jiang et al.[15] 2019	China	Pros., cohort	3107 (30 ICUs)	KDIGO	65.5	61.2	38.8	HTN (39.3%),HF (7%),DM (17.1%), CKD (6.5%), COPD (5.3%)	Male sex, older age, sepsis, hypotension, drugs	51		AKI-27.7 Non-AKI-6.8	3-11 (average, 7)	2-6	
Ahmed et al.[14] / 2021	Sudan	Pros	211	KDIGO	41	64	36	DM (31%), HTN (14%),Resp dx (4%), GIT(5%), CNS (2%).	Male sex, middle age, increasing length of ICU stay, mechanical ventilation, sepsis	29	62	AKI-41	2-45 days (average , 22.5)	-	Recovery-48%, discharged on RRT-11%
Adelaja et al.[13] 2019	Nigeri a	Prospect ive cohort	100	RIFLE and AKIN	41.3	59	41	-	Younger age, male sex,head injury, sepsis, malignancy, cardiothoracic, obstetrics	54	-	AKI-61.5 Non-AKI-35	10.2+-9.4	11.1+-10	Survival 14.9%
Passoni et al 2019.[12]	Brazil	Ret/ cohort	1500	KDIGO	53	-	-	HTN (40.6), DM (16.1 %), cancer (8.2%)	Middle age, sepsis	40.5	13	AKI-39.1	12-39	13-31	-
						Population characteristics			Epidemiological Data for AKI				Length of ICU stay		
Author	Countr y	Study type	No of px	Criteria for AKI	Mean ag (yrs)	Male (%)	Female (%)	comorbidities	Risk factors for AKI	Incidence	RRT for AKI	Mortality (%)	With AKI	Without AKI	Outcome
Masewu et al.[16]2016	DRC	Prospect ive cohort	476(7 ICUS)	AKIN	52	57	43	HTN (4 6 %),DM (20.4%), stroke (8.8%), HF (1.8%)	Male sex, CKD, NSAID, sepsis	52.7	-	AKI-58	-	-	
Banda et al 2020.[11]	India	Retr cohort	280	KDIGO	36	51.1	48.9	DM (13%),HTN (27%), HIV (38.5%)	Young age, NSAID, HIV	52.9	-	AKI-68	-		
Minja et al 2019.[17]	Tanzan ia	Pros. Cohort	320	KDIGO	35	56	44	CVD (34%), DM (16%), surgery, HTN, malignancy (6%)	Sepsis, drugs, DM	55.3	-		-	-	
Aylward et al 2019.[18]	South Africa	Pros. Cohort	849	KDIGO	42.5	58.9	41.1	HTN (31.6%),DM (13.6%),CK D (7.7%), active TB (6.1%)	Length of stay, DM, sepsis, hypovolaemia, vasopressors	58.5	-	AKI-31.8 Non-AKI-7.23	-	-	CKD-12.7
Oweis et al.[19] 2020	Jordan	Retrospe ctive	2530	AKIN	54.3	58	42	HTN (45.7%), DM (45.9%), HF (6.7%)	Sepsis, neurological disorder	31.6		AKI-58 Non-AKI-51.3			
Halle et al 2018.[10]	Camer oun	pros. Cohort	2402	KDIGO	56	54.7	45.3	HTN (32.2%), DM (17.6%)	Male sex, middle age, infections	22.3	10	36.9	-	-	Recovery-84.2 CKD1.1 Partial recovery-14.1
Kim et al.[20]2015	Korea	retrospe ctive	335	RIFLE				HTN (35%), DM (25%)	Surgery, nephrotoxin	15.5	34.6	AKI-40.4, Non-AKI-21.3	14	15	Recovery-17

Yokota et al.[21] 2017	Brazil	Prospective	200	KDIGO	Elderly			DM, HTN (70.3%)	Sepsis, longer ICU stay	27		AKI-48.1 Non-AKI-15.7	11.4	5.2	
Santos et al 2015.[22]	Brazil	prospective	27	RIFLE	50	59.3	40.7	HTN, DM, heart dx		55.6		AKI-44.4			
Herrera-Mendez et al 2015.[23]	Mexico	prospective	360	AKIN	49	54.8	55.2	HTN, DM	Sepsis, shock, MODS	20.3		AKI-26.1,Non-AKI-16.6			
Boltansky et al.[24]2015	Chile	Retrospective	1769	AKIN		47		HTN (44%), DM (22%)		28.9		AKI-13.3 Non- AKI-6.0			

Abbreviations: AKIN - Acute Kidney Injury Network;HIV - Human Immunodeficiency Virus; KDIGO - Kidney Disease Improving: Global Outcomes; RIFLE - Risk, Injury, Failure, Loss, End-stage kidney disease; RRT – Renal replacement therapy; HTN-Hypertension; DM-Diabetes Mellitus, COPD- Chronic Obstructive Pulmonary disease,CKD- Chronic Kidney disease; CVD- Cerebrovascular disease,IHD-Ischaemic heart disease; PVD- Peripheral Vascular Disease, MODS- multiple organ dysfunction syndrome, Pros- prospective, R- Retrospective, DRC- Democratic Republic of Congo, AKI- Acute kidney injury

DISCUSSION

This study was aimed at reviewing the existing epidemiological studies on ICU-related AKI in LMIC. Our findings show that incidence rate of AKI was high, ranging from 29-58% based on the population studied and AKI definition criteria applied. The most common risk factors for AKI were modifiable and mortality rate was high.

The high incidence of AKI in developing countries may be due to higher occurrence of communicable diseases, poor health seeking attitude and delay of appropriate intervention. In addition, most of the critically ill patients from the studies reviewed, had comorbidities such as hypertension, diabetes mellitus[8,12,14-16], probably increasing the disease burden and worsening the outcome. Other comorbidities present include, COPD, malignancies, CKD, ischaemic heart disease, HIV and peripheral vascular diseases.[11,14,16-19] The presence of comorbidities increase the risk for AKI directly or indirectly by altering the renal autoregulatory processes leading to renal hypoperfusion and injury.[28]

The young and middle age groups were mostly affected and this probably reflects the lower average life-span in LMIC compared to advanced countries. Furthermore, some of the risk factors for AKI such as sepsis, hypovolaemia from injuries, HIV and use of nephrotoxic medicines tend to be commoner in the younger age group. There were more critically ill males with AKI compared to females and this may be because in many LMIC, males tend to have better access to health care, being the head of the family and bread winner.

The risk factors reported in the studies reviewed include young and middle age groups[12-14], male sex[8,12,14,15], sepsis[12,13,15], surgeries[13], hypovolaemia, head injury[13], mechanical ventilation[14], HIV[11], nephrotoxic medicines such as NSAIDs[11,16,17] and increasing length of ICU stay.[14,18] Sepsis was a commonly reported risk factor and cause of AKI in critically ill patients across most of the studies reviewed. Sepsis was associated with worsened morbidity, leading to an increase in ICU stay[13,14,16-19]. Sepsis increases the risk for AKI by 48.1%.[20] The pathophysiological mechanisms of sepsis-induced AKI in critically ill patients is complex, often leading to glomerular, interstitial and tubular damage possibly explaining its severity and poor treatment outcomes.[25]

Besides sepsis, another critical risk factor for AKI is baseline renal dysfunction. Jiang et al, in a large multicenter study involving 30 ICUs using KDIGO AKI definition criteria observed that

AKI patients already had worse baseline renal function when compared with those without AKI.[15] Similarly, Masewu et al, in a large multicenter prospective study verified that AKI had worse baseline serum creatinine.[16] Hence, critically patients with background renal impairment should be carefully monitored and interventions promptly instituted to prevent further deterioration.

The length of ICU stay was higher in patients with AKI compared to those without. This may be attributed to the increased severity of illness and prolonged treatment required in those who develop AKI and sometimes other organ(s) dysfunction. Increased length of hospital stay among the critically ill is associated with increased the out-of-pocket health costs and further impoverishment of patients and their families.

The risk of death associated with AKI in the ICU is also high in LMIC and can be ascribed to late recognition, severity of illness and the limited resources available for the prompt management of the complication.[11,13,26] Furthermore, the presence of community and hospital acquired infectious diseases in developing nations contributes to this increase in patients' morbidity and mortality.[8,13,14,27,28] This study showed a mortality rate of 25.7% [8] to 61.5% [13] in patients with AKI compared to 6.8% [6] to 51.3% [18] in those without. Adelaja et al reported that the presence of AKI in critically ill patients resulted in poor outcome with a mortality rate of 65% compared to those without AKI, having a mortality rate of 35%.[13] These values were higher compared to what was reported in a larger multicenter study from China, with AKI patients having mortality rate of 27.7% and non -AKI patients having 6.8%.[15] Other studies had similar pattern, thereby confirming that AKI increases morbidity and mortality in critically ill patients.[18,19] However, the study conducted in Jordan showed an almost equivalent mortality rate between patients with (58%) and without AKI (51%). The reason for this observation is unclear but may be due to a generally severely ill cohort or inefficient ICU treatment protocols.

The limited number of articles reviewed may not adequately reflect the epidemiology of AKI in the ICUs of LMICs. However, the lack of national AKI registries in most of these countries makes the current study findings valuable.

CONCLUSION

This systematic review demonstrates that the burden of AKI in critically ill patients in developing countries is enormous. Having noted the methodological differences across studies, it is reasonable to conclude that the high incidence of AKI and its contributory factors are persistent in LMICs with the associated poor outcomes. The information provided in this study provides opportunities for promptly recognising high-risk patients and modifiable factors responsible for AKI in critically ill patients, thereby reducing the adverse outcomes. Relevant specialists should co-produce a simple AKI risk assessment tool to promptly identify at-risk patients and intervene.

More methodologically sound large prospective studies that would consider extensive potential risks factors are required from LMIC.

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