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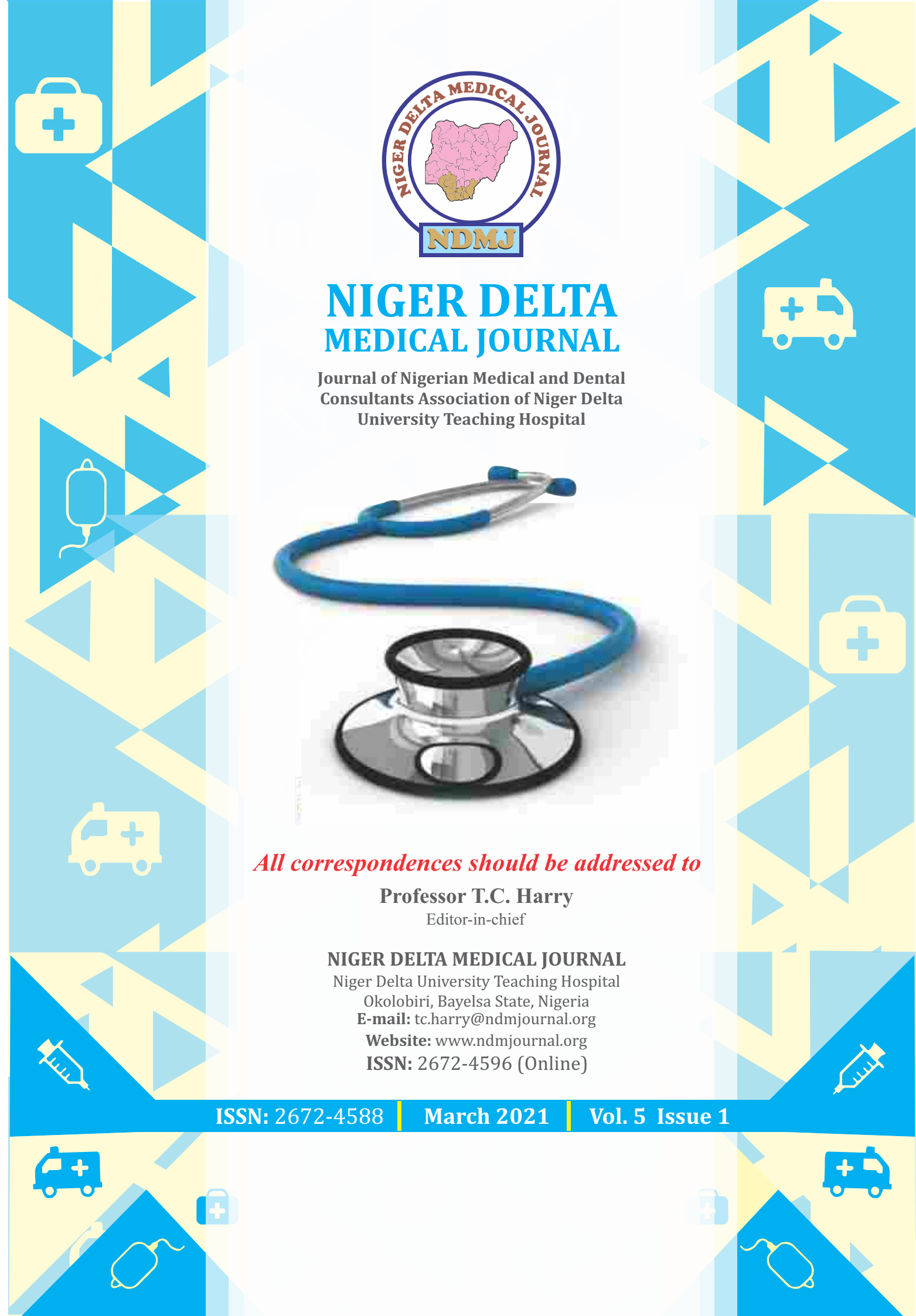
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EDITORIAL: TURNING THE CURVE

Tubonye C. Harry, FRCOG, FRCP, FWACS

Editor-in-Chief

*Niger Delta Medical Journal* 2021;5(1):5-6

Margaret Keenan, 90, made history by being the first recipient¹ of the Pfizer & BioNtec² (BNT162 (mRNA) Covid-19 vaccine in UK on the 8th December 2020 for protection against the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and this represented the massive roll out in UK to stymie the rampage of the Covid-19 pandemic. Sadly it came too late for some, including two colleagues whose tributes are in this issue.

In this issue, Dambo³ et al provide a commentary calling for review of nomenclature in antenatal service delivery.

The pathological variables in patients presenting with nasopharyngeal carcinoma in the tertiary centre in Ibadan, Nigeria is retrospectively reviewed by Foluke⁴ over a 10 year period with fascinating insights.

Pughikumo et al⁵ explores MTHFR gene mutation, the C677T variant in our local pregnant women in Bayelsa State, Nigeria with interesting findings.

Covid-19 vaccine is still unavailable in Nigeria at the time of going to press. Ballah et al⁶ report of their innovative low tech approach in providing care in a tertiary centre in Bauchi State, Nigeria on patients infected with Covid-19.

In this issue we have tributes to two outstanding clinicians⁷⁻¹⁰, late Professor D.J.

O'Donohue and Professor A.O.U. Okpani who sadly died of complications of Covid-19, whose life and times have impacted on healthcare delivery in the Niger Delta region of Nigeria.

References:

1. Mahase E. How was the first covid vaccine approved? How will it be rolled out, and who will get it? *BMJ* 2020, **371**:m4759;3-9
2. Wu SC. Progress and Concept for COVID-19 Vaccine Development. *Biotechnol J* 2020;**15**(6):1-2.
3. Dambo N.D, Aigere EOS, Jeremiah I. Commentary: Antenatal booking status: Is it time for a review of nomenclature? *Nig Del Med J* 2021;**5** (1): 7 - 10
4. Foluke OS Clinico-pathological pattern of nasopharyngeal carcinoma presentation at the radiation oncology clinic, University College Hospital, Ibadan: a 10-year retrospective review. *Nig Del Med J* 2021;**5** (1): 11 - 22
5. Pughikumo DT, Pughikumo CO, Alade T. The distribution of the methylenetetrahydrofolate reductase (mthfr) gene, c677t substitution amongst an indigenous population of pregnant subjects in Bayelsa State, Nigeria *Nig Del Med J* 2021;**5** (1): 23 - 28
6. Ballah A, Yusuf BJ, Ibrahim AS, Dunga J, Zuwaira H, Maigari I. High flow nasal

- oxygen therapy in Covid-19 patients; our experience in a low resource setting. *Nig Del Med J* 2021; **5** (1): 29 - 33.
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10. John CT. Tribute Prof AOU Okpani. *Nig Del Med J* 2021; **5** (1): 39.

COMMENTARY

ANTENATAL BOOKING STATUS: IS IT TIME FOR A REVIEW OF NOMENCLATURE?

Dambo N.D¹, Aigere EOS², Jeremiah I³

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The role of antenatal care in improving maternal and fetal outcomes has been demonstrated as it affords the opportunity for the risk status of the patient to be determined and adequate preparations made to mitigate identified risks¹. This role in improving foetal and maternal outcomes is highlighted by the latest position of the World Health Organisation (WHO) which recommends eight, as the minimum number of visits provided by a skilled birth attendant during the antenatal period as against four which was previously recommended by the organisation².

Risks identified prior to pregnancy or during the antenatal period determine the class of facility (primary, secondary or tertiary) and the cadre of the skilled birth attendant who should provide care^{1,3}. A minimum of four antenatal visits attended by a pregnant woman has been used as marker of quality of the antenatal care provided but there is evidence to suggest that the services offered during the course of each visit may be a better marker of antenatal care⁴. Factors such as the cadre of personnel providing care, presence of a care plan (nutrient supplementation, routine investigations, number and timing of visits, access to a multi-disciplinary team) and the facility where care is provided are known to influence the outcome of a

pregnancy⁵. These factors are often simplified and referred to as the booking status of the antenatal client. From hospital-based studies, several authors^{6,9} in Nigeria have defined an unbooked patient as a woman who did not receive hospital care during pregnancy. Some qualify booking status based on whether the antenatal care is delivered by trained personnel⁸ or not, while others qualify the booking status based on cadre of the health facility that provided the pregnant woman with antenatal care and the number of antenatal visits the woman had⁹. These definitions are imprecise as they do not go further to specify who qualifies as a trained personnel regarding the delivery of antenatal care and also do not define the minimum criteria a hospital must have for a woman who receives care to be regarded as a booked patient. Using the criteria provided, women who received care in private hospitals, licensed hospitals owned by faith based organisations primary health care centres and facilities where care is led by registered by midwives would have been classified as unbooked alongside women who had no antenatal care or those who were cared for by a traditional birth attendant. This is particularly important because from observations in some Nigerian tertiary hospitals, patients who receive care elsewhere and

are referred (properly or otherwise) to the aforementioned hospitals are usually categorized as unbooked patients, while some hospitals classify them as 'booked elsewhere'. Either way, this places these patients at a disadvantage when compared to the 'booked patients'. There is evidence to show that women classified as unbooked may pay higher fees, have a longer waiting time, and have a higher risk of poor obstetric outcomes⁶⁻¹⁰.

The health care landscape in Nigeria has changed tremendously in terms of policy, equipment, and personnel. Regarding policy, the Ministry of health has with the support of the WHO and other partner agencies, developed a task shifting and task sharing (TSTS) policy and many states of the federation are in the process of adopting it. A task shifting policy is one of the strategies geared at improving access to health care for many people and communities who are currently underserved¹¹. As regards maternal health, an implementation of this policy will lead to lower cadre health workers such as community health extension workers being trained to provide reproductive health services where the risk of morbidity and mortality is considered to be low¹². Also of importance in the policy section is the introduction of the Basic Health Care Provision Fund (BHCPF) which provides financial access to a minimum level of packages (including maternal health services) at the primary health care level as well as improved infrastructure for primary health care centres¹³. The TSTS policy and the BHCPF put together serve to mitigate the problem of access to healthcare as they reduce the manpower deficit and reduce the financial and infrastructural barrier to accessing healthcare.

An increase in the number of qualified specialist obstetricians and the awarding of the membership position after the part 1 exams in the Faculty of Obstetrics and Gynaecology in the West African College of Surgeons has translated to increased availability of specialist care outside the tertiary hospital settings¹⁴. While tertiary centres still take the lead in terms of research and training of personnel, some private facilities and secondary health centres are able to provide maternal care to a level that matches what is obtained at the tertiary level. This does not solve the challenge of specialist care being domiciled mainly in the urban areas with

the rural areas suffering a deficit. The Voluntary Obstetrician Scheme (VOS) as put forward by the Society of Gynaecologists and Obstetricians in Nigeria (SOGON) in July 2016, demonstrated that it can provide specialist care to rural settings¹⁵. If funded and expanded, the VOS can in the long term tackle this challenge.

With the identified changes in policy and personnel as regarding maternal care, it may no longer suffice to classify a patient as either booked or unbooked as this simple classification does not speak to the quality of care a woman has received during the antenatal period. Maternal care in the UK may be based in the hospital or in the community. The risk level determines if care is provided by a midwife, general practitioner (GP) or specialist obstetrician¹⁶. The Nigeria Demographic Health Survey of 2018 (NDHS 2018)¹⁷ shows that women living in urban areas had a higher chance of receiving antenatal care from a skilled birth attendant than those living in a rural area (83.6% vs 56.1%). These women are denied access to quality antenatal care by a myriad of factors including health worker shortages and the absence of health care facilities. The *Abiye* maternal health program in Ondo state, Nigeria has provided evidence that increasing access to quality maternal health services has a role in reducing maternal morbidity and mortality¹⁸. Task shifting as a strategy for increasing access to quality health care was used in the *Abiye* program. With a deficit in the human resource for health, the role of community health workers in improving access to antenatal services has been investigated.

In a study from Jigawa State, Nigeria the use of community health extension workers to provide antenatal services led to 11.9 - 21.3% of pregnant women receiving care after a one-year period of study as against a baseline of < 1-6%. In the community used as a control group, antenatal service coverage remained at 3% of the pregnant population¹⁹.

In a study conducted in Tanzania, community health workers were able to reduce the average time to booking for antenatal care over a sixteen month period from 22 weeks to 16 weeks ($p < 0.0001$) thus allowing PMTCT services and other antenatal interventions to be delivered at an earlier gestational age²⁰.

There is evidence from around the developing economies that community health workers with more than three months pre-service training are able to provide antenatal care in the communities they serve. Being situated in the facilities with regular forays into the community allows them to identify women in need of reproductive health services and then bring these women into the formal healthcare network where basic care can be provided and referral services also provided when deemed to be necessary thus leading to improved maternal care^{21,22}.

To recognize the access to reproductive health services provided by these frontline health care workers who serve in rural areas and provide an entry point for women into the formal healthcare network and away from the road leading to maternal morbidity and mortality, a change in nomenclature as regards the antenatal booking status of a pregnant woman may be necessary.

Perhaps stating the level of care (Consultant obstetrician, specialist registrar, family physician, medical officer, midwife, CHEW, no care) received during the antenatal period and the place of care (private hospital, primary health facility, secondary health facility, tertiary health facility) with regulatory guidelines clearly stating the extent of care that can be provided at each level/cadre may lead to better stratification of antenatal clients especially when they are referred from one facility to another and help to provide personalized care. While changing the nomenclature does not equate to improved care, it removes the barrier of being classified as 'unbooked' and helps to improve access to the same level of care given to 'booked' patients. Alongside this, the provision of more accredited facilities and staff, and a change in culture of the care givers will go a long way to improve maternal outcomes.

In conclusion, the present system of categorizing care received during the antenatal period excludes a large percentage of pregnant women from receiving quality care at the time of delivery and repudiates the care provided by lower cadre frontline health workers. Changing the nomenclature opens the door dialogue that can increase access to

antenatal care and reduce adverse obstetric outcomes.

REFERENCES

1. Yeoh PL, Hornetz K, Dahlui M. Antenatal Care Utilisation and Content between Low-Risk and High-Risk Pregnant Women. *PLoS One*. 2016;11(3):e0152167. Published 2016 Mar 24. doi:10.1371/journal.pone.0152167
2. World Health Organization. WHO recommendations on antenatal care for a positive pregnancy experience. Geneva, Switzerland, 2016 [<http://apps.who.int/iris/bitstream/10665/250796/1/9789241549912-eng.pdf?ua=1>] Accessed 18th September 2020.
3. Singh, S., Doyle, P., Campbell, O.M.R. *et al*. Management and referral for high-risk conditions and complications during the antenatal period: knowledge, practice and attitude survey of providers in rural public healthcare in two states of India. *Reprod Health* **16**, 100 (2019). <https://doi.org/10.1186/s12978-019-0765-y>
4. Hodgins S, D'Agostino A. The quality-coverage gap in antenatal care: toward better measurement of effective coverage. *Glob Health Sci Pract*. 2014;2(2):173–181. Published 2014 Apr 8. doi:10.9745/GHSP-D-13-00176.
5. Gudayu TW, Araya BM. Outcomes among Mothers Who Gave Birth in the Health Facility: Does Birth Preparedness and Complication Readiness Have a Role? *Obstet Gynecol Int*. 2019;2019:5147853.
6. Ogu RN, Alegbeleye JO. Improving maternal health: Women's attitude to antenatal care utilization is crucial. *Clin Obstet Gynecol Reprod Med* 2018;4 doi:10.15761/COGRM.1000209
7. Iklaki CU, Inaku JU, Ekabua JE, Ekanem EI, Udo AE. Perinatal outcome in unbooked teenage pregnancies in the

- University of Calabar teaching hospital, Calabar, Nigeria. *ISRN Obstet Gynecol*. 2012; 2(4):246-983. doi:10.5402/2012/246983
8. Osungbade KO, Ayinde OO. Maternal complication prevention: evidence from a case-control study in southwest Nigeria. *Afr J Prim Health Care Fam Med*. 2014;6(1):E1-E7. Published 2014 Dec 12. doi:10.4102/phcfm.v6i1.656
 9. Owolabi AT, Fatusi AO, Kuti O, Adeyemi A, Faturoti SO, Obiajuwa PO. Maternal complications and perinatal outcomes in booked and unbooked Nigerian mothers. *Singapore Med J* 2008; 49(7) : 526
 10. Okonofua F, Imosemi D, Igboin B, Adeyemi A, Chibuko C, Idowu A, et al. (2017) Maternal death review and outcomes: An assessment in Lagos State, Nigeria. *PLoS ONE* 12(12): e0188392. <https://doi.org/10.1371/journal.pone.0188392>
 11. Deller B, Tripathi V, Stender S, et al. Task shifting in maternal and newborn health care: key components from policy to implementation. *Int J Gynaecol Obstet*. 2015;130:S25-S31. doi:10.1016/j.ijgo.2015.03.005
 12. Task Shifting and Task Sharing policy for essential health care services in Nigeria. Federal Ministry of Health. Abuja, Nigeria. August 2014. <https://advancefamilyplanning.org/sites/default/files/resources/Nigeria%20task%20shifting%20policy-Aug2014%20REVISED%20CLEAN%20Approved%20October%202014.pdf> (Accessed 3 January 2020)
 13. Uzochukwu, B., Onwujekwe, E., Mbachu, C. et al. *Int J Equity Health*. 2018;17:100. <https://doi.org/10.1186/s12939-018-0807-z>
 14. Omigbodun A. The membership certification of the West African College of Surgeons and its relevance to the needs of the West African sub-region. *J West Afr Coll Surg*. 2012;2(3):83-87.
 15. Fasubaa OB. Primary health care and voluntary obstetricians scheme in Nigeria: For impact and change. *Trop J Obstet Gynaecol* 2016;33:133-4
 16. Standards for Maternity Care – RCOG. 2008. <https://www.rcog.org.uk/globalassets/documents/guidelines/wprmaternitystandards2008.pdf>. Accessed February 4, 2020.
 17. National Population Commission (NPC) [Nigeria] and ICF. 2019. Nigeria Demographic and Health Survey 2018 Key Indicators Report. Abuja, Nigeria, and Rockville, Maryland, USA: NPC and ICF.
 18. Mimiko O. Experiences with Universal Health Coverage of Maternal Health Care in Ondo State, Nigeria, 2009 - 2017. *Afr J Reprod Health*. September 2017; 21(3):9-16
 19. Uzundu CA, Doctor HV, Findley SE, Afenyadu GY, Ager A. Female health workers at the doorstep: a pilot of community-based maternal, newborn, and child health service delivery in northern Nigeria. *Glob Health Sci Pract*. 2015;3(1):97-108. Published 2015 Mar 5. doi:10.9745/GHSP-D-14-00117
 20. Lema IA, Sando D, Magesa L, et al. Community health workers to improve antenatal care and PMTCT uptake in Dar es Salaam, Tanzania: a quantitative performance evaluation. *J Acquir Immune Defic Syndr*. 2014;67 Suppl 4(Suppl 4):S195-S201. doi:10.1097/QAI.0000000000000371
 21. Lassi ZS, Das JK, Salam RA, Bhutta ZA. Evidence from community level inputs to improve quality of care for maternal and newborn health: interventions and findings. *Reprod Health*. 2014;11 Suppl 2(Suppl 2):S2. doi:10.1186/1742-4755-11-S2-S2
 22. Olaniran A, Madaj B, Bar-Zev S, et al. The roles of community health workers who provide maternal and newborn health services: case studies from Africa and Asia. *BMJ Global Health* 2019;4:e001388.

Original Article.
**CLINICO-PATHOLOGICAL PATTERN OF NASOPHARYNGEAL
CARCINOMA PRESENTATION AT THE RADIATION ONCOLOGY
CLINIC, UNIVERSITY COLLEGE HOSPITAL, IBADAN:
A 10-YEAR RETROSPECTIVE REVIEW**

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ABSTRACT

Background

Nasopharyngeal cancer (NPC) represents the most common head and neck malignancy in most Nigerian centers. Although it is uncommon among all cancers, it has high significant morbidity and mortality associated with it.

Objective

This review aimed to document and evaluate the clinical presentation pattern and histological types, treatment and outcomes of patients diagnosed with NPC at the Radiation Oncology clinic, University College Hospital Ibadan, Nigeria.

Materials and Methods

A descriptive retrospective study of all patients who were histologically diagnosed with NPC and treated from 2001 to 2010. A proforma was used to extract patient data such as sociodemographic characteristics, clinical characteristics at presentation, histological diagnosis, treatment regimen and treatment outcome. The statistical analysis was carried out using SPSS v23.

Results

A total of 211 cases of NPC was analyzed during the study period. Majority, 150 (71.1%) were male and the modal age group was 21-30 years. A continuous increase in the number of NPC cases was observed through the years, with a significant increment in the number of cases in 2010 (38 [18.0%]). Most, 131 (62.1%) of the patients consumed smoked/salted fish. The most common presenting symptom and sign was nasal blockage in 175 (82.9%) and cervical lymphadenopathy in 207 (98.1%) respectively. WHO-3 was the most prevalent histological type in 154 (73%). Majority 178 (84.4%) of the patients had concurrent chemo-radiation therapy and 187 (88.6%) of all patients were treated with radical radiotherapy at presentation. The number of patients with symptom free interval (SFI) within two years of radical treatment was 75 (40.1%).

Conclusion

The duration of illness before presentation was quite poor in this study with a duration of as long as 33 months was recorded. There is an obvious need for a more active and robust awareness campaign for NPC and cancers generally both locally and nationally.

KEYWORDS: Nasopharyngeal, Clinico-pathological, Carcinoma, Cervical lymphadenopathy, Radiation-therapy.

INTRODUCTION

Globally, nasopharyngeal cancer (NPC) is the 24th most common malignancy, accounting for 0.7% of the global cancer burden as reported in 2011.¹ Though it is known as a fairly rare cancer, it has a high mortality rate with about 50,000 deaths out of 80,000 cases annually.² Nasopharyngeal carcinoma is the most common type of head and neck cancer, and it has been shown to have distinctive racial, ethnic and geographical predisposition.³ This behaviors explains its rare incidence in the USA (0.7/100,000 per year)⁴, but more common occurrence in Southern China with incidence rate of 50/100,000, Southeast Asia 6.2/100,000 inhabitants respectively⁵, as well as in the Middle East (5.4/100,000) and North African countries (5.1/100,000).⁶ Reports from cancer registries in Nigeria, both the Ilorin Cancer Register and the Ibadan Cancer Register put NPC at 2% of the total cancers reported January 2001 and December 2010.^{3,7} The Ilorin study reported a total of 30 patients with NPC over the ten-year study period with a male to female ratio of 2:1.⁷ On the other hand, the Ibadan study which covered a 20-year review period reported 586 cases of NPC in males and 288 in females.³ A nine-year cohort study reported 75 cases of NPC in Lagos state (male to female ratio 1.7:1) which constituted 1.1% of the total cancer cases recorded during the study period.⁸

Undifferentiated squamous cell carcinoma (WHO type-3) is overwhelmingly the most frequent histologic type and it has been strongly associated with Epstein-Barr virus infection, which is present in over 90% of cases

of NPC.⁹ Epstein Barr Virus (EBV) is considered a critical step in the progression of NPC from normal nasopharyngeal epithelial cells to precancerous lesions, although only a fraction of the EBV-infected population go on to develop NPC.¹ This virus is ubiquitous globally, hence additional factors like genetic and environmental factors must be involved to explain the striking global variation of NPC.¹⁰ Many studies have reported increased risks of NPC associated with certain foods eaten within high-risk areas including salted fish and certain preserved foods and hot spices, all of which are high in nitroso compounds and volatile nitrosamines.¹

Misdiagnosis of NPC in its early stage is highly possible due to its relatively uncommon nature in this environment and its non-specific signs.⁴ Some of these early presentations are usually that of epistaxis, nasal obstruction, nasal discharge and serious otitis media.⁵ In more advanced cases, presentation includes difficulty in breathing, cervical lymphadenopathy, and cranial nerve involvement. Most NPC patients usually present in advanced stages of disease and by virtue of the anatomical location of this tumor, curative surgical resection may not be achievable.⁶ However, NPC is highly radiosensitive and external beam radiotherapy has been the mainstay of primary treatment even in cases with nodal metastasis.⁶ Majority of studies have investigated the efficacy of Intensity-Modulated Radiation Therapy (IMRT) in the treatment of NPC. Sheng-Fa Su et

al investigated the outcomes of patients treated with IMRT alone and a combination of chemotherapy and IMRT. They reported that the 5-year overall survival (OS), local relapse-free survival (LRFS), and distant metastases-free survival (DMFS) were respectively high (83.0%, 90.4% and 84.0%), with treatment failure rate low among early disease group as compared to advance locoregional group which had the highest incidence of relapse and death. They concluded that IMRT alone and IMRT in combination with chemotherapy provided no significant benefit to locoregionally advanced NPC.¹¹

In a study in Taiwan, the 1-year overall survival rates were 25%, 36% and 48% for patients with no treatment, chemotherapy and radiotherapy, respectively.⁽¹²⁾ The researchers concluded that radiotherapy to the primary tumor sites could be considered for patients with stage IVC NPC and that a combination of radiotherapy and chemotherapy might have potential survival benefits.^{12,13} In Nigeria, Aliyu et al reported a median survival time of 22 months and an overall disease-free survival rates of 67% and 46% at 12 and 24 months respectively; with longer survival rates experienced by patients who presented at stage I.¹⁴ Notable among prognostic factors that dictate treatment outcome is the histological type, age of patient at diagnosis and treatment modality.^{12,15} Also, the diagnosis of NPC requires a good knowledge of the clinico-pathological pattern of the disease and a high index of suspicion, especially at the early stage. This study aimed to review the pattern of clinical presentation and histological types of NPC as seen over a ten-year period (2001-2010) at the Radiation Oncology Clinic, University College Hospital Ibadan.

PATIENTS AND METHODS

This was a retrospective review of all cancer patients who were histologically diagnosed

with nasopharyngeal carcinoma and treated at the Radiation Oncology clinic of the University College Hospital, Ibadan between January 1st 2001 and December 31st 2010. A proforma was used to extract patient data such as sociodemographic characteristics, clinical characteristics at presentation, histological diagnosis, treatment regimen and treatment outcome. Cases without histological diagnosis and treatment reports were excluded from the study. Descriptive statistics such as frequency, proportion, mean and standard deviation was carried out. Discrete data was summarized using mean and standard deviation while categorical variables were summarized using frequency and proportions. The statistical analysis was carried out using SPSS v23. Ethical clearance to conduct the study was obtained from the Joint Ethical Review Committee of the University of Ibadan/University College Hospital (UCH), Ibadan.

RESULTS

Figure 1 presents the trend of NPC cases between January 2001 and December 2010, it was observed that as the years progressed, the facility experienced an exponential increase in the number of NPC cases being managed; the number cases managed in 2010 (38 [18.0%]) was found to be more than four-times those managed in 2001 (9 [4.27%]). The geographical spread from our study showed that 69 (32.7%) of the patients were from the South-Southern part of the country, 66 (31.3%) South-East, 48 (22.7%) South-West, while 4 (1.9%) were from the North-East (Figure 2).

The socio-demographic characteristics of the patients is presented in table 1, it was observed that majority of the patients 51 (24.2%) were between 21-30 years, about twenty-three percent 48 (22.8%) were between 41-50 years. The average age of patients during the period under review was 40.8 ± 15.7 years. Most of the patients were males 150 (71.1%), married 149 (70.6%), have attained tertiary education 114

(54.0%) were employed 164 (77.7%) and identified with the Igbo 66 (31.3%) Yoruba 48 (22.7%) and others 69 (32.7%) ethnic groups respectively.

Table 2 shows the social characteristics of the patients. Consumption of smoked/salted fish 131 (62.1%) was highly prevalent among the patients, similarly, result of alcohol and smoking pattern shows that 20 (9.5%) consumed alcohol alone, 6 (2.8%) smoking alone while 27 (12.8%) participated in both smoking and alcohol consumption. Figure 3 below shows a multiple bar chart of gender frequency by age group at presentation. At all age group, NPC was more prevalent among all age groups especially among patients between the ages of 41-50years. The result shows that majority of the patients presented more than 12months 129 (61.1%) after onset of illness (figure 4).

Based on the WHO classification, Type III (undifferentiated carcinoma) was the commonest histopathological variant reported in 154 (73.0%) of studied patients and this was followed by differentiated non keratinized squamous cell carcinoma accounting for 45 (21.3%) of cases, while the least variant was well differentiated non keratinizing squamous cell carcinoma seen in 12 (5.7%) of patients (Table 3). Figure 5 shows signs and symptoms of patients at presentation. Cervical lymphadenopathy was the commonest sign (98.1%) followed by rhinorrhea (76.3%) and the least clinical sign at presentation was proptosis (4.7%). Similarly, the commonest clinically diagnosed symptom at presentation was nasal blockage (82.9%) followed by epistaxis (28%), headache (20.4%), Dysphagia (20.4%) while sore throat (6.2%) was the least diagnosed symptom at presentation. Metastasis was present in 21 (10%) patients at presentation. The commonest site was bone metastasis in 12

(57.1) patients (Figure 6).

Figure 7: shows the treatment regimen received by NPC patients. Majority of the patients had concurrent chemo-radiation therapy 178 (84.4%) and some had neo-adjuvant chemotherapy before radiation therapy 33 (15.6%). Few of the cases received palliative radiotherapy 24 (11.4%), while a total of 187 patients (representing 88.6% of all patients) were treated with radical radiotherapy at presentation. Table 4 depicts the treatment outcome; the number of patients with symptom free interval (SFI) within two years of radical treatment was 75 (40.1%) and loco-regional recurrence was 61 (32.6%) out of the 187 patients. Meanwhile, loco-regional recurrence at two year follow up showed increase in prevalence with respect to clinical stage of NPC at presentation (3 (16.7%) in stage II to 22 (44.0%) stage IVA&B). Also, distant metastasis was more prevalent in stage III and IVA&B 8 (6.7%) and 9 (18.0%) respectively.

DISCUSSION

Nasopharyngeal carcinoma, a relatively uncommon cancer² poses a diagnostic challenge due to its clinical features at presentation that may be indistinguishable with other causes of sore throat, nasal blockage and ear infection. In view of this, this study was carried out as a retrospective review of the clinico-pathological presentation of NPC in order to raise the index of suspicion when such clinical features are encountered.

During the period under review, the number of patients with NPC managed in the facility increased annually. This average steady increase was in corroboration with previous cohort study (2004-2008) in the same setting³. Similarly, a study in Indonesia showed a relatively steady rise in NPC cases from 1996-2005 (5). Conversely, a decrement in NPC rate

was reported in USA¹⁶. The increase in annual number of cases in this study may be a real increase as a result of increasing incidence of NPC in Nigeria. It could also be as a result of increasing awareness among referring medical practitioners, thus resulting in more referrals for specialist treatment.

There was a male preponderance of NPC in study and this is slightly more than in some Nigerian studies, like Omoseebi et al in Lagos⁸ and Okwor et al in Ibadan.¹³ On the other hand, this is slightly less than the ratio reported in endemic areas.⁵ The age of patients with NPC ranged from 15-70years with the highest peak in the third (21-30years) and fifth decade (41-50years) of life for both males and females and in agreement with a previous study in Nigeria¹⁷ and indonesia.⁵

Similar to other studies in Nigeria and other endemic areas consumption of smoked-salted fish, smoking and use of alcohol were the major identifiable risk factors.^{6,7} However, self-reporting of smoking or alcohol consumption alone appeared to be low. The study by Abraham *et al*⁶ had about half of their patients reporting alcohol consumption as against slightly below a quarter in our study. The low incidence of cigarette smoking in our study as compared to Alabi *et al* with 23.3% in their study⁷ may be as a result of all other forms of tobacco consumption were not explored in detail during history taking because chewing of tobacco and kola nut is not uncommon. Findings from this study shares with those found in Tanzanian patients, this may be due to similarities in geographical distribution of the shared aetiological risk factors for NPC.

The geographical spread from our study showed that 86.7% of the patients were from the southern part of the country and only 13.3% is from the north. This large disparity may be

due to the location of the facility itself with resultant distance constraints to the patients from the northern part and the fact that there are also two functioning radiotherapy centers in the north for NPC treatment (Abuja and Zaria). Southern Nigeria has an endemic Burkitt's lymphoma incidence owing to EBV infection¹⁸ and our study revealed high incidence of type III NPC. Though, previous studies^{1,9} have reported the relationship of EBV and especially type III NPC, we may not be able to extrapolate it to our study since EBV was not specifically evaluated for.

We also observed poor time to presentation as majority of the patients presented after one year of illness. This general late presentation of patients in this study is in contrast to what is obtainable in developed and endemic regions of the world where presentation is at an average of two months.¹⁵ This late presentation may be attributed to poverty, ignorance, use of alternative, and traditional medications, delayed referral and low index of suspicion from general practitioners. Healthcare in Nigeria presently is mostly paid out of pocket even though there is a National Health Insurance Scheme in operation. It is also possible that most of the patients may not have easy access to information and thus seek healthcare late.

The histologic pattern of NPC in this study is typically what is found in the literature^{5,19}, especially in endemic regions where type III is by far the most common. In regions where type III is the most common, Epstein Barr virus (EBV) infection has been implicated as a risk factor.^{16,20} In our study EBV antibody titre was not determined, but it has been reported that in developing countries transmission is mainly through the saliva and occurs very early in life because of crowded living

conditions and low hygiene standards.²¹ Reports of Burkitt's lymphoma endemicity in the southern part of Nigeria also strongly suggest the possibility of high infection rate of EBV.¹⁸ This is because the southern part of Nigeria falls within the lymphoma belt of equatorial Africa and as such a very high incidence rate of EBV infection has been reported.²¹

Cervical lymphadenopathy was the most common and virtually a universal clinical feature, occurring in close to 100% of cases in this study. This is comparable with reports from literature in both endemic and non-endemic regions of NPC as the most common clinical features.^{21,6,8,22} Cervical lymph node involvement already shows a loco-regional spread, indicating that majority of presenting cases is already at the advanced stage. Nasal blockage, rhinorrhea and epistaxis were also common symptoms while proptosis was the least presenting clinical feature.

A study by Adewuyi SA et al in Zaria reported that 75.6% of their patients received neo-adjuvant or induction chemotherapy prior to the use of radiotherapy to downstage the disease in locally advanced disease.²³ They also stated that concomitant chemo-radiation was not used due to long waiting time on the radiotherapy machine and that chemotherapy followed by radiotherapy in sequence was the mode of treatment with these patients. The above study finding is contrary to the findings in our study where majority of the patients (84.4%) had concurrent chemo-radiation therapy. Only 33 (15.6%) patients had neo-adjuvant or induction chemotherapy (cisplatin and 5-fluorouracil (5FU) before radiotherapy and this is mainly for those with distant metastasis and very large loco-regional spread. However, the actual contribution of each treatment regimen was not quantifiable. This is because patients were found not to be consistent with chemotherapy schedule due to financial constraints, beliefs systems or even due to side effects like myelosuppression.

LIMITATIONS

- Follow up was a major challenge in this study, about half of the patients were lost to follow up during the period under review. Also,
- The non-standardization of data entry into the patient's case notes made data retrieval difficult.

CONCLUSION

The clinico-pathological pattern of NPC in our study, a non-endemic area was consistent with other studies in Nigeria and in endemic regions. There was an upward trajectory in the number NPC cases. Also, NPC is at high peak in 3rd and 5th decade of life and majority of the cases have poor timely presentation. Even though there are facilities for megavoltage radiotherapy and chemotherapy in Nigeria, the outlook for better treatment outcome is bleak. Therefore, it is expedient to conduct this type of study periodically to monitor the changes in NPC trend and pattern for quick intervention. Patients with persistent nasal symptoms should be encouraged to go for early evaluation to aid early detection and treatment, in order to reduce mortality and morbidity due to NPC. There is a need for further analytical studies to characterize NPC with respect to the actual presence and role of EBV in patients, and factors associated with development of NPC in Nigeria. Design of a standard patient history and assessment questionnaire for NPC patients will help in having more detailed information such as eliciting for cranial nerve syndromes. There is a need for a more active and robust awareness campaign for NPC and cancers generally both locally and nationally.

Conflicts of interest

There are no conflicts of interest.

Acknowledgment

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REFERENCES

1. Ahmedin Jemal, DVM P, Freddie Bray P, Melissa M. Center M JFM. *Global Cancer Statistics*. CA Cancer J Clin [Internet]. 2011;**49**(2):1,33-64.
2. Society AC. Cancer Facts & Figures 2015. Am Cancer Soc. 2015. p. 1-56.
3. Adisa AO, Adeyemi BF, Oluwasola AO, Kolude B, Akang EEU LJ. Clinico-pathological profile of head and neck malignancies at University College Hospital, Ibadan, Nigeria. *Head Face Med*. 2011;**7**(1):1-9.
4. Wang KH, Austin SA, Chen SH, Sonne DC GD. Nasopharyngeal Carcinoma Diagnostic Challenge in a Nonendemic Setting: Our Experience with 101 Patients. *Perm J*. 2017;**21**:1-5.
5. Adham M, Kurniawan AN, Muhtadi AI, Roezin A, Hermani B, Gondhowiardjo S et al. Nasopharyngeal carcinoma in Indonesia: Epidemiology, incidence, signs, and symptoms at presentation. *Chin J Cancer*. 2012;**31**(4):185-96.
6. Abraham ZS, Massawe ER, Ntunaguzi D, Kahinga AA, Yahaya JJ MS. Clinico-pathological profile of nasopharyngeal carcinoma at Muhimbili National Hospital, Dares Salaam, Tanzania. *Int J Otorhinolaryngol Head Neck Surg*. 2019;**5**(4):922-5.
7. Alabi BS, Badmos KB, Afolabi OA, Mo Buhari MO S-BS. Clinico-pathological pattern of nasopharyngeal carcinoma in Ilorin, Nigeria. *Niger J Clin Pr*. 2010;**13**(4):445-8.
8. Omoseebi O., Akinde OR., Banjo AF. BB. Histopathological Pattern of Nasopharyngeal Malignancy in Lagos University Teaching Hospital. *Int J Sci Eng Res*. 2015;**6**(5):1733.
9. Sani M. Mado IA, Umma IA, Robinson WD JF. Prevalence of malaria parasitaemia among febrile Nigerian children with severe malnutrition in Northwestern Nigeria. *Niger J Basic Clin Sci*. 2018;**15**(1):1-4.
10. Pan XB, Li L, Qu S, et al. The efficacy of chemotherapy in survival of stage II nasopharyngeal carcinoma. *Oral oncology* 2020;**101**:104520. doi: 10.1016/j.oraloncology.2019.104520
11. Su SF, Han F, Zhao C, Huang Y, Chen CY, Xiao WW, et al. Treatment Outcomes for different subgroups of nasopharyngeal carcinoma patients treated with intensity-modulated radiation therapy. *Chin J Cancer*. 2011;**30**(8):565-73.
12. Yeh S, Tang Y, Lui C, Huang E. Treatment Outcomes of Patients with AJCC Stage IVC Nasopharyngeal Carcinoma: Benefits of Primary Radiotherapy. 2006;**36**(181):132-6.
13. Okwor VC, Fagbamigbe AF FO. Survivorship of patients with head and neck cancer receiving care in a tertiary health facility in Nigeria. *Cancer Manag Res*. 2017;**9**:331-8.
14. Aliyu UM, Folasire AM, Ntekim AI. Treatment outcome of patients with nasopharyngeal carcinoma in Nigeria : An institutional experience. *Prec Radiat Oncol*. 2018;**2**:68-75.
15. Yee-Lin V, Pooi-Fong W S-BA. Nutlin-3, A p53-Mdm2 Antagonist for Nasopharyngeal Carcinoma Treatment. *Mini-Reviews Med Chem*. 2017;**18**(2):173-83.
16. Argirion I, Zarins KR, Ruterbusch JJ, Vatanasapt P, Sriplung H, Seymour EK et al. Increasing incidence of Epstein-Barr virus-related nasopharyngeal carcinoma in the United States. *Cancer*. 2020;**126**(1):121-30.
17. Ochicha O AA. Nasopharyngeal Cancer in Kano - A Histopathologic Review. *Niger J Basic Clin Sci*. 2019;**16**(1):38-41.

18. B. B. A review of the literature on childhood Burkitt lymphoma in Nigeria. *Niger J Paediatr.* 2018;**43**(1):1-7.
19. Wang Y, Zhang Y MS. Racial Differences in Nasopharyngeal Carcinoma in the United States. *Cancer Epidemiol.* 2014;**37**(6):1-15.
20. Tabuchi K, Nakayama M, Nishimura B, Hayashi K HA. Early Detection of Nasopharyngeal Carcinoma. *Int J Otolaryngol.* 2011;2011:638058
21. Hämmerl L, Colombet M, Rochford R, Ogwang DM PD. The burden of Burkitt lymphoma in Africa. *Infect Agent Cancer.* 2019;**14**(1):1-6.
22. Roy C, Choudhury KB BS. Basaloid squamous cell carcinoma of nasopharynx: An extremely rare variety of tumour of nasopharynx. *J Indian Med Assoc.* 2011;**109**(5):343-4.
23. B. B. A review of the literature on childhood Burkitt lymphoma in Nigeria. *Niger J P a e d .* 2 0 1 6 ; **4 3** (1) : 1 - 7 . 9712201820252933380102030402001200220032004200520062007200820092010**Numberofcas**
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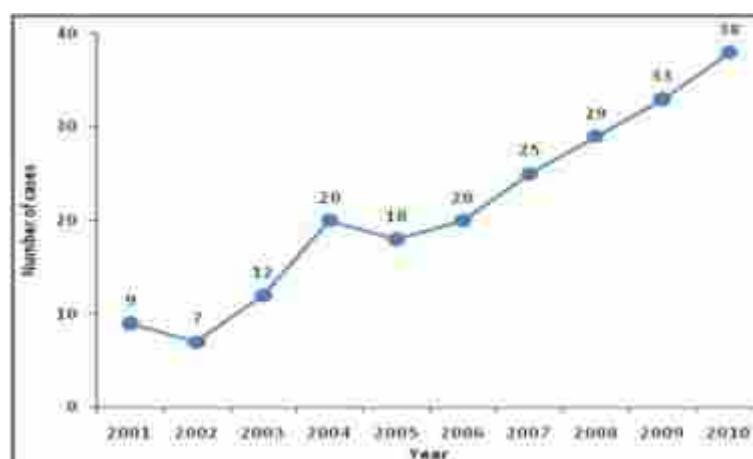


Figure 1: Trend of NPC cases over study period

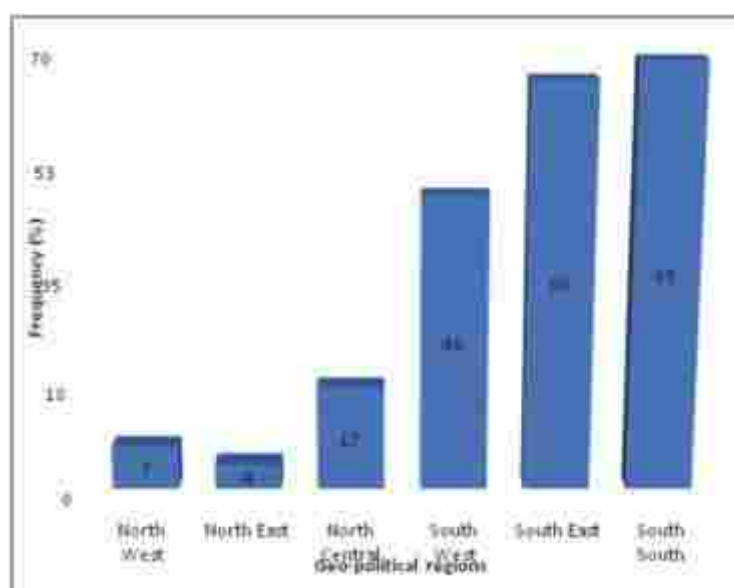


Figure 2: Distribution of presented patients by geo-political regions

Table 1: Socio-demographic characteristics of patients

Characteristics	Number of patients	Percentage (%)
Age group (years)		
11-20	17	8.1
21-30	51	24.2
31-40	33	15.6
41-50	48	22.8
51-60	41	19.4
61-70	19	9.0
>70	2	0.9
Gender		
Male	150	71.1
Female	61	28.9
Marital status		
Single	56	26.5
Married	149	70.6
Others	6	2.8
Level of education		
Secondary education	86	40.8
Tertiary	114	54.0
No formal education	11	5.2
Employment status		
Employed	164	77.7
Unemployed	47	22.3
Ethnicity		
Yoruba	48	22.7
Igbo	66	31.3
Hausa/Fulani	28	13.3

Table 2: Distribution of smoked/salted fish consumption and social habits in the patients with nasopharyngeal carcinoma

Characteristics	Frequency	Percentage (%)
Consumption of smoked/salted fish		
Yes	131	62.1
No	80	37.9
Social habit		
None	158	74.9
Use of Alcohol	20	9.5
Smoking	6	2.8
Smoking & use of alcohol	27	12.8

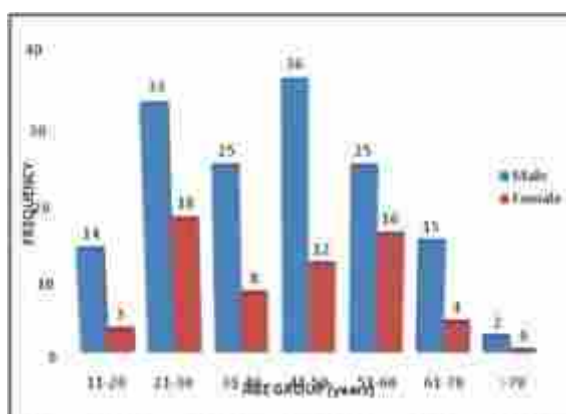


Figure 3: The distribution of the patients with nasopharyngeal carcinoma according to gender and age group at presentation

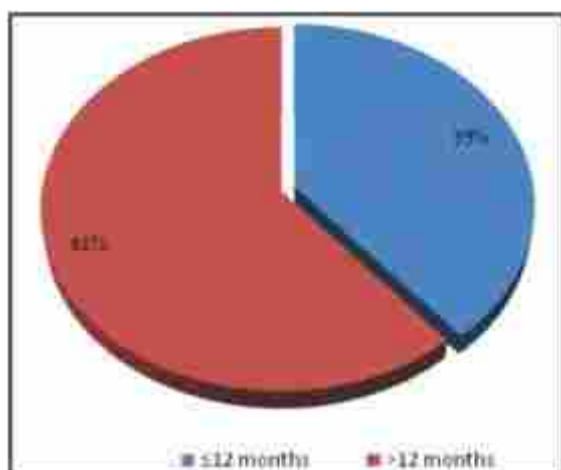


Figure 4: Duration of illness before presentation (months)

Table 3: WHO Histology Classification

WHO classification	Number of patients
WHO-Type I (Well differentiated non keratinizing squamous cell carcinoma)	12 (5.7%)
WHO-Type II (Non differentiated keratinized squamous cell carcinoma)	45 (21.3%)
WHO-Type III (Undifferentiated carcinoma)	154 (73.0%)

Figure 5 Distribution of signs and symptoms at presentation

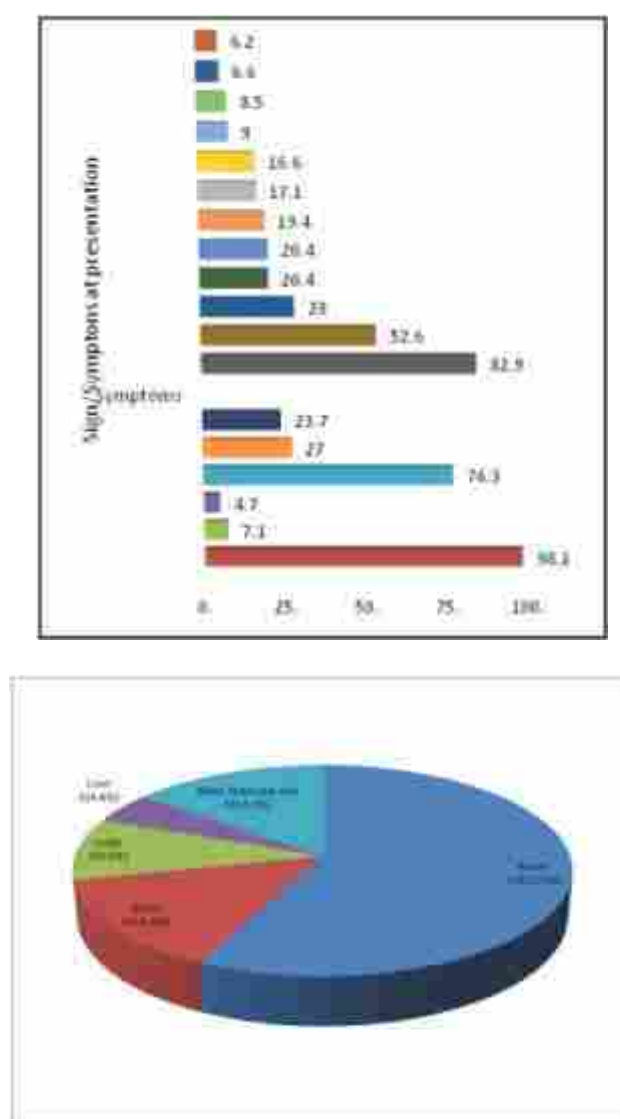


Figure 6: Pie chart showing the distribution metastatic site at presentation

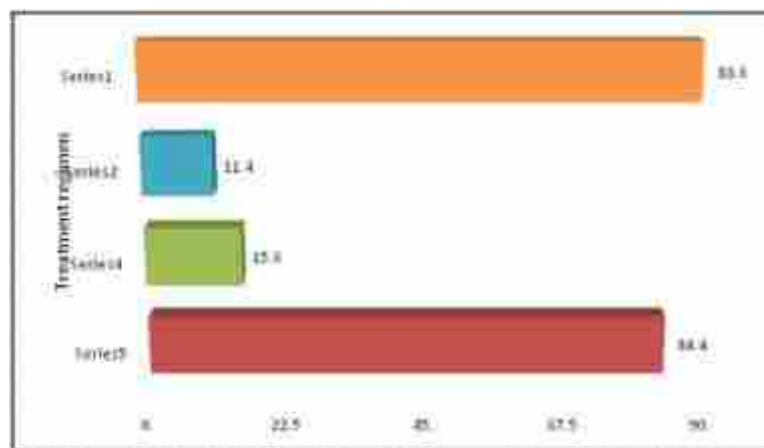


Figure 7: Treatment regimen received

Table 4: Two years treatment outcome in patients after receiving radical treatment for nasopharyngeal carcinoma (N= 187)

Clinical staging	Two (2) years SFI	Loco-regional recurrence	Distant metastasis	Total patients
I	-	-	-	-
II	10(55.6%)	3(16.7%)	5(27.8%)	18
III	53(44.5%)	36(30.3%)	8(6.7%)	119
IVA & B	12(24.0%)	22(44.0%)	9(18.0%)	50
IVC	-	-	-	-

SFI = symptom free interval

Original Article

THE DISTRIBUTION OF THE METHYLENETETRAHYDROFOLATE REDUCTASE (MTHFR) GENE, C677T SUBSTITUTION AMONGST AN INDIGENOUS POPULATION OF PREGNANT SUBECTS IN BAYELSA STATE, NIGERIA**Pughikumo Dibo Tabot¹, Pughikumo Crosdale Ogho², Alade Tolulope³**¹Department of Physiology, Faculty of Basic Medical Sciences,
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ABSTRACT

Background: It is established that race as well as geographical location has an impact on disease presentation and prevalence. There is a general paucity of data for indigenous black populations as regards the genetics of endothelial and thrombo-embolic disorders including pre-eclampsia.

Objective: The aim of this study is to determine the prevalence of the C677T polymorphism of the MTHFR gene, which has been implicated as a risk factor pre-eclampsia in an indigenous black population of pregnant women in Bayelsa state, Nigeria.

Methods: The genotypes of 124 randomly selected pregnant women were determined for the C677T polymorphism (C-T substitution) of the methylenetetrahydrofolate reductase (MTHFR) gene by DNA amplification using PCR-RFLP and the amplicon digested using HINF1 enzyme. The frequency of the substitutions was determined by counting the alleles from the observed genotypes and Chi-test used to determine the conformity of the genotype frequency distribution to Hardy-Weinberg proportion.

Results: The CC genotype was found in 116 subjects (93.5%) and CT genotype in 8 subjects (6.5%) No subject had the TT genotype (0%). Genotype frequencies of CC, CT and TT were thus 0.935, 0.065, and 0.000 respectively. The allele frequencies were C – 96.8%, T – 3.2% respectively.

Conclusion: The result showed a low prevalence of the C-T polymorphism of the MTHFR gene in an indigenous black population of pregnant women in Bayelsa State, Nigeria

KEYWORDS; MTHFR gene; C677T polymorphism; pre-eclampsia; pregnancy.

Introduction

The methylenetetrahydrofolate reductase enzyme is important in folate dependent homocysteine metabolism.¹ Epidemiological studies by Baushyet *al*² suggests that mild elevations of homocysteine are associated with endothelial dysfunction and thrombo-embolism including preeclampsia, neural tube defects, and psychiatric abnormalities. The MTHFR gene is a 20kb long gene having 11 exons and is mapped onto position 1p36.3. There are several polymorphisms but the most clinically relevant variants are the C677T (exon 4) and A1298C (exon 7) variants.³ The C677T variant is a result of a C-T substitution at nucleotide 677 which converts alanine to valine in the 222nd position.⁴ This substitution produces a thermolabile enzyme with reduced enzymatic activity. The deficiency is an autosomal recessive disorder and homozygous individuals (TT) are highly susceptible to hyper-homocysteinemia with lower levels of both red blood cell and plasma folate levels.^{5,6}

The incidence of this polymorphism has been shown to vary among ethnic populations with prevalence ranging from 7- 42%.^{1,7,8} Patients with 50% residual activity due to the thermolabile form of the reductase were first reported amongst 17% of 212 North American patients with coronary artery disease.³ Most previous studies have been conducted amongst blacks domiciled in temperate regions, especially African-Americans; reports on black Africans have been relatively scanty.^{1,7,8} In African-Americans, the mutation (polymorphism) was noted to have a very low prevalence and there were no homozygotes compared to Caucasians.⁹ This suggests that racial differences have a stronger contribution to the predisposition to the disease than geographical location. Thus the aim of this study is to determine the prevalence of the C677T polymorphism of the MTHFR gene in an indigenous black population of pregnant

women in Bayelsa state, Nigeria

Methodology

A total of 124 subjects were randomly selected from amongst women attending antenatal clinic at the Federal Medical Centre, Bayelsa State, Nigeria. Bayelsa state is a state in southern Nigeria with a predominantly Ijaw ethnic population. It is located in the Niger Delta region of Nigeria at Latitude (04° 15° North) (05° 23° South), Longitude 05° 22° West and 06°45° East.

Subjects were mainly from the Ijaw ethnic population and a few from the Ibo and Delta regions. Ethical approval was sought and obtained and informed consent was obtained from each subject. 5 ml of venous blood was collected from each subject into an EDTA bottle. The analysis was carried out in the molecular genetic laboratory of the Department of Medical Laboratory Sciences, Niger Delta University, Wilberforce Island, Bayelsa state.

DNA Extraction: DNA Extraction using DNA Miniprep extraction kit supplied by InqabaBiotech West Africa Limited. Pure DNA was stored at -20°C.

Genotyping: The extracted DNA was genotyped by polymerase chain reaction (PCR) and restriction fragment length polymorphism (RFLP) using the *Hinf*I enzyme by methods previously described by Frosst *et al* 1995³, using primers 5'-TGAAGGAGAAGGTGTCTGC GGA-3' and 5'-AGGACGGTGCGGTGAGA GAGTG-3'. PCR was done using 25µl volume. Initial denaturation was done at 94°C for 5min, followed by 35 cycles of denaturation at 94°C for 40s. The annealing temperature was at 58°C followed by an extension for 40s at 72°C and a final extension for 7min at 72°C and the genotypes were determined by the length of the PCR products digested with the *Hinf*I restriction enzyme.

Amplification and restriction products were analyzed using 2% agarose gel electrophoresis. Allele frequencies were calculated by counting genes from the observed genotypes.

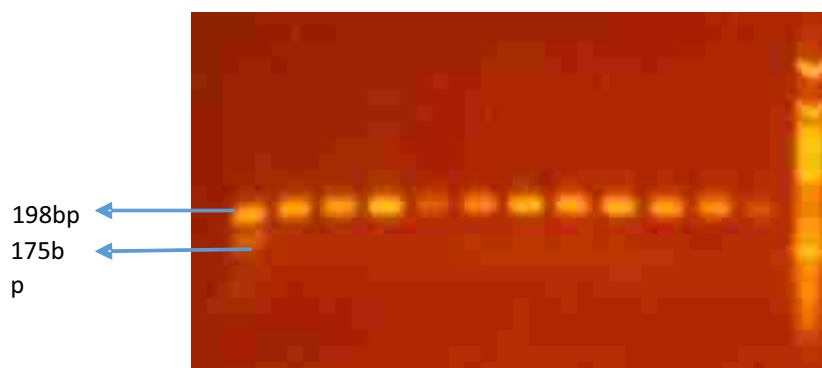


FIGURE 1: Showing RFLP analysis of the MTHFR PCR products with *HinfI* enzyme. Wild type homozygous remains uncut and gives 1 band and the heterozygous (CT) gives three bands, (198bp, 175bp, 23bp), 23bp was run-off the gel. Lane 1 shows the homozygous genotype (CC), Lane 2-12, shows the heterozygous (CT) genotypes

Results and Discussion

Table 1 shows the genotyping results for the C677T polymorphism. A total of 124 individuals were sampled and 116 of the subjects had the CC genotype (93.5%), 8 subjects had the CT genotype (6.5%) and none had the TT genotype (0%). Chi-test was used to assess how the genotype frequency conformed to Hardy Weinberg proportions. Genotype frequencies of CC, CT and TT were 0.935, 0.065 and 0.000 respectively. The frequency of the C-allele was found to be 0.977 and T-allele frequency was found to be 0.320. The result of the present study showed that the 677 CC homozygous genotype has the highest percentage, while the 677 TT genotype was absent in the entire sampled population. This is in agreement with findings from previous studies^{1, 3, 7, 9, 10} which showed a 0% in the TT genotype among African – Americans i.e. the mutation was absent in homozygous state. Our

study has shown a consistency in the distribution of gene frequency within an ethnic population i.e. the indigenous African and African American (TT-0%) despite difference in geographical location. The T-allele frequency of 0.32 in our study is within the range of 0.32-0.90 reported in previous studies on black Africans.⁹ The result of our study on the MTHFR gene polymorphism confirms the findings that African blacks have a very low prevalence of the C677T mutation^{1,7,9,10,11} Studies in Brazilian blacks showed a slightly higher prevalence of the mutant allele (12.0%)⁷ with 2% having the TT genotype. But this again would have been a result of the mixed genes of Brazilian blacks for which previous studies indicated up to 20-30% of Caucasian genes.⁷

Conclusion

This low prevalence of the mutant gene in Black Africans as compared to a higher frequencies in Caucasian, Asian and Indian population, (24% - 40%)⁷ agrees with previous suggestion that the mutation might have occurred outside Africa after the first split of the human population and this may serve as a focus for further research into the probable cause of the mutation which may be the consequences of a selective advantage or disadvantage outside or inside Africa.⁷

Contribution to knowledge

This research has been able to demonstrate a low prevalence of the C-T polymorphism of the MTHFR gene in an indigenous black pregnant population.

Table 1: MTHFR genotypes and allele Frequency distributions in the sampled population

	GENOTYPES			ALLELES	
	CC	CT	TT	C	T
Observed Number	116	8	0	240	8
Frequencies	0.935	0.064	0.000	0.977	0.032
Percentage	93.5%	6.4%	0.0%	96.8%	3.2%

Acknowledgment

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References

1. Boushey, C.J, Bereshfford, S.S.A, Pmenn, G.S, Motulsky, A.G. A quantitative assessment of plasma homocysteine as a risk factor for vascular diseases. *J.A.M.A.*, 1995;**274**:1049-1057.
2. Vamdan, R, Upandra, Y, Pradeep, Kumar. Prevalence of methylenetetrahydrofolate reductase C677T polymorphism in Eastern Uttar Pradesh. *Indian Jour. Hum. Gen*, 2012; 18-21
3. Frost, P, Blom, H.J, Miles, R, Goyette, P, Sheppard, C.A, Mathew, R.G. *et al.* A candidate genetic risk factor for vascular disease: a common mutation in methylenetetrahydrofolate reductase. *Nat Genet* 1995;**10**:111-15.
4. Zhongxia, G, Hoffman, B. S, Daniel, K, Jingwei, Yu. Prevalence of the C677T substitution of the methylenetetrahydrofolate reductase (MTHFR) gene in Wisconsin. *Genet. Med.* 2003; **5**:458-459.
5. Mikherjee, M, Joshi, S, Bagadi, S, Dalvi, M, Rao, A, Shetty, KR. A Low prevalence of the C667T mutation in the methylenetetrahydrofolate reductase gene in Asian Indians. *Clin. Gen* 2002; **61**:155-159.
6. Bortolini, M.C, Welmer, T.A, Franco, MHLP, Salzano, F.M, *et al.* Genetic studies in three South American black populations. *Gene Geog.* 1992; **6**:1-16.
7. Franco, R.T, Araujo, A.G, Guerreiro, J.F, Elion, J, Zago, M.A. Analysis of the 677 C-T mutation of the Methylenetetrahydrofolate Reductase Gene in different Ethnic groups. *ThrombHaemost* 1998; **79**:119-121.
8. Whitehead, As., Gallagher P., Mills, L, Kirke, PN., Burk, H., Molloy, Am *et al.* A genetic defect in 5-10 methylenetetrahydrofolate reductase in neural tube defects. *Q. Jour. Med.* 1995; **88**:763-766.
9. Setareh, T.E, Edward, A.C, Maire, A.C. Heterogeneity in the prevalence of methylenetetrahydrofolate reductase gene polymorphisms in ofolate reductase in African. Americans. *Thromb. Res*, 1996;**83**:195-198.

- women of different ethnic groups. *Diet. Assoc.* 2003; **103**:200-207.
10. Marie-Claude, B, Phillippe, D, Juan, R, Passa, P, Froguel, P.H, James, R.H., Letters to the editor: Differences in methylenetetrahydrofolate reductase genotype frequencies, between whites and blacks: Prevalence and parental origin of de novo 1.5 MB duplication in Charcot Marie-Tooth Disease Type 1A. *Am Jour. Hum. Genet.* 1997; **60**:229-30.
 11. Togozoghu, S.I, Alikasfoglou, M., A.E, Aytemir, K, Ozer, N, Ovunc k. *etal.* Methylenetetrahydrofolate reductase genotype and the risk and extent of coronary artery disease in a population with low plasma folate. *Heart.* 1991; **81**:518-522.
 12. Lori, Hill. Racial Differences in the Genetics of Preeclampsia, thesis and dissertation Virginia Commonwealth University. 2011.
 13. Zhang, J, Meikle, S, Thumbe, A. Severe maternal morbidity associated with hypertensive disorders in pregnancy in the United States. 2003; **22**: 203-212.
 14. Caughey, A.B, Stotland, N.E, Escobar, G.J. Maternal ethnicity and paternal ethnicity and parental ethnic discordance: predictors of preeclampsia. *Obstet Gynecol* 2005; **106**:156-161.
 15. Brown, H.L, Chireau, M.V, Jallah, Y, Howard, D. The "Hispanic Paradox" an investigation of racial disparity in pregnancy outcomes at a tertiary care medical center. *Am Jour. Obstet Gynecol* 2007; **197**: 197e191-92.
 16. Tanaka, M, Jaamcia., G, Kaiser, M., Hills, E, Soimet *al.* Racial Disparity in hypertensive disorders of pregnancy in New York state: a 10-year longitudinal population – based study. *Am Jour. Public Health* 2007; **97**:163-170.
 17. Thelma, E., Patrick, Robert, W., Powers, A., R., Daftary *et al.* Homocysteine and folic acid is inversely related in black women and preeclampsia. *Hypert.* 2004; **43**:1279-282.
 18. Stone, J.L, Lockwood, C.J, Berkowitz, G.S, Alvarez, M, Lapinski, R, Berkowitz RI. Risk factors for severe preeclampsia. *Obstet. Gynecol.* 1994; **83**:357-361.
 19. Eskenazi, B, Fenster, Sidney, S. A multivariate analysis of risk factors for Preeclampsia. *Jama.* 1991; **266**:237-241.
 20. Gudmason, V, Stansbie, D., Scott, J, Bowman, A, Nicaud, V, Humphries S.C677T (thermolabile alanine/valine) polymorphism in methylenetetrahydrofolate reductase (MTHFR), its frequency and impact on plasma homocysteine concentration in different European populations. *Atheroscl.* 1998; **136**: 347-354.
 21. Verhoef, P, Stamfer, M.J, Stabler, S.P, Reynolds, R.D, *et al.* Homocysteine metabolism and risk of myocardial infarction: relation with vitamin B6, B12 and folate. *Am J Epidemiol.* 1996; **143**:345-359.
 22. Walker, M.c, Smuth, G.N, Perans, S.I, Keely, E.d, Garner PRS. Changes in homocysteine levels during normal pregnancy. *Am I. Obstet Gynecol.* 1999; **789**: 660-664.
 23. Welsbery, I, Tran, P, Chritensen, B, Sibani, S, Rozen, R., A second genetic polymorphism in methylenetetrahydrofolate reductase (MTHFR) Associated

- with decreased enzyme activity
Mol. genet. Metal. 1996;**64**: 169-172.
24. Molly, Am, Daly, S, Mills, JL, kirke, PN, Whitehead, As, Ramsbeohom D. Thermolabile Variant of 5, 10 methylenetetrahydrofolate reductase associated with low red-cell folate: Implications for folate intake recommendations. *Lancet*, 1997;**347**:1591-1593.
25. Bailey, LB, Gregory, JF. Polymorphisms of methylenetetrahydrofolate reductase and other enzymes; metabolic significance, risks and impact on folate requirement. *Jour. Nutrit.* 1999;**129**: 919-922.
26. Abbate, R, Sardil, Pepe, G, Marcucci, R, Brunelli, T, Prisco, D, Fatinic, C, Capanni M, Simonetti, T, Genisini, GF. The high prevalence of thermolabile 5 - 10 methylenetetrahydrofolate reductase (MTHFR) in Italians is not associate to an increased risk for coronary artery disease (CAD). *ThrombHaemost.* 1998;**79**:727-730.
27. Patricia, E.M, John. T.B, Brandt, D.K, Dennis, K.P, Thomas, W.P. The incidence of the gene for thermolabile methylenetetrahydrofolate reductase in African. Americans. *Thromb. Res*, 1996;**83**:195-198.

Audit Report

HIGH FLOW NASAL OXYGEN THERAPY IN COVID-19 PATIENTS; OUR EXPERIENCE IN A LOW RESOURCE SETTING.

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INTRODUCTION

In December 2019, a novel coronavirus¹, SARS-CoV-2, was identified as the pathogen causing coronavirus disease (COVID-19) in Wuhan, China and was declared on March 11, 2020, as a pandemic by the World Health Organization. This disease has spread around the entire globe because of its great contagiousness and has led to a severe public health problem. In Nigeria, the first case was reported on 27th February, 2020 in Lagos State while here in Bauchi State, the index case was on 23rd of March, 2020. As at 15th January, 2020, Nigeria has recorded over 109,000 cases with 85,000 recoveries and 1,420 deaths.² Although, over 80% of patients present with mild respiratory symptoms, some patients infected with SARS-CoV-2 have developed severe pneumonia and respiratory failure, often requiring specialized oxygen therapy or mechanical ventilation in either high dependency units (HDU) or intensive care

units (ICU). This situation has led to an increase pressure on the few available mechanical ventilators, oxygen delivery devices and ICU staff.^{3,4}

In most developing countries, especially those of sub-Saharan Africa, intensive care medicine or critical care services are poorly developed having faced with enormous challenges such as inadequate man-power, lack of equipment and inadequate training among other things has challenged us from the beginning of COVID-19 to categorize patients into three groups; mild, moderate and severe and patients who will require oxygen therapy in addition to other supportive treatment.^{4,5} We adopted the early warning signs (EWS) and any patient who tested positive by rt-PCR and has any three of the signs below was admitted into either the ICU or HDU for oxygen and other supportive therapy.

Age	> 65yrs male and > 60 yrs females
Pulse rate	≤ 55 beats/min
Respiratory rate	< 10 or > 30 breath per min
Oxygen saturation	< 92% on oxygen
Systolic blood pressure	≤ 90mmHg
Temperature	< 35 or > 39
Level of consciousness	drowsy, lethargy, coma, confusion

Each parameter has a score of 2; indication for oxygen therapy is 6.

CASE ANALYSIS OF ELEVEN PATIENTS REQUIRING HIGH FLOW NASAL OXYGEN

A total of twenty six (26) out of two hundred and eighty three (283) patients who tested positive to COVID-19 by rt-PCR required oxygen therapy. Of the 26 patients admitted that required oxygen therapy, none was mechanically ventilated. 11 out of the 26 were treated using high flow nasal oxygenation starting from 10litre per minutes. Four (4) out of the eleven patients were diabetic and hypertensive and only two of them showed features suggestive of COVID-19 on x-ray. Ground glass opacity in both mid and lower zones of the lungs was seen however, the lung

markings were preserved. Two (2) were only diabetic with a relative normal x-ray findings. Another two (2) were only hypertensive and their x-rays showed only cardiomegaly with unfolding of the aorta while three (3) had no comorbidity and all their X-rays showed consolidation with partial loss of lung marking behind the heart in the left lower zones. All our eleven patients had elevated white blood cell count not less than 13,000/dl and platelets were within normal limit.^{6,7,8} All the patients were initially treated with Meropenem 2g stat, then 1g twice daily, Azithromycin 500mg daily, zinc sulphate 20mg twice, Hydroxychloroquine 200mg twice daily, subcutaneous Clexane 80mg stat then 40mg daily and dexamethasone 8mg daily.⁹⁻¹³

Table 1

CHARACTERISTICS OF PATIENTS

Patient	Age	Sex	BMI	SPO ₂	EWS score on admission
1.	80	M	29.2	80	6
2.	78	M	34.8	79	8
3.	69	F	23.3	84	6
4.	65	M	23.4	86	6
5.	68	M	33.6	82	6
6.	70	M	22.9	68	8
7.	64	M	26.1	72	6
8.	62	F	32.8	68	8
9.	67	M	31.2	86	6
10.	72	M	24.7	79	8
11.	61	M	29.5	69	10

The mean age of the patients was 68.7years, 81.8% (9) were male while 18.2% were females. The mean BMI was 28.3 while the mean saturation among patients that required HFNO was 78%. The minimum EWS score admitted was 6 while 10 was the highest EWS score. All patients were given incremental oxygen starting from 10litres/minute until saturation was at least 92%. The maximum flow required to achieve at least 92% was 30litres/min. out of the 11 patients, 7(63.6%) were weaned and

returned to the Sani Sami COVID-19 treatment center and 4 (39.3%) died. The maximum duration of oxygen therapy was 8 days while the minimum duration was 2 days. Of the three that died, one had long standing hypertension and was diabetic for 10 years, the second was a chronic kidney disease patient on dialysis while the third was a known diabetic who was amputated 2years ago on account of poorly controlled blood sugar.

Patient	Comorbidity	Laboratory findings	Radiological findings
1.	Nil	WBC-20,000 Platelets 438,000	Consolidation, loss of lung marking behind the heart in the left lower zones.
2.	Hypertension	WBC-13,800 Platelets 372,000	Features only suggestive of hypertension
3.	Hypertension + DM	WBC-18,300 Platelets 308,000	Features only suggestive of hypertension
4.	Nil	WBC-19,900 Platelets 408,000	Consolidation, loss of lung marking behind the heart in the left lower zones.
5.	DM	WBC-18,800 Platelets 438,000	Wide spread consolidation on both lungs
6.	Chronic kidney disease on dialysis	WBC-28,000 Platelets 152,000	Ground glass opacity in both mid and lower zones of the lungs
7.	Hypertension + DM	WBC-16,800 Platelets 354,000	Ground glass opacity in both mid and lower zones of the lungs
8.	DM	WBC-17,000 Platelets 158,000	Normal finding
9.	Hypertension + DM	WBC-14,000 Platelets 338,000	Features only suggestive of hypertension
10.	Hypertension	WBC-16,700 Platelets 328,000	Features only suggestive of hypertension
11.	Nil	WBC-13,800 Platelets 278,000	Consolidation, loss of lung marking behind the heart in the left lower zones.

HIGH FLOW NASAL OXYGENATION

High flow nasal oxygen (HFNO) provides higher concentration and flow of oxygen, resulting in decreasing anatomic dead space by preventing rebreathing and ensure positive end-expiratory. The positive end expiratory (PEEP) effect oxygenates the airway and the warm water creates vapors which loosens mucus so the alveoli can fully expand. In hypoxemic respiratory failure, the use of supplemental oxygen therapy is considered the first line of treatment. This can be administered using bag valve mask, non-rebreathing bag, nasal cannulas etc. These devices mainly supply low flow oxygen.¹⁴ HFNC washes carbon dioxide (CO₂) out of the upper airways there by reducing the anatomical dead space. Subsequently, the work of breathing is improved and respiratory rate lowered by reduction in anatomic dead space. Apart from improving oxygenation and decreasing of anatomical dead space, HFNO therapy decreases metabolic demand of breathing, decreases production of carbon dioxide and gives better comfort to patient compared to mechanical ventilation. It also improves work of breathing and improves clearance of secretion.^{14,15}

For some critical care physicians, the issue of aerosolization of virus in HFNO raises a lot of concern. Although, compared to intubation and mechanical ventilation, Tran et al¹⁶ found no increased risk of health care workers with HFNO.

CONCLUSION

In a low resource setting like ours where there are very few mechanical ventilators, inadequate manpower to man a COVID-19 ICU, HFNO provides an effective treatment option for patients infected by SARS-CoV2. It also reduces ICU length of stay and it is safe for the health workers.

REFERENCES

1. Lu R, Zhao X, Li J, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. *Lancet* 2020; **395**:565-74.
2. Nigerian Centre for Disease Control. (NCDC). COVID-19 Nigeria Situation Dashboard; Viewed Online on 2020. <https://covid19.ncdc.gov.ng/>. Accessed on 3rd September 2020.
3. Yang BY, Barnard LM, Emert JM, et al. Clinical characteristics of patients with coronavirus disease 2019 (COVID-19) receiving emergency medical services in King County, Washington. *JAMA Network Open* 2020; **3**(7):e2014549.
4. NHS England. Specialty guides for patient management during the coronavirus pandemic: Guidance for the role and use of non-invasive respiratory support in adult patients with COVID19 (confirmed or suspected). Version 3 ED, 2020.
5. Truog RD, Mitchell C, Daley GQ. The toughest triage – allocating ventilators in a pandemic. *N Engl J Med*. 2020; **382**(21):1973-1975.
6. Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW et al. Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized with COVID-19 in the New York City Area. *JAMA*. 2020; **323**: 2052–2059
7. Terpos E, Ntanasis-Stathopoulos I, Elalamy I, Kastritis E, Segertanis T, Politou M et al. Hematological findings and complications of COVID-19. *American Journal of Hematology* 2020; **95**:834-847
8. Klok FA, Kruip MJHA, van der Meer NJM, et al. Confirmation of the high cumulative incidence of thrombotic

complications in critically ill ICU patients with COVID-19: An updated analysis. *Thromb Res* 2020; **191**:148-150.

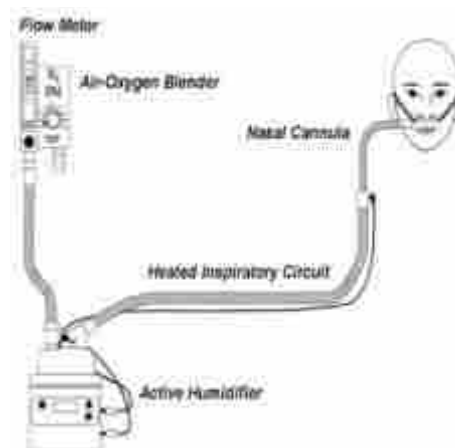
9. Arshad S, Kilgore P, Chaudhry ZS, et al. Treatment with hydroxychloroquine, azithromycin, and combination in patients hospitalized with COVID-19. *Int J Infect Dis* 2020; **97**:396-403.
10. Lagier JC, Million M, Gautret P, et al. Outcomes of 3,737 COVID-19 patients treated with hydroxychloroquine/azithromycin and other regimens in Marseille, France: a retrospective analysis. *Travel Med Infect Dis* 2020; **36**:101791.
11. Vaduganathan M, van Meijgaard J, Mehra MR, Joseph J, O'Donnell CJ, Warraich HJ. Prescription fill patterns for commonly used drugs during the COVID-19 pandemic in the United States. *JAMA* 2020; **323**:2524-6.
12. Singh AK, Majumdar S, Singh R, Misra A. Role of corticosteroid in the management of COVID-19: a systemic review and a clinician's perspective. *Diabetes MetabSyndr* 2020; **14**:971-8.
13. Artifoni M, Danic G, Gautier G, et al. Systematic assessment of venous thromboembolism in COVID-19 patients receiving thromboprophylaxis: incidence and role of D-dimer as predictive factors. *J ThrombThrombolysis* 2020; **50**:211-6.
14. Drake MG. High-flow nasal cannula oxygen in adults: An evidence-based assessment. *Ann Am Thorac Soc* 2018; **15**:145-55.
15. Segovia B, Velasco D, Jaureguizar Oriol A, Diaz Lobato S. Combination therapy in patients with Acute Respiratory Failure: High-flow nasal cannula and Non-invasive Mechanical Ventilation. *Arch Bronchoneumol.* 2019 ;**55**:166-167
16. Tran K, Cimon K, Severn M, Pessoa-Silva CL, Conly J. Aerosol generating procedures and risk of transmission of acute respiratory infections to healthcare workers: a systematic review. *PLoS One*.



HFNO system



Non re-breather mask.



HFNO device

Tribute: Late Professor Donal Joseph O'Donoghue MD, FRCP (London), OBE

15th August 1956 - 3rd January 2021

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The death of Professor Donal O'Donoghue came with shock and great sadness to us all. He was aged 64 years and died peacefully at the critical care unit of Stepping Hill Hospital in Stockport Manchester on Sunday 3rd January 2021 after battling with COVID-19.



In Manchester, he led the re-organisation of renal services and established the first managed clinical network in England where he helped build excellent service delivery, research and quality training and brought innovations to patient care. He was the National Director for Kidney Care "Kidney Tsar" at the Department

Donal qualified in physiology and medicine from University of Manchester with a career spanning over 35 years. He trained in Internal Medicine and Nephrology in the East Midlands and North-West England, Paris (as a Medical Research Council travelling fellow) and in Edinburgh Scotland. He started his renal career as a Consultant Renal Physician in 1992 at the Salford Royal Hospital Manchester and later became Professor of Renal Medicine at the University of Manchester with research interests in healthcare systems, quality improvement and innovation in education and service delivery. He was a dedicated and highly distinguished Nephrologist, with a huge national and international reputation. He was awarded an OBE (Order of the British Empire) on the Queen's Birthday Honours in June 2018 in recognition dedicated service to kidney patients.

of Health between 2006 and 2013 where he led the implementation of the Renal National Service Framework as National Director of Kidney Care at the Department of Health. During this time he chaired the National Directors Forum, the Vascular Board and the Pandemic Influenza Clinical and Operational group. He was a member of Liverpool Clinical Commissioning Group Governing Body. He was the Chair of the Greater Manchester, Lancashire and South Cumbria Clinical Senate, which provides clinical advice to commissioners. Donal was Medical Director of the Greater Manchester Academic Health Science Network and the past president of the Renal Association from 2016 until 2018 and also the inaugural past president of the multi-professional British Renal Society.

Donal until his death was the Registrar at the Royal College of Physicians London since 2018

and was responsible for professional leadership, membership matters, global engagement and supporting the President in system wide engagement to improve patient care and outcomes. He was a strong advocate for diversity within the Royal College of Physicians and the NHS workforce especially affecting the Black, Asian and Ethnic minority (BAME) groups in the UK. He was a Mentor with the NIA from its start in 2015, continuing to support the programme and offer expert guidance to Fellows up until his death in early 2021.

The tragic loss of Prof O'Donoghue was felt across the international renal community as he was a friend to many, and worked tirelessly to drive positive change for patients with kidney disease contributing to the International Society of Nephrology Commission for the Advancement of Global Nephrology (ISN-COMGAN). He is passionate about professionalism in medicine, innovation and quality improvement in kidney care. On a personal level, he was my mentor and was the warmest, welcoming person, you could wish to meet. He was unpretentious, genuine, funny, and above all charming. He was a champion of global advancement of nephrology and this is evident in his incredible support to the development of renal care in the Niger Delta Region of Nigeria which is a project that is dear to his heart through the partnership between

the renal department at the Salford Royal Hospital and the University of Port Harcourt Teaching Hospital renal unit under the platform of the International Society of Nephrology and the UK Renal Association. He tirelessly supported training and service development and was the guest speaker to the Nigeria Association of Nephrology in 2006 sharing his experience from the implementation of the National Service Framework for Kidney Health in Primary Care in the UK.

He was chair of the patient support charity "Kidney Care UK" since 2016 and was a real source of encouragement and motivation to many patients. He was such a professional and kind man with so much warmth for his patients, championing their access to excellent kidney care and experience at the highest level. A report he co-authored in 2015 showed that vulnerable elderly people, died unnecessarily of acute kidney injury because of inadequate care in NHS hospitals—a conclusion he described as "a real opportunity for quality improvement." He's as passionate about Manchester United football club as he is about NHS care.

He is survived by his wife Marie, his three children and four grandchildren and our condolences, thoughts and prayers go out to them. Let his memories be a blessing to us all.

Obituary

PROF. ANTHONY OKPANI

(10th January 1955 - 23rd January 2021)

Emeritus Professor Kelsey Atangamuerimo Harrison, NNOM, DSc, FRCOG
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The announcement of the death of Anthony Okpani came as a rude shock from which I am yet to recover. We had known ourselves for the best part of forty years. He qualified from University of Ibadan in 1979, but it was in 1981 that we first met at University of Port Harcourt Teaching Hospital. He was one of four foundation doctors in the post registration residency programme in obstetrics and gynaecology, and I was one of his three teachers. The others were

Dr. Celestine John and Dr. Nimi Briggs, who headed the department. Conditions were exceptionally austere and difficult for everybody, and they were to remain so for many years.

As well as being a good human being, Okpani had a pioneering instinct, he worked exceptionally hard, he was able to take full advantage of the little that was available – and they were very few in those days. Against the odds, he prospered and eventually became a respected professor in the discipline. He earned much respect by doing all this through merit. Based all the while at University of Port-Harcourt and its teaching hospital, he was seen as a committed professional who served both



institutions well, and who also did sterling work for the Society of Gynaecology and Obstetrics of Nigeria as one of its leading lights particularly in that society's Eastern sector.

Tony was a delightful man. As well as being his teacher and a mentor, I was to benefit from the association in several ways. One was unique. 1998 saw my relocation from Nigeria to Finland on my retirement. To mark the event and the occasion, he and Celestine John quietly authored, in my absence abroad, a moving article to mark my retirement, and got it published as a commentary in a respected medical journal¹. Talk

of being gracious, he had it. The gesture will remain with me for as long as I live.

I heard that he played the game of hockey quite competently. Unfortunately, I never had the privilege of seeing him wield the field hockey stick. To the immediate family members, I pray that you all be granted the fortitude to bear the loss.

30 January 2021.

Reference:

1. John CT, Okpani AOU. Commentary. Kelsey A Harrison. Forty years legacy in Tropical Obstetrics and Gynaecology. *African Journal of Reproductive Health* 2000, 4 (2):109 – 111.

TRIBUTE TO LATE PROFESSOR ANTHONY OKPANI UGUBA OKPANI

(10th January 1955 – 23rd January 2021)

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One of the most difficult tributes to write is one in which you forever think of the person in the present but must accept the sad inevitable reality.

I got to know late Tony 40 years ago when we were young residents, in the nascent Residency Programme in Obstetrics & Gynaecology (O&G) of the University of Port-Harcourt Teaching Hospital which was initially domiciled in rural General Hospital, Emohua. Tony passed the primaries of the National Postgraduate Medical College Examinations in O&G in November 1981 at first attempt, whilst in Emohua, to the consternation of us the residents! It was a feat! We competed and cooperated fiercely, a unique trait that gendered camaraderie in the climes of scarce and limited clinical resources, until our relocation to the then General Hospital, Port-Harcourt in August 1983. Tony thrived in the then immense challenges to postgraduate training¹ and became a Fellow of the West African College of Surgeon in Obstetrics & Gynaecology in 1989 after duly passing the prescribed examinations. I left for the United Kingdom in September 1984 after obtaining the primaries of both the National Postgraduate Medical College & the West African College of Surgeons in Obstetrics and Gynaecology respectively. I obtained the membership of the Royal College of Obstetricians and Gynaecologists in 1989

We were to meet again in 2003 when I returned to explore the prospects of my relocation plan from the United Kingdom. He was at that time, the Head of Department of O&G and his generosity and magnanimity knew no bounds. He reminded all who cared to listen that we were the pioneers of residency in the unit. This bond of collegiality remained till I relocated in 2012 and the profound role he played in my reintegration was a testament to his character. He attended the 16th Inaugural Lecture of the Niger Delta University (NDU) which was delivered by me². Furthermore, he participated as a guest lecturer³ on the *Deans Lecture Series* of NDU which was initiated by me in my capacity then as Dean of the Faculty of Clinical Sciences and sponsored by the pharmaceutical company, Pfizer. Additionally, it was he who nominated me as the Vice-Chairman of the Eastern sector of the Society of Gynaecology and Obstetrics of Nigeria's (SOGON) executive council when the position became vacant.

We had time to share the anecdotes of yesteryears. We attended SOGON's sector & national meetings as well as the annual conferences of the West African College of Surgeons. Our travels also took us to several countries including Brazil, Dubai and Rwanda.

He was a quintessential gentleman, with a legendary wry sense of humour. He was a friend to all including the junior residents and a source of succor to his three children: Charles – Consultant Urologist, Mary - Senior Registrar in Paediatrics & Francis – Chemical Engineer with a master's degree; whom he raised as a single parent following the untimely demise of his childhood-love wife. He enjoyed his role as Chairman of the Eastern Sector of SOGON. His

commitment was rewarded by 2 successive best performing National Sector awards from SOGON. His last act before his sad demise was to post a set of anticipated preparatory questions to residents on the SOGON Eastern sector platform which was dedicated to educational activities. May his soul rest in perfect peace.



February 2020 @ the West African College of Surgeons Conference Abuja



April 2018 @ FIGO Regional Conference Dubai

References:

1. Harrison KA. Tribute to late Prof AOU Okpani. *Nig Del Med J* 2021; **5**(1): 36.
2. Harry TC. 16th Inaugural Lecture. Aid to AIDS: a journey of serendipity. *Nig Del Med J* 2019; **3**(1): 18-28.
3. Okpani AOU. Deans Lecture Series: Manpower requirements in Nigeria's health sector: the unmet need to maximize our gains. *Nig Del Med J* 2017; **1**(3): 16-33.

PROFESSOR ANTHONY U. OKPANI

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The sudden death of Tony left me in a sudden state of shock. 'Tony' as he was fondly called started with us at the University of Port Harcourt Teaching Hospital from its original site in Emuoha. He was our first trainee. He was brilliant and hard working.

We (Emeritus Professor K A. Harrison, Emeritus Professor N.D Briggs and myself- his original teachers) were proud of him and watched him rise to the rank of Professor, Head of our Department; a committed SOGON member and until his sudden death, the Chairman Eastern Sector.

He went through some traumatic moments in his life but through them all he overcame and has never found wanting in any aspect of his life. He took the blows of life and came out each time stronger.

I was involved in all aspects of his life; academic, social and personal.

I feel broken and sad, very sad. He never forgot to visit me from time to time and our talk ranged from the departmental academic progress and all aspects of life and living. As in all things I give thanks to God and pray for him and his children.

We can't forget, we shall miss him and may his soul rest in perfect peace.