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EDITORIAL

MEDICAL GENETICS AND EDUCATION

The recent dramatic cures announced for diseases like sickle cell disease, Spinal Muscular atrophy, Beta Thalassemia using revolutionary gene editing techniques and gene therapies, the availability of advanced genetic tests, raises the question of what currently goes into our medical training regarding medical genetics and genomics education. The human genome project was completed in 2005 that confirmed humans had only between 20000 and 23,000 gene pairs and that mutations in our genomes caused about 7000 known genetic diseases that affects millions of families worldwide. Ghana is no exception and at the Department of Child Health and now armed with access to whole genome sequencing investigations in the USA (Through Rare diseases Ghana Initiative) we are beginning to diagnose a whole new range of diseases hitherto thought non-existent in our environment. Rare diseases like Rubenstein- Taybi syndrome, Wilson's disease, SCN1A mutation epilepsy (Dravet syndrome), Gauchers disease to name a few are being seen in the Department. It has already been observed at the Neuro- Developmental clinic for instance that our children tolerate much lower doses for epilepsy drugs than what is prescribed in the books. The issue of pharmacogenetics comes in here where the variation in drug metabolizing enzymes could be a factor. In 1892 Sir William Osler said, "if it were not for the great variability among individuals, medicine might as well be a science and not an art'.

The brilliant gene editing techniques and known as CRISPR Cas9 or Clustered regulatory Interspaced Palindromic repeats associated protein 9 which acts as a' genetic tailor' has moved rapidly from being a laboratory technique to the clinical bedside. We depend on our survival as humans on our ability to repair mutations. Xeroderma pigmentosum is an example of such a failure. Mutations are the driving force of nature. Imagine copying a book such as the bible or the Koran as happens in DNA replication. Monks used to do that job. There were huge errors. This tool marks a new revolution in medical practice to treat genetic diseases.

There are references to genetic diseases and the diagnosis in a few articles. Is our clinical workforce trained to handle this major shift going on? I envisage laboratory reports dotted with genetic language in the near future. There is the issue of having your private genetic biodata available to insurance companies and the whole world. What are the undergraduate and post graduate institutions doing about these rapid developments regarding basic training in genetics? Bennet et al suggest we need to foster excitement about medical genetics specialties early upon entry to medical school as well as throughout their training. The content of genetic training should be looked at by our Curriculum review committees serving the medical schools. Genetic counselling training has begun at the West African Genetic Medicine Centre(WAGMC) , Legon and it is hoped our population will be served with their expertise. The public deserves to be informed by health professionals about the nature of disease and the role of genes. There is no surveillance and registry for rare genetic diseases and this should be quickly established so we can participate in International trials for new drugs.

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ORIGINAL ARTICLES

EXPLORING THE CAUSES OF LOW REPORTING OF MEDICO-LEGAL ISSUES IN GHANA: PERSPECTIVES OF KEY INFORMANTS IN THE HEALTH SECTOR

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Abstract

Objective: The study aimed at exploring factors leading to medico-legal issues and why they are under reported.
Methodology: This was a qualitative study in which 16 key informants were interviewed with a semi-structured questionnaire. Ethical approval was obtained from the Ghana Institute of Management and Public Administration (GIMPA) Ethical Review Board. Data was analysed thematically. A written informed consent was obtained from each participant.
Results: A medico-legal issue arose if the standard of care was perceived to have been breached or when a complaint was not managed according to the complainant's expectations. Reasons for low reporting included the long emotionally exacting and expensive adjudication process. Additionally, procedures at the facilities to address complaints are considered non-transparent and prejudicial. Finally, interviewees were credulous believing in predetermined death. They have the attitude of 'leave judgement to God.' Even if the victim wants to take the matter up, others may impress upon them to stop it.
Conclusion: The study concludes that factors leading to medico-legal issues include a breach in the approved standard of care of the patient and whether the complainant is unhappy with the handling of the matter. The emotionally and financially exacting nature of dealing with these issues, and the perceived unfair processes account for the low reporting. Belief in fatalism is a contributory factor.

Key words: *Medico-legal, reporting, contributory factors*

Introduction

The ethics of the medical profession hinge on the fundamental values of autonomy, confidentiality, justice, beneficence, and non-maleficence[1]. Medical professionals have a legal duty to comply with these ethical principles in their day-to-day practice. This is because ignorance of, or deviation from these and the possible fall outs thereof, may lead to an occurrence of a medico-legal issue. Another reason is that even when the professional has acted in good faith, the action may not stand the scrutiny of the legal system when subjected to strict analysis. With the increasing number of medico-legal issues worldwide, it is imperative that medical professionals are conversant with fundamental legal issues in medical practice through continuing medico-legal education.

The most frequent forms of medico-legal issues faced by medical professionals are medical negligence, professional misconduct, false imprisonment, assault and battery, euthanasia, and vicarious liability[2]. Others are misdiagnoses or failure to diagnose, failure to obtain an informed consent[3] failure to warn the patient of the known risks involved in treatment and improper treatment.[4]

It is the case that legal implications may arise from the mere alteration in the fundamental practice of medicine and the health practitioner must be aware of this. Practitioners must be mindful of the risks that their medical practice is faced with daily, both from the legal perspective and from the patient's perspective. It is common knowledge that a well-publicized malpractice suit can do irreparable damage to the reputation and practice of a practitioner and their organisation. However, many Ghanaian practitioners are not concerned because few really get reported or sued. Others know that scandals involving them or the facilities may only appear in the media and nothing more so they seem unperturbed.

Anecdotally, it is known that even with the best of intentions and effort, adverse events may occur. However, how they are dealt with may predict how far the issue goes. Often, an honest explanation and a sincere apology may be all it takes to prevent a lawsuit. Unfortunately, most clinicians think that this would imply the admission of guilt and make them vulnerable to a claim. However, all clinicians are encouraged to apologise to the patient where necessary.[5]

Worldwide, medico-legal suits against private and public healthcare providers have soared especially with regards to suits relating to maternal and child health. This is reported to have the potential to severely affect reproductive health services in South Africa.[6] With

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public sector providers, the breach of medical guidelines and practices have been attributed to low-resources and lack of proper management systems.[6] On the other hand, the private sector has been criticised for its non-existent accountability systems coupled with increased patient assertiveness resulting from enhanced knowledge of their rights.[6] Legislative and dispute resolution framework have seen them also faced with increasing medico-legal suits.[6]

In Ghana, there is the perception among healthcare workers that patients can be treated anyhow as though there are neither laws nor professional ethics guiding their conduct.[7] These healthcare workers behave like, "we are doing you a favour therefore, you cannot complain".[7] Unfortunately, most of the populace are not aware of the laws which ensure their rights and privileges. Hence, they hesitate to register their disapproval when these rights are disregarded - advertently or otherwise.[7] The country's difficult economic situation further complicates the issue. Poor people are usually uneducated or under-educated, unempowered and vulnerable, and they overly spiritualise every situation and have 'a-give-it-to-God' attitude. They are ignorant of their entitlements and are unable to launch a complaint at the court and see to its logical conclusion due to lack of funds, and because they feel like they do not have a choice. However, the recognition of healthcare as a human right empowers the holders of these rights to demand accountability from the obligation bearers.[8]

The main objective of this study was to explore the reasons for low reporting of medico-legal issues in Ghana in spite of the fact that such issues do exist in Ghana.

Materials and Methods

The study was a retrospective, purposive study. It was a qualitative study involving the interview of officials who were knowledgeable, communicative, impartial and willing to shed light on the subject matter. They held key positions in the various health institutions and had information germane to the topic of interest. These people were selected because of the positions they held and the pertinent roles they played in Ghana's health sector. Their views, perceptions and experiences on the common causes of medico-legal problems, as well as the factors that determine whether a patient formally reports an incident or not were explored. Also, patients who had suffered an unfortunate incident and the relations of patients who sadly passed away during or following medical treatment were interviewed.

A semi-structured interview guide developed by the primary author was used. The interview instrument was used to organise and guide the interviews. The guide included interviewee-specific, follow-up questions within and across the interviews. Probing and follow-up questions were used as and when necessary, during the interview. Different categories of interviewees were administered with specific questions.

Study Sites and Population

The Ministry of Health (MOH), the Ghana Health Service (GHS), the Medical and Dental Council (MDC), the Korle-Bu Teaching Hospital (KBTH), the Greater Accra Regional Hospital (GARH), the Attorney-General's Department (AGD), a law firm, and the homes and workplaces of patients and their relations were used. The study population comprised officials of the regulatory bodies, notably the MDC, GHS, MOH, KBTH, GARH, and the AGD. These officials receive and deal with such matters of medico-legal issues. Also, a lawyer from a private law firm as well as patients and relations of patients who had suffered an adverse outcome and may have resorted to one form of redress or the other, were among the interviewees. The study aimed to sample a total of 17 persons, but one person declined the interview. It was over a six-week period.

Sampling Technique

Purposive sampling method was used. In purposive sampling, individuals are chosen to participate in the research because they have certain experiences and knowledge of a specific phenomenon, reside in a specific location, or some other reason.[9] This sampling method allows the deliberate selection of individuals and/or research settings that will enable the gathering of information to answer research questions.[9] It is the primary sampling approach used in qualitative research.[10,11]

The Principal Investigator (PI) interviewed two sets of persons. The first set comprised 10 predetermined key informants mainly from the health sector. Key informants are persons with enormous knowledge and/or impact and can shed light on issues of interest. In this study they included the following officials: one person each from MDC, MOH, KBTH and AGD, two each from GHS and the GARH, one private legal practitioner and a patient advocate. These individuals were selected to participate in the research as they were officials of regulatory and other agencies deemed to have knowledge and experience in the administration and practices of the health sector of Ghana. They had also been involved in medical litigation. In particular, the private legal practitioner handles human rights cases including those from the health sector. The other set of interviewees were six persons – two patients and four patient relations. These were chosen because they had experienced a medico-legal issue directly (the patients) or indirectly (patients' relations). The administered questionnaire consisted of four parts. The first part was the demographics which was answered by every interviewee. The second part consisted of questions answered by all victims (patients) and patients' relations. The third part consisted of general questions answered by all officials, while the last part was customised to the specific category of officials interviewed. The questionnaire (interview guide) is attached as appendix.

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Data Source

A primary data source was used to gather the data. Primary data source is the data collected for a specific reason, that is, data collected originally from the source, first-hand (new data would be collected directly). This data type is unpublished, valid, and objective compared to secondary data. A semi-structured interview guide was used.

Research Instrument and Data Collection Procedure

Recorded interviews were conducted. Participants were informed that interviews were going to be audio-recorded and their permission was sought. Consenting participants were told that they were at liberty to stop the recording at any point during the interview. The duration of the interviews was between 20 and 90 minutes, the average duration was about 45 minutes.

Reliability and Validity

Reliability is how consistently a particular research method measures a specific variable. A measurement is considered reliable if the same result can be repeatedly obtained by using the same method under the same conditions.[12] Each category of study participants was administered the same questionnaire. The responses received for the various questions were identical, showing the questionnaire was reliable. Validity refers to the process by which researchers can establish that their findings are authentic to the experiences of the participants. It assesses the quality and rigor of the study[9] which our study showed.

Data Handling and Analysis

The participants interview guides were coded. The audio recordings were transcribed and coded to conform to that used for the guides. A commercial entity was contracted to transcribe the audio recordings. To ensure confidentiality, a confidentiality agreement was signed before the commencement of the work. The transcripts were secured in a passworded file on a computer. The data was analysed using thematic analysis.

Ethical Considerations

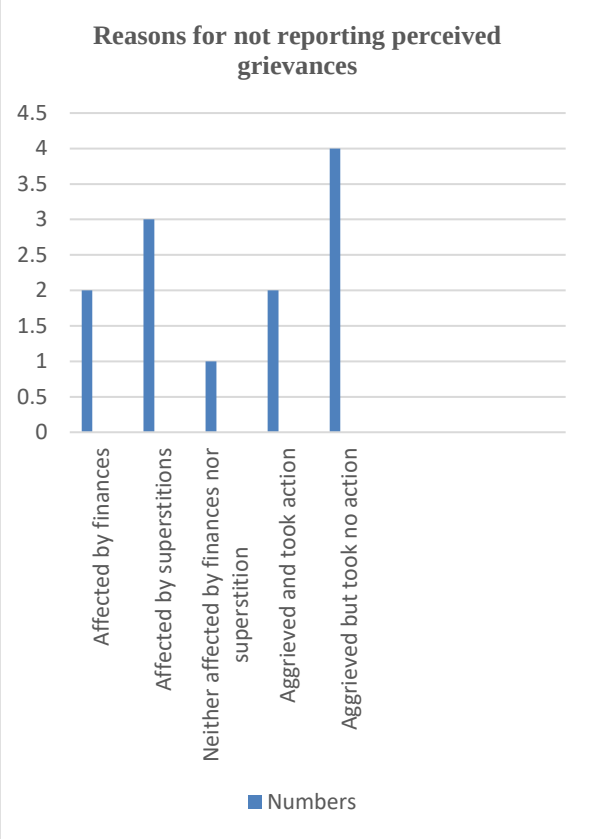
- Ethical approval was obtained from the GIMPA Ethical Review Board, a copy attached.
- A written informed consent was obtained from all the participants.
- Data was in the custody of the PI.
- The transcriber signed a non-disclosure agreement, valid for 3 years.
- All recordings were coded using unique serial numbers to ensure anonymity.

Results

The table below shows a total of six respondents made up of two patients and four patient relations, and their responses in terms of whether they reported their grievances, and which of them did not report based on finances or superstition or otherwise.

One aggrieved respondent who took no action was neither affected by finances nor superstition. He just did not see how he was likely to win a case against a very senior doctor.

		Numbers	%
1.	Affected by finances	2	33.3
2.	Affected by superstitions	3	50.0
3.	Neither affected by finances nor superstition	1	16.7
4.	Aggrieved and took action	2	50.0
5.	Aggrieved but took no action	4	66.7



Bar Graph showing respondents affected by finances or superstition and those who were not so affected.

Interviewees believed in fatalism which is that some happenings in our life are predetermined and will happen as and when they will, and nothing can stop them. One interviewee responded:

"Until recently, the issue of malpractice was left to superstitious beliefs, because a lot of people believe that if it is not your turn to die, you won't die. People think that it is only God who determines who dies and at what point in time. So, for that matter, if you go to

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the facility and something unfortunate happens and you die, then it is your time to die….".

For the reason for not complaining formally following a medical mishap, interviewees' responses included the ignorance of what constitutes a mishap.

A respondent said:
"……..people [the public] *don't even know that there is a remedy or there are rights in law when you* [the patient] *fall victim to medical negligence. For a lot of people, precedence has told them that, 'Look, uh, even if you go to talk about it* [the mishap]*, it won't end anywhere, so why worry yourself" just leave it!'…….*

Also, the long, emotionally exacting, and expensive adjudication process was found to be deterring as some interviewees complained:

'Look, we don't have money because litigation is expensive- you waste money. Also, it can take many years before a verdict is given; so why should we [complainants] *bother ourselves? The person is already dead. Making claims or seeking justice would not bring the person back to life, so, let it be'. I mean let's leave it* [forget about the mishap].

Additionally, it was found that many interviewees were laid back with reporting issues, speaking up against the wrongs of society or even litigating. One respondent said:

"……my in-laws, family and pastor said uh, (hisses) the usual Ghanaian thing, 'gyai ma no ka' [let sleeping dogs lie]. *They said it* [the death] *has already happened, and (hisses) so it was not necessary. So, I shouldn't sue because it would be a waste of time as she had already died and it* [suing] *won't bring her back. I also thought, 'Yeah, you can't fight an institution and win', you'll just be bullied"* (Abdul, patient's relation).

I mean a lot of patients are intimidated by some of these issues [medico-legal issues] *that come up, hence they're unable to speak up when they become victims of malpractice"* (Torgbui, patients advocate).

Finally, the procedures in place at the health facilities to address complaints from service users are considered non transparent and prejudiced against the complainant.

Therefore, the victims would rather go to the court of public opinion to complain where they know they would be heard, sympathised with, and judged most kindly. These points are alluded to by these quotes:

"Mm, they [the complainants] *don't trust in the laid down procedures. `They presume that the facility would shield its own by covering up any untoward findings. However, at the radio stations at least you get the attention and people to sympathize with you. There are instances where people will say that 'I don't like the team that you have put together. I want to bring my own team to come and investigate.'*

Also, perhaps the promptness of response to their issues, is a challenge. So, they want to go out there, and get the public to just bash [castigate] *us and then we'll fall in line* [act professionally] (laughs) ……" (Ama, nurse).

Discussion

The findings are supported by the 2014 Healthwatch report 'Suffering in Silence' which found out that less than 50% of victims of malpractice report the incident. The reasons are either because they are ignorant of the complaint process or because they doubt that anything noteworthy would result from the complaint made.[13] Therefore, even when one is unjustly treated there is the likelihood that no redress would be sought. In fact, even if the victim tries to take the matter up, it is most likely that the family, friends, and society in general may impress upon the one to 'allow sleeping dogs lie'.

The belief of the African that every occurrence in this world is attributable to a higher power and certainly our entry and exit from it, contributes to our non-reporting. This is borne from a respondent's quotation above that, "*People think that it is only God who determines who dies and at what point in time".* This may explain the 'give it to God' attitude that most people are socialised into.

Also, the protracted, emotionally draining and costly nature of the judicial process, is a factor for this non-reporting.

The average Ghanaian has low income and hence any endeavour that is financially exacting is deterring. In 2019, the monthly individual living wage in Ghana was reported to be about GHS 900.00 (about USD 154.78), which was an increase of about GHS 40.00 (about USD 6.87) from the previous year.[14]

The case of *Dr E L A Chinbuah and Captain J K Nyamekye v The Attorney General* wa as determined, after five years.[15] One can imagine how much money was spent. Unfortunately, one of the plaintiffs passed on during this arduous court process.

Furthermore, the Ghanaian is generally laid back with respect to registering their disapproval with issues that boarders on their ill treatment. *There is a certain culture of silence in Ghana.* Unfortunately, when a person tries to defy the status quo, neighbours and relations impress upon him/her to 'move on'. This is reflected in another response that, *"gyai ma no ka"* [let sleeping dogs lie].
The fact that potential complainants consider the complaint procedures at the health facilities non transparent and prejudiced against them is another factor. This is evidenced by the quote, *"Mm, they* **[the complainants]** *don't trust in the laid down procedures. They presume that the facility would shield its own by covering up any untoward findings.* Patients are generally suspicious of the system and any finding that exonerates the system, is judged as confirming their

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perception. They find more solace in the media, especially the electronic and social media which serve as courts of public opinion, and sympathetic to their plight.

Melberg et al found that the populace may just lack information about what constitutes a medico-legal case and how to go about reporting same.[16] This corroborates our finding that the populace is largely ignorant of medico-legal issues. This is supported by the report of the 2014 Healthwatch report 'Suffering in Silence' which found that less than 50% of victims of malpractice reporting the incident. The reasons are either because they are ignorant of the complaint process or because they doubt that anything noteworthy would result from the complaint made.[13] The fatalistic belief of the Ghanaian comes into play. 'Whatever will happen will happen'. Thus, death will occur not so much because of one's negligence but that it is bound to happen. Some supernatural powers are responsible for our entry and exit from the world. No one comes earlier nor leaves later than is predetermined. This responsibility is not bequeathed to any mortal. In effect there is a feeling of learned helplessness where one believes death or malpractice or negligence is outside one's ability to prevent and once it occurs, there is nothing that can be done.

Limitations

The sample size of fifteen sixteen (16) key informants was too small to allow for generalization. A future study will require a larger sample size.

Another limitation was the small number of facilities used for the interviews. That did not allow for a variety of responses. A future study will need to use many more facilities from different parts of the country.

Finally, the profession of the PI (as a medical doctor) may have interfered with the responses received: the complainants may have been apprehensive about speaking frankly to the issues due to the fact that the complaints were about the colleagues of the interviewer.

Conclusion

The dissatisfied client may complain formally through the laid down processes at the health facility or informally in the media, that is electronic or print. Often, the latter is preferred as most of the clients have no confidence in the formal process due to a variety of reasons. These include lack of clarity for the process, and the presumption that the healthcare worker would be shielded. Other reasons are the long and expensive adjudication process, the fatalistic views about life of the Ghanaian, leading to laid back attitudes and general ignorance about what constitutes medico-legal issue. It is recommended that more public awareness is created among clients and the populace to understand their rights and to empower them to be able to stand up for their rights. Medical personnel must also be taken through in-service or continuous professional development to recognise the need to be circumspect with respect to medico-legal issues and to accept and apologise when such negligence occurs to reduce the chances of medico-legal suits.

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DISEASE BURDEN AND OUTCOME OF NEONATAL ADMISSIONS AT THE TAMALE TEACHING HOSPITAL, GHANA: A PROSPECTIVE STUDY

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Abstract

Objective: To determine the pattern of diseases and factors affecting the outcome of neonates admitted at the Tamale Teaching Hospital Neonatal Intensive Care Unit (TTH NICU) over three months.

Methodology: A hospital-based prospective cohort design was used to collect data from participants. A sample size of 399 neonates (participants) admitted into the NICU from 1st March 2021 to 10th June 2021. Data was obtained using KoboCollect, exported into Excel for cleaning, coding and analysed using SPSS version 20.

Results: This study screened a total of 450 neonates under 28 days admitted in the NICU of Tamale Teaching Hospital, Ghana, over three months. Fifty-one of them were rejected, and 399 were included in the final analysis. The mean birth weight was 2600 g (±810g), with 33.1% of the neonates having low birth weight. Three hundred and forty-one (341) (85.5%) neonates survived, while 58 (14.5%) died during hospitalisation. The pattern of diseases showed that neonatal sepsis (37.3%, n=149/399), small for gestational age or low birth weight (SGA/LBW) (33.1%, n=132/399), neonatal jaundice (28.1%, n=112/399), prematurity (23.6%, n=94/399), birth asphyxia (13.5%, n=54/399) and congenital anomalies (7.8%, n=31/399) were the most common causes of admissions. All variables which had an association with neonatal mortality ($p < 0.05$) were entered into a binomial logistic model, prematurity (AOR=6.974, 95% CI: 1.766-27.537; p=0.006) was the main predictor of mortality.

Conclusion: The common causes of admission and deaths in the TTH NICU during the study were neonatal sepsis, prematurity, birth asphyxia, LBW/SGA and neonatal jaundice. This highlights the need for interventions to address these conditions as we strive to reduce institutional neonatal mortality.

Key words: *Neonatal mortality; NICU, Disease; Prospective study, Tamale*

Introduction

Globally, an estimated 130 million neonates are born every year[1], out of which approximately 2.5 million die in the first 28 days of life, three-quarters of these deaths happen in the first week of life, and over a quarter occur within the first 24 hours of life [1,2]. According to the United Nations Inter-Agency Group for Child Mortality Estimates UN IGME[3], a considerable percentage (47%) of all under-five deaths occurred in the first 28 days of life. Almost all (98%) of neonatal deaths occur in developing countries [3]. The probability of dying of under five years children is higher in their first month of life [1]. In the Global Health Observatory of WHO in 2018, the global neonatal mortality rate stood at 17.7 per 1000 live births. It was projected that between the years 2018 and 2030, an estimated 27.8 million neonates would lose their lives if the current global reduction rates of neonatal mortalities are maintained [4]. The African Region had the highest rate of neonatal deaths at 27.2 per 1000 live births, with the Eastern Mediterranean and Southeast Asia recording 25.9 and 20.2 per 1000 live births, respectively[1]. West and Central Africa recorded the highest neonatal mortality rate of 30.2 per 1000 live births in 2017. This figure was 9 times higher than high-income countries that recorded 3.0 per 1000 live births[4]. Sub-Saharan Africa, together with Southeast Asia, was responsible for 79% of the entire global burden of neonatal deaths in 2017 [4]. However, these two regions have the slowest progress in reducing the rates of neonatal mortality [5].

Although sub-Saharan Africa recorded an annual reduction rate of 1.8% in neonatal mortality from 1990 to 2018, about one million neonates still die every year, partly due to the increased fertility rate in the region [3,4,6]. In 2012, Ghana recorded a neonatal mortality rate of 39 per 1000 live births, which decreased to 30 per 1000 live births in 2014 [7, 8]. Four years later, a significant improvement resulted in a further decline in NMR, resulting in 23.9 per 1000 live births (WHO, 2018). This significant improvement could be attributed partly to the Ghana National Newborn Health Strategy and Action Plan (GNNHSAP) 2014-2018, a policy rolled out by the Ghana Ministry of Health to reduce NMR from 30 per 1000 to 21 per 1000 live births [7]. The common and major causes of neonatal deaths around the world are preventable. They include prematurity, respiratory distress syndrome, sepsis, jaundice, and birth asphyxia[2]. In high-income countries (HIC), most neonatal deaths

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are non-preventable and caused mainly by congenital anomalies. However, deaths occurring in low-and middle-income countries (LMICs) are mainly attributable to prematurity, sepsis, jaundice, etc, which are preventable[1]. With the use of simple and cost-effective measures (such as good and hygienic birth practices, care of the umbilical cords, the use of antibiotics for all forms of neonatal sepsis, kangaroo mother care for preterm babies, early initiation of breastfeeding, and immediate skin-to-skin practice to keep babies warm), 75% of all neonatal deaths in LMICs can be avoided [5].

Global initiatives such as the Millennium Development Goals (Goal 4) and the Sustainable Development Goals (Goal 3) have had some success. However, neonatal mortality is still unacceptably high, and if pragmatic measures are not put in place, most LMICs will not achieve SDG 3. According to Anuradha, Rajesh Kumar [9], health facility-based interventions have the potential to reduce neonatal mortality by 23.50%. Therefore, NICU care is significant for improving the survival of neonates. Most studies [2, 10-12] on neonatal mortality in the NICU have been done retrospectively in different parts of the world and Ghana. Walana, Acquah[13] did a retrospective study in TTH NICU utilising data from the years 2013 to 2015, when the TTH NICU was not as well equipped as it is presently. Therefore, a 3-month prospective study was carried out to determine the pattern of disease and factors affecting the outcome of neonates admitted at the Tamale Teaching Hospital Neonatal Intensive Care Unit This prospective study allowed for complete data regarding neonatal morbidity and mortality.

Materials and Methods

Study Design

A prospective cohort study was carried out among neonates admitted to the NICU of the Tamale Teaching Hospital from 1st March 2021 to 10th June 2021.

Study Area

This study was carried out in the Neonatal Intensive Care Unit of the Tamale Teaching Hospital (TTH). TTH is a tertiary hospital located in the Tamale Metropolis, the administrative capital of the Northern Region of Ghana and affiliated with the University for Development Studies, School of Medicine. TTH with a bed capacity of 800 is the only referral hospital serving all five regions (Northern, Savannah, North East, Upper West and Upper East) in the northern belt of the country, parts of the Oti and Bono East regions as well as some residents of Burkina-Faso and Togo who live in towns that share boundaries with Ghana. TTH NICU is a 40-bed capacity and provides neonatal healthcare services to babies.

Study Population and Sampling Technique

A sample size of 399 neonates was included in this study. The study population included all neonates admitted into the NICU at the time of data collection. However, neonates who died within an hour of admission or were brought to the NICU for observation were excluded from the study. Neonates delivered at home or other facilities and admitted to the NICU with missing data were also excluded due to the difficulty in obtaining such data. A consecutive non-probability sampling method was used to recruit participants. Each consecutive neonate admitted to the NICU and met the inclusion criteria was enrolled in the study.

Data Collection Procedure

Permission was obtained from the NICU nurses, and with their assistance; mothers/relatives whose babies qualified to be part of the study were introduced to the principal investigator (PI) and research assistant. Upon providing information about the study, informed consent was obtained from parents or guardians. The researcher and the two research assistants performed screening at the time of admission. After obtaining consent, data was collected at admission, during admission and at exit (discharged alive or dead). Data for all variables (dead or discharged home alive, final diagnosis and other variables of interest) were obtained from medical records at admission, updated during the hospital stay, and confirmed at discharge. The nurses and doctors were contacted when there was uncertainty about the information of the included participants. Follow-up was terminated at discharge, transfer or death. The ones who opted for discharge against medical advice were not added to the analysis. The survivors in this study represented neonates who had been discharged home or transferred to different hospitals. Neonates who had low birth weight or were small for the gestational age (LBW/SGA) or both were categorized together.

Sample Size

Using Cochrane's formula, a sample size of 385 was calculated. However, 5% of the calculated sample size was added to cater to attritions, resulting in a total of 399 participants. A p (estimated proportion of the population) of 50% was used because we did not know the size of the population. A 50% proportion is used when the population of interest is unknown and this helps in achieving maximum sample size (Kotrilik, 2001; Shete, 2020). A precision of 5% was used because it is more practical and feasible compared to 1% which will require a larger sample size. Using a precision of 10% might also mean that the sample size will be small raising concerns about reliability. Again, a precision of 5% is the most common and accepted level of precision in health research. An addition of 5% of the estimated sample was purely based on resources. A higher percentage will mean an increase in sample size. This research was done towards the award of a postgraduate degree, which was funded by the principal investigator.

Study Instruments

The instrument for data collection (questionnaire) was adapted from previous studies (Demisse et al., 2017; Desalew et al., 2020; Orsido et al., 2019), modified to

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suit the present study, and pretested a month earlier in the same NICU before the start of data collection. The questionnaire was designed and entered into a software called KoboCollect (https://www.kobotoolbox.org/), which was used for the data collection.

Quality Control

The link to the software for data collection was shared with the research assistants, who were trained on how to use it. A two-week period was allowed for research assistants to get accustomed to the use of the application. Pretesting of the tool was done in the study area, and one week was given for research assistants to explore how to obtain data on the neonates from the electronic medical record system of the hospital. Each data form submitted via the Application (KoboCollect) was reviewed by the principal investigator to check for missing data. Data forms with incomplete data of up to 50% of variables of interest were rejected, and such participants were removed from the study. After data collection, the data was exported from the KoboCollect to Microsoft Excel 2010, and data cleaning and coding were done and prepared for analysis.

Ethical Considerations

Ethical clearance was obtained from the Committee on Human Research, Publications and Ethics, Kwame Nkrumah University of Science and Technology, Kumasi (reference number: CHRPE/AP/093/21). Written permission was also obtained from the Tamale Teaching Hospital research and development department, and copies were sent to the NICU through the unit head. Informed consent was also obtained from mothers of neonates in the study. The study posed no physical harm to participants. All data obtained from the study were treated with utmost anonymity and confidentiality.

Data analysis and Presentation

All data was captured using KoboCollect, exported to Microsoft Excel for data cleaning, and then analysed using SPSS version 20. Descriptive statistics such as means and standard deviations were used to determine mean age at admission, sex, Apgar score, birth weight, and admission temperature. Resuscitation status, diagnosis, referral status, etc., were presented using frequency counts and percentages. All selected variables such as Admission age, sex, APGAR score at 5th min, Birth weight, admission weight, resuscitation, immediate skin-to-skin care, breastfeeding initiation, oxygen therapy, CPAP, prematurity, birth asphyxia, neonatal sepsis, and neonatal jaundice were analysed in cross-tabulation (chi-square). Variables, which were significantly associated with the outcome of admission (p-value <0.05), were further considered for binomial regression to determine the predictors of outcome.

Odds ratios were reported with their 95% confidence intervals (CIs), and the statistical significance was determined at a p-value of <0.05. Results were presented as tables, histograms, and narrative summaries.

Results

Neonatal Characteristics

A total of 450 neonates were screened at the end of data collection and 399 met the inclusion criteria and were recruited and included in the data analysis. Fifty-one (51) were rejected; 25 were brought to the NICU for observation, 15 died within an hour of admission, 5 asked for discharge against medical advice (DAMA) and the remaining had incomplete data. The descriptive statistics of neonatal characteristics are shown in Table 1.

Table 1. Neonatal Characteristics (Descriptive Statistics)

Kg: Kilogramme; Min: Minimum; Max: Maximum; SD: Standard Deviation; ºC: Degree Celsius

Variable	No. of participants	Min	Max	Mean (SD)	Median
Age at admission (days)	399	0	28	4.13 (±4.97)	2.00
Birth weight (Kg)	348	0.5	5.1	2.6 (±0.81)	2.70
Weight at admission (Kg)	399	0.6	5.9	2.54 (±0.83)	2.60
Length of stay in NICU (days)	399	1	28	6.55 (±5.66)	5.00
Temperature at admission (ºC)	399	32	40	36.56 (±1.39)	36.70
Age at outcome (days)	399	1	28	10.91 (±6.92)	9.00

The age (days) at admission ranged from 0-28, with a mean of 4.13 (±4.97) days. Thirty-seven percent (37%) (n=125/339) of the neonates had an Apgar score of less than 7/10 in the first minute, and 18% (n=62/399) had an Apgar score of less than 7/10 in the fifth minute. Mortality in neonates with low Apgar score (<7/10) was 25% (n=31/125) in the first minute and 42% (n=26/62) in the fifth minute. A mean birth weight of 2.60 Kg (±0.81Kg) was recorded. Twenty-nine percent (29%, n=100/348) of neonates had low birth weight (LBW) (<2500g), 7% (n=25/348) had very low birth weight (VLBW) (<1500g) and 2% (n=7/348) had extremely low birth weight (ELBW) (<1000g). Mortality was 15% (n=15/100) for LBW, 40% (n=10/25) in VLBW and 43% (n=3/7) in those with ELBW. The mean temperature recorded was 36.56 ºC (±1.39).

The majority of the neonates admitted into the NICU were males (56.9%, n=227). About half (49.1%, n=196/399) of the neonates had immediate skin-to-skin contact with their mothers. For those who received immediate skin-to-skin care, 59.2% (n=116) had it within 30 minutes, 5.6% (n=11) in about an hour, and 1.0% (n=2) had it over an hour later. However, 34.2% (n=67) of neonates' mothers could not tell the time it took for their babies to be placed in skin-to-skin contact with them. Mortality was 7.7% (n=15/196) among

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neonates who had immediate skin-to-skin contact and 21.2% (n=43/203) among those who did not have immediate skin-to-skin contact with their mothers. Fifteen percent 15% (n =59/399) of neonates were resuscitated, and about 42% (n=25/59) of those who were resuscitated died (95% CI: 29.87-54.87; p=<0.001). Breastfeeding was initiated in the delivery room for only 33.8% (n=135) of the neonates. The majority of the neonates (54.3%, n=209) were delivered in TTH, and 27.1% (n=108) of neonates were referred from other health facilities to the NICU.

Pattern of Diseases

The leading causes for admission to the NICU included neonatal sepsis, neonatal jaundice, prematurity, birth asphyxia, congenital anomalies, and others (Figure 1).

In a Chi-square test (Table 2), the following were all statistically significant with the outcome of admission; thus, prematurity OR=2.4, 95% CI: 1.67-3.36; p=<0.001), birth asphyxia (OR=2.5, CI: 1.48-4.14; p=0.001;), neonatal sepsis (OR=2.9, 95% CI: 1.46-5.80; p=0.002;), neonatal jaundice (OR=3.9, 95% CI: 1.63-9.38, p=0.001;) and SGA/LBW (OR=0.4, 95% CI: 0.25-0.76; p=0.003;). In binomial logistic regression (Table 3), prematurity was the main predictor of mortality (AOR=6.97, 95% CI: 1.77-27.54; p=0.006).

Table 2. Association between Pattern of Disease and Outcomes of NICU Admissions

Variable	Survived	Died	x^2	df	*p*-value
Prematurity			19.923	1	<0.001
Yes	67	27			
No	274	31			
Birth asphyxia			11.452	1	0.001
Yes	38	16			
No	303	42			
Neonatal sepsis			9.796	1	0.002
Yes	138	11			
No	203	47			
Neonatal jaundice			10.56	1	0.001
Yes	106	6			
No	235	52			
SGA/LBW			8.773	1	0.003
Yes	103	29			
No	238	29			

Kg: Kilogramme; LBW: Low Birth Weight; NICU: Neonatal Intensive Care Unit; SGA: Small for Gestational Age

Table 3. Predictors of neonatal outcome

Variable	AOR	95% Confidence Interval	P-value
Prematurity			
Yes	6.97	1.77, 27.54	0.006
No	Ref	Ref	Ref
Birth asphyxia			
Yes	0.33	0.05, 2.08	0.239
No	Ref	Ref	Ref
Neonatal sepsis			
Yes	1.75	0.49, 6.26	0.388
No	Ref	Ref	Ref
Neonatal jaundice			
Yes	0.60	0.17, 2.16	0.436
No	Ref	Ref	Ref
SGA/LBW			
Yes	0.30	0.14, 0.63	0.002
No	Ref	Ref	Ref

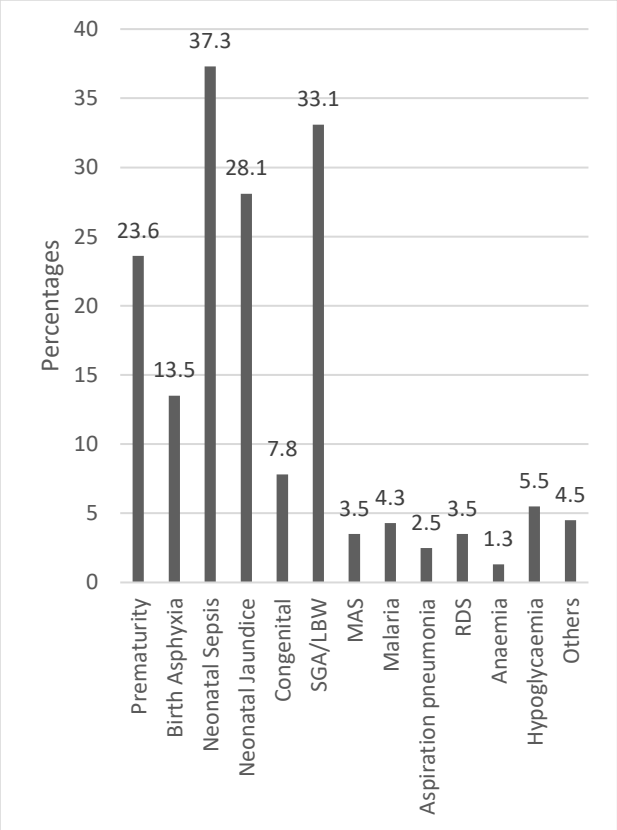

Figure 1. Patterns of Diseases in the NICU. MAS: Meconium Aspiration Syndrome; NICU: Neonatal Intensive Care Unit; SGA/LBW: Small for Gestational Age/Low Birth Weight; RDS: Respiratory Disease Syndrome

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Outcome of Admission

About 85.5% (n=341) of neonates in this study survived, and the remaining 14.5% (n=58) died (95% CI: 11.05 - 17.95). The total crude mortality rate in this study was 14.5% (n=58), in which 44.8% (n=26) were males and 55.2% (n=32) were females.

Discussion

The majority of the neonates admitted were males; this corroborates with other studies conducted in Ethiopia[2], Nigeria[14], and Ghana[11,13]. Ochoga and colleagues[14] have attributed the high number of male neonates in the NICU over females partly to cultural beliefs that more value is placed on the male baby over the females; hence, they will quickly be sent to the hospital when they are unwell. It could also be due to biological factors where surfactant markers like lecithin, phosphatidylglycerol, and phosphatidylinositol turn to appear earlier in females than males, making the females have relatively well-developed lungs than males at the time of birth[15,16].

The Apgar score is a tool used to tell the vitality of a newborn and has been proven to be essential in determining a newborn's survival[17]. In this study, 31% of the neonates had an Apgar score less than 7/10 in the first minute, and 15.5% had an Apgar score less than 7/10 in the fifth minute, a remarkable improvement in the vitality of the neonates in the fifth minute, which may be a sign of good resuscitation practices. Studies by Andegiorgish, Andemariam[18], Annan and Asiedu[17], Desalew, Sintayehu[19], and Owusu, Lim[11] found an association between Apgar score at 5 minutes and neonatal mortality. In a study by Annan and Asiedu[17], there was a significant association between the Apgar score of a neonate and its survival. Findings in this study agree with earlier findings that assert that neonates with Apgar scores of less than 7/10 in the fifth minute of life were more likely to record higher neonatal mortality as compared to their counterparts who scored ≥7/10[11, 20].

Thirty-eight percent (38%) of neonates in the present study had birth weights less than 2.5 kg. A Chi-Square analysis found a significant association between birth weight and neonatal outcome (VLBW, p=0.001 and ELBW, p=0.006). However, a binomial regression did not find birth weight as a predictor of neonatal mortality. In the study of Andegiorgish, Andemariam [18], nearly half (40.9%) of all ELBWs died. The case fatality rate for LBW was 24.8% in the study of Gunasekhar and Somasekhara[21]. Cavallin and colleagues attributed the burden of morbidity and mortality in the NICU to LBW[22]. In this study, 40% (n=10/25) of VLBW and 42.9% (n=3/7) of ELBW babies also died.

One cost-effective means of providing good thermo-regulation is by ensuring skin-to-skin contact between mother and baby. However, this current study found that, in the delivery room, more than half of the neonates did not get skin-to-skin contact with their mothers; nonetheless, some had skin-to-skin contact within 30 minutes of birth. Other neonates also received skin-to-skin care after 30 minutes, which does not qualify for immediate skin-to-skin care. It is noteworthy that immediate skin-to-skin care in this study is the mothers' self-report, and its accuracy cannot be ascertained. Nonetheless, the rate of skin-to-skin care in this study is higher than in the study by Abdul-Mumin, Dawuni[23]. There was high mortality among neonates who did not receive immediate skin-to-skin care following birth. This is similar to the studies by Cavallin, Bonasia[22], Demisse, Alemu[2], and Tekleab, Amaru[24] who also reported high cases of mortality due to hypothermia. In a Chi-Square analysis, this study also showed that neonates with hyperthermia had 4.28 (95%CI: 1.66-11.02; p=0.001) odds of dying compared to those who had normal body temperature. This conforms with the study by Desalew, Sintayehu[19] that, neonates with high temperature (fever) on admission were almost seven times more likely to die compared with their counterparts with normothermia.

The present study found that neonates who were resuscitated had an increased risk of mortality compared to their counterparts who were not resuscitated. This could be explained by the fact that neonates who required resuscitation had very poor vitality, as seen in their Apgar scores. It could also be because resuscitation is not optimally done (poor thermal control, the use of inappropriate devices and inadequate provider skills)[23,25]. Inadequate optimal post-resuscitation care and transport to the NICU may also contribute to the risk of death among resuscitated neonates. Providers of neonatal care, especially newborn resuscitation, should be adequately trained to offer such services.

Early initiation of breastfeeding is very essential in ensuring the immunity of infants to prevent infections and also a means of providing warmth for the neonates. It also positively influences the duration of exclusive breastfeeding[1]. It is one of the tested and tried means recommended by WHO to aid in the survival and thriving of neonates. In this study, less than half of the neonates, initiated breastfeeding in the delivery room. Early initiation of breastfeeding is key in preventing neonatal death, but ,Orsido, Asseffa[25] found in their study that breastfeeding in the first hour was seldom practiced or promoted. Desalew, Sintayehu[19] reported that neonates who did not initiate breastfeeding within 24 hours were 12 times more likely to die. In the current study, 84.5% (n=49/58) of neonates who died did not have breastfeeding initiated in the delivery room. However, poor vitality and early referral could be the reason for not achieving early initiation of breastfeeding.

The leading causes of admissions to the NICU and subsequent mortality in this study were neonatal sepsis, prematurity, neonatal jaundice, small for gestational age or low birth weight (SGA/LBW), and birth asphyxia. This agrees with studies conducted in Ghana and other LMICs[13,17,19,24]. This further confirms the WHO assertion that most neonatal deaths in LMICs are preventable (WHO, 2018; Demisse et al., 2017).

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Prematurity was the main predictor of mortality (AOR=6.974, 95% CI: 1.766-27.537; p=0.006). This can be explained by the high prevalence of complications associated with prematurity in our study, such as jaundice, sepsis, asphyxia and LBW. All these increase the risk of mortality in preterm neonates, explaining the reason for prematurity being a predictor of neonatal deaths consistent with other studies [2,13,17,19,24].

About half of the deaths in this study were early neonatal mortality; this is, however, lower than the finding of Farah et al. (2018), who recorded 96% of early neonatal mortality. This can be linked to different circumstances surrounding labour and delivery and immediate newborn care interventions.

The study-specific mortality rate in TTH NICU was 14.5%. This rate agrees with similar rates reported by other studies in Ghana, Nigeria, and Ethiopia[2,13,14]; all these other studies employed a retrospective design. The rate in this study was higher than the NMR in studies conducted in Eritrea[18]. Nonetheless, the finding in the current study was also lower than the 51.8% reported by Annan and Asiedu[17] in Ghana using a prospective design, the 33.3% reported by Weddih, Ahmed[26] in Mauritania that employed a retrospective design and the 23.1% that was reported in Ethiopia using a prospective design[24]. These different findings amongst studies could be explained partly by the variations in study design, sample size, type of hospital setting, and differences in the resources of the various hospitals where the studies were conducted.

Limitations

The strength of this present study hinges on it being the first prospective study to the best of our knowledge in the Tamale Teaching Hospital regarding the pattern and burden of diseases and factors affecting the outcome of admissions into the NICU. In interpreting the findings of this study for generalization, one needs to carefully consider the fact that this study was done in just three months; the duration was short and did not include all seasons of the year.

Another important limitation of the study is the single institution study site. This affects the generalizability of the findings.

Conclusion

The common causes of admission and deaths in the TTH NICU during the study were neonatal sepsis, prematurity, birth asphyxia, LBW/SGA and neonatal jaundice. This highlights the need for interventions to address these conditions as we strive to reduce institutional neonatal mortality.

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Author Contribution

Conceptualization: Sylvia Phaphali Adzitey; **Supervision:** Alhassan Abdul-Mumin, Victor Mogre; **Writing – original draft:** Sylvia Phaphali Adzitey; **Writing – review & editing:** Sylvia Phaphali Adzitey, Alhassan Abdul-Mumin, Victor Mogre.

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PREDICTING FACTORS OF LENGTH OF STAY AT A NEONATAL INTENSIVE CARE UNIT IN A TERTIARY HOSPITAL IN GHANA

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Abstract

Objective: The aim of this research was to determine the factors that influence the length of stay in the NICU of the Korle Bu Teaching Hospital (KBTH), Accra.

Methodology: This was a retrospective study involving 249 preterm infants who were admitted and discharged from the NICU, KBTH from November 2021 to October 2022. The multivariable negative binomial regression model was used to assess the factors associated with the number of hospital days among the newborns.

Results: The median number of days stayed in the NICU was 12 days (IQR: 8-21).

Predictor of shorter length of stay in the NICU was preterm infants with birthweight between 1500-2499g (aβ: -0.39, 95% CI: [-0.54, -0.24], p<0.001). Predictors of prolonged length of stay in the NICU were late initiation of breastmilk feeding (aβ: 0.31, 95% CI: [0.01, 0.60], p=0.040), preterm infants with neonatal jaundice (aβ: 0.15, 95% CI: [0.02, 0.28], p=0.023), neonatal sepsis (aβ: 0.44, 95% CI: [0.30, 0.57], p<0.001), and necrotising enterocolitis (aβ: 0.37, 95% CI: [0.16, 0.58], p<0.001).

Conclusion: Preterm infants who initiated breastmilk feeding late, developed neonatal sepsis, necrotising enterocolitis and neonatal jaundice were more likely to stay longer at the NICU. While those with birth weight between 1500-2499grams were likely to stay for a shorter period.

Key words: *length of stay, preterm, neonatal sepsis, necrotising enterocolitis*

Introduction

Preterm infants are likely to stay in a neonatal intensive care unit (NICU) for a longer period. This is because of their small size and the complications they may develop while on admission. Preterm infants are at the greatest risk of mortality. However, they may have to be nursed for long periods to gain adequate weight when they survive. In the process, they may develop complications such as late onset infections which would require antibiotics treatment for a longer period.[1] A prospective hospital-based study conducted in Ethiopia showed that, preterm infants who develop health care associated infections (HAIs) are more likely to have extended hospital stay.[1] In a systematic review with studies mostly from developed countries, it was found that preterm infants with necrotising enterocolitis, bronchopulmonary dysplasia, and retinopathy of prematurity are at high risk of prolonged length of stay (LOS).[2] It has been reported that being a male, very immature and small for gestational age are associated with prolonged length of stay.[3,4] In Port Harcourt, Nigeria, West[5] reported in a prospective hospital-based study that, LOS averagely ranged between 20 days for late preterm infants and 60 days for the extreme preterm infants. In Ethiopia, preterm infants with respiratory distress syndrome spent averagely 11 days to recover.[6] Thus, it is important for a facility or healthcare provider who sees to the day-to-day affairs of these infants to know the average LOS. Accurately predicting LOS at the NICU allows the health care providers to plan their resources, make decisions, counsel and educate parents. Most studies on LOS have come from high-income countries.[3,4,7] However, most preterm deliveries and mortalities are in low-and-middle-income countries (LMIC) like Ghana.[8]

In Ghana although there have been efforts to improve newborn and preterm survival over the past few years,[9,10] data on LOS of preterm infant admitted at the NICU is limited. Hence, it is vital to assess the possible factors that contribute to prolonged LOS in the NICUs in Ghana. Prolonged LOS could affect quality of care, patient safety and patient outcome.[11] The finding would help the care providers to plan administratively, conduct quality improvement research and help educate the parents of these vulnerable children. Thus, this study aimed to find the predictors of LOS among preterm infants admitted at the NICU of the Korle Bu teaching Hospital (KBTH), Accra.

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Materials and Methods

Study Design and Site

This is a retrospective study involving preterm infants admitted and discharged from the NICU, KBTH, Accra. The NICU of KBTH receives patients from the southern part of the country. It is a 60-bed capacity which takes care of preterm and term infants with varied complications. The average monthly admissions are about 150 infants. Forty-eight percent of these are preterm infants with varied conditions like respiratory distress syndrome, neonatal sepsis, neonatal jaundice, anemia of prematurity, and perinatal asphyxia. They are discharged home when they are not in distress, have

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achieved good thermoregulation in kangaroo mother care (KMC), have no acute medical or surgical condition that would endanger their survival at home, mother is able to take care of the baby and baby is gaining adequate weight.

Study Population

All preterm infants, 26-36 weeks post-conception, admitted and discharged alive in the NICU, KBTH from November 2021 to October 2022.

Exclusion Criteria

We excluded all preterm infants who died during the study period and those who stayed in the NICU for less than a day. Patients with missing information on sex, birth weight and gestational age were excluded. Furthermore, preterm infant with congenital anomalies and those who were transferred to other departments were also not included.

Study Variables

Data were extracted from the electronic medical records using Microsoft Excel 2016 spreadsheet. The variable of interest was length of NICU stay till discharge home. LOS was determined using days the infants were admitted to the day they were discharged home, and it was considered the dependent variable. Data were collected on the following independent or predictor variables: sex, gestational age (based on Modified Ballard's score),[12] mode of delivery, birth weight, time of initiation of feeds, time to achieve full feeds, co-morbidities (neonatal sepsis and or meningitis, necrotizing enterocolitis, neonatal jaundice, congenital anomalies, and infant of diabetic mother). We also collated data on maternal factors like age, occupation and maternal co-morbidities such as chronic hypertension, preeclampsia-eclampsia, gestational hypertension, gestational diabetes, sickle cell, asthma and HIV/AIDS. All the preterm infants admitted during the period in question constituted the study group. Patients were excluded if their data was incomplete.

Sample Size Estimates

The study sought to assess the length of stay in NICU among preterm newborns admitted and discharged alive. Due to the skewness observed in other studies,[2,13] and the study objective to estimate the median LOS, we adopted the sample size for continuous variables, given by $n=(z*\sigma/e)^2$, where, σ is the standard deviation of the length of stay, z is the standard normal score corresponding to the desired level of confidence and e is the margin of error. By approximation the standard deviation with interquartile range of 8 days,[14] at a 95% confidence level and a desire margin of error of 1 day, the minimum required sample size for the study is $n=(1.96*7\text{days}/1\text{day})^2 = 188.2$. However, due to the secondary data analysis and facility-based data extraction nature of the study, a total of 249 samples were successfully extracted within the study defined period and used for analysis.

Statistical Analysis

Stata IC version 16 (Stata Corp, College Station, TX, US) was used to analyze the data. Categorical characteristics of the study participants were described using frequency and percentages. Normally distributed continuous variables were summarized using the mean and standard deviation. Non-normally distributed variables were described using the median and interquartile range. The bar chart was used to describe the percentage of mothers with specific maternal conditions as well as the percentage of neonates with specific neonatal co-morbidities. The number of children were also described by the number of hospital days using the bar chart. The number of hospital days was categorized into the following four groups: <3 hospital days, 3-7 hospital days, 8-28 hospital days and >28 hospital days. The pie chart was used to describe the percentage of neonates according to the categories of number of hospital days.

The median and interquartile range of number of hospital days was estimated across all the maternal and child characteristics observed in the study. For characteristics with 2 categories, the Wilcoxon rank sum test was used to test the equality of medians between the two groups. For characteristics with 3 or more categories, the Kruskal Wallis test was used to test the equality of medians between the categories. For the categorized version of the length of stay, the Fisher's exact test was used to assess the association between the length of stay and the observed maternal and child characteristics.

The multivariable negative binomial regression model was used to assess the factors associated with the number of hospital days among the newborns. Both the crude and adjusted estimates were provided. Variables with significance level below 0.100 from the bivariate analysis (Wilcoxon rank sum test or Kruskal Wallis test) were only considered for the multivariate analysis. The 95% confidence interval of all crude and adjusted estimates and their corresponding p-values from the negative binomial regression model were estimated and provided in the analysis. All statistical analysis were considered significant at an alpha of 0.05.

Results

Characteristics of Child and Mother in the Study

A total of 249 children were considered for the analysis. The median age of the mothers was 30 years (IQR: 25-35 years). More than half of the newborns were males (51.8%). Most of the newborn (62.2%) were delivered through caesarean section. The median birthweight was 1,560 grams (IQR: 1,300-1,890 grams) with 13 below 1000 grams. The median gestational age at birth was 33 weeks (IQR: 31-34 weeks) with only 1 born before 28 weeks' gestation and 25.3% of them born between 28 and 31 weeks. Less than a quarter (23.3%) initiated breastfeeding during the first day, a third (33.3%) on day 2, 20.9% on day 3, 19.3% between day 4 and 7 and 3.2% after 7 days. Exclusive breastfeeding

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was practiced for 75.5% of the newborns, formula was given to 13.7% and 10.8% received both breastmilk and formula. (Table 1)

Table 1: Characteristics of study participants

	Total
Characteristics	**N=249**
Mother's age in years: Median (IQR)	30.0 (25.0-35.0)
Mother's age group	
15-19 years	23 (9.2)
20-29 years	84 (33.7)
30-39 years	125 (50.2)
40-49 years	17 (6.8)
Occupational class	
I	8 (3.2)
II	23 (9.2)
III-1	10 (4.0)
III-2	50 (20.1)
IV	96 (38.6)
V	42 (16.9)
Unknown	20 (8.0)
Sex	
Female	120 (48.2)
Male	129 (51.8)
Mode of delivery	
CS	155 (62.2)
SVD/BBA/Vacuum	94 (37.8)
Birthweight in grams: Median (IQR)	1560 (1300-1890)
Birthweight category	
<1,000 grams	13 (5.2)
1,000 to <1,500 grams	103 (41.4)
1,500 to <2,499 grams	133 (53.4)
Gestational age in weeks: Median (IQR)	33 (31-34)
Gestational age at birth category	
<28 weeks	1 (0.4)
28-31 weeks	63 (25.3)
32-33 weeks	84 (33.7)
34-36 weeks	101 (40.6)
Initial day of breastfeeding	
Day 1	58 (23.3)
Day 2	83 (33.3)
Day 3	52 (20.9)
Day 4-7	48 (19.3)
Day 8-14	8 (3.2)
Type of Feeds	
EBM	188 (75.5)
Formula	34 (13.7)
Mixed	27 (10.8)
Age of attainment of full feeds	
1-7 days	72 (28.9)
8-14 days	100 (40.2)
15-21 days	30 (12.0)
>21 days	18 (7.2)
Missing	29 (11.6)

Maternal Conditions

The most common maternal conditions were hypertension (36.9%) and ante-partum hemorrhage (15.7%). (Figure. 1)

Neonatal Co-Morbidities

The most common neonatal co-morbidities among the preterm infants were neonatal jaundice (61.8%), neonatal sepsis & meningitis (48.6%), and respiratory distress syndrome (28.1%). (Figure 2)

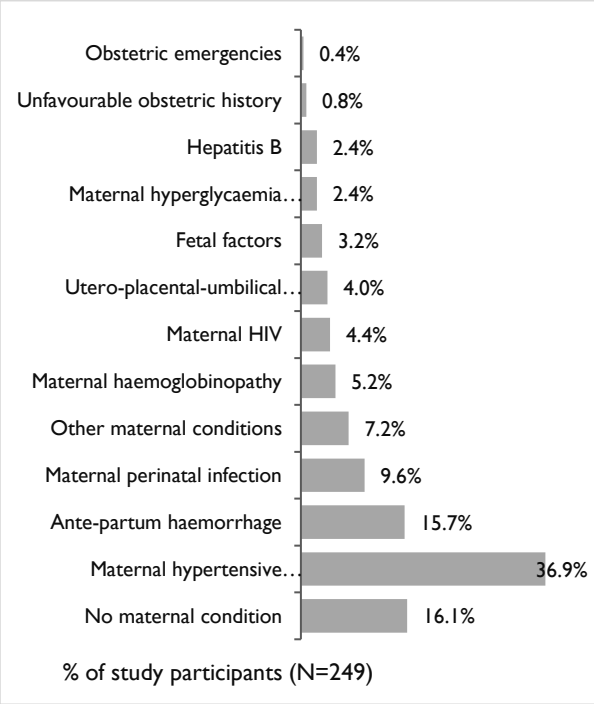

Figure 1: Prevalence of maternal conditions among mothers of the preterm infants

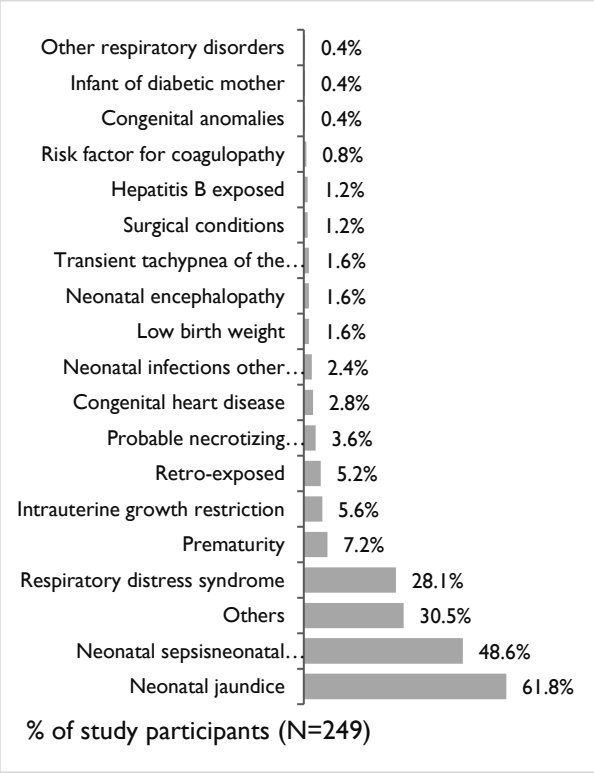

Figure 2: Prevalence of neonatal co-morbidities among study participants

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Length of stay in the NICU

The median number of days stayed in the hospital was 12 days with an interquartile range from 8 to 21 days. Among the 249 low birth weight neonates, 5.6% stayed for less than 3 days, 19.3% stayed for 3-7 days, 62.2% stayed for 8-28 days and 12.9% stayed beyond 28 days. (Figure 3)

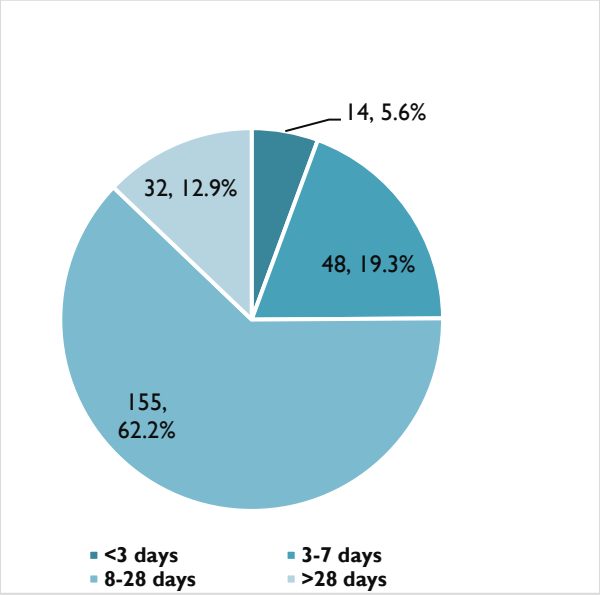

Figure 3: Length of stayed in the NICU

Bivariate Association Between Preterm Infant and Maternal Characteristics and Length Of Stay in the NICU

The median number of hospital days was statistically significantly higher among neonates with less than 1,000 grams of birth weight (29 days, IQR: 25-38 days) compared to neonates with 1,000 to <1,500 grams (18 days, IQR: 12-27 days) and neonates with 1,500 to 2,499 grams (8 days, IQR: 6-13 days) (p<0.001). Also, the median number of hospital days was significantly higher among neonates born before 32 gestational weeks (23 days, IQR:14-31 days) compared to newborns between 32-33 gestational weeks (13 days, IQR: 8.5-21 days) and 34-36 weeks (8 days, IQR: 5-12 days) (p<0.001). The median hospital days was lowest among neonates who initiated breastfeeding on day 1 (7 days, IQR: 3-11 days), followed by day 2 (10 days, IQR: 7-16 days), day 3 (14 days, IQR: 11-26 days) then days 4-7 (17 days, IQR: 12-25 days) and then days 8-14 (32.5 days, IQR: 19.5-39.5 days) (p<0.001). The median hospital days was highest among neonates who were given exclusive breastfeeding (13 days, IQR: 8-23 days) compared to neonates given formula only (8.5 days, IQR: 6-16 days) and mixed feeding (12 days, IQR: 7-23 days) (p=0.023). (Table 2). Table 2 also shows the association between preterm infant and maternal characteristics and the category of length of stay using the Fisher's exact test. (Table 2)

Bivariate association between preterm infant co-morbidities and length of stay in the NICU

The median number of days was statistically significantly higher among preterm infants with neonatal jaundice (13 days, IQR: 8-23 days) compared to those with no neonatal jaundice (10 days, IQR: 6-19 days) (p=0.017). Also, the median hospital days was higher among neonates with neonatal sepsis & meningitis (17 days, IQR: 12-28 days) compared to those with no neonatal sepsis & meningitis (9 days, IQR: 6-13 days) (p<0.001). The median hospital days was higher among neonates with respiratory distress syndrome (14 days, IQR: 9-26 days) compared to those with no respiratory distress syndrome (12 days, IQR: 7-18 days) (p=0.015**).** The median hospital days was higher among neonates with probable necrotizing enterocolitis (27 days, IQR: 10-26 days) compared to those with no probable necrotizing enterocolitis (12 days, IQR: 7-19.5 days) (p<0.001). (Table 3)

Table 3 also shows the association between preterm infant co-morbidities and the category of length of stay using the Fisher's exact test. (Table 3) None of the maternal conditions were statistically significantly associated with the number of hospital days of the neonates from both the Wilcoxon rank sum test and the Fisher's exact tests.

Multivariable analysis of the factors associated with the length of stay in the NICU

The adjusted negative binomial regression model showed that the average hospital days was 11% less among male newborns compared to female newborns (aβ: -0.11, 95% CI: [-0.23, 0.02], p=0.088) although not statistically significant. The average hospital days was 39% less among neonates with birthweight between 1500 to 2499 grams compared to neonates with birth weight less than 1,500 grams (aβ: -0.39, 95% CI: [-0.54, -0.24], p<0.001). Compared to neonates born before 32 weeks' gestation, the average hospital days was 22% and 42% less among neonates within 32–33 weeks' gestation (aβ: -0.22, 95% CI: [-0.39, -0.05], p=0.011) and 34-36 weeks' gestation (aβ: -0.42, 95% CI: [-0.60, -0.24], p<0.001). The average hospital days stayed for newborn infants who initiated breastfeeding on day 4 and beyond was 31% higher compared to those who initiated on day 1 (aβ: 0.31, 95% CI: [0.01, 0.60], p=0.040).

The average hospital days was 15% higher among neonates with neonatal jaundice (aβ: 0.15, 95% CI: [0.02, 0.28], p=0.023), 44% higher among neonates with neonatal sepsis & meningitis (aβ: 0.44, 95% CI: [0.30, 0.57], p<0.001), 37% higher among those with probable necrotising enterocolitis (aβ: 0.37, 95% CI: [0.16, 0.58], p<0.001) and 32% higher among those with neonatal infections other than NNS (aβ: 0.32, 95% CI: [0.00, 0.63], p=0.047). (Table 4)

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Table 2: Bivariate association between infant and maternal characteristics and length of stay in the hospital

		Number of days		Length of stay category				
		Stayed in hospital		<3 days	3-7 days	8-28 days	>28 days	
Characteristics	**N**	**Median (IQR)**	**P-value**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**P-value**
Overall	249	12.0 (8.0-21.0)		14 (5.6)	48 (19.3)	15 (62.2)	32 (12.9)	
Mother's age in years: Mean [±SD]				32.5 (28.0-36.0)	30.0 (26.5-33.5)	30.0 (25.0-36.0)	30.0 (24.0-34.0)	0.55 K
Mother's age group			0.850K					0.78 F
15-19 years	23	13.0 (9.0-25.0)		1 (4.3)	2 (8.7)	16 (69.6)	4 (17.4)	
20-29 years	84	12.0 (7.0-18.5)		4 (4.8)	18 (21.4)	52 (61.9)	10 (11.9)	
30-39 years	125	12.0 (7.0-22.0)		9 (7.2)	23 (18.4)	76 (60.8)	17 (13.6)	
40-49 years	17	12.0 (7.0-24.0)		0 (0.0)	5 (29.4)	11 (64.7)	1 (5.9)	
Occupational class			0.593 K					0.23 F
I	8	9.0 (7.0-13.5)		0 (0.0)	2 (25.0)	5 (62.5)	1 (12.5)	
II	23	11.0 (6.0-27.0)		2 (8.7)	6 (26.1)	10 (43.5)	5 (21.7)	
III-1	10	16.0 (8.0-19.0)		0 (0.0)	2 (20.0)	6 (60.0)	2 (20.0)	
III-2	50	11.5 (8.0-27.0)		1 (2.0)	10 (20.0)	27 (54.0)	12 (24.0)	
IV	96	12.0 (7.0-17.0)		8 (8.3)	19 (19.8)	65 (67.7)	4 (4.2)	
V	42	12.0 (9.0-20.0)		3 (7.1)	5 (11.9)	29 (69.0)	5 (11.9)	
Unknown	20	18.0 (8.0-25.0)		0 (0.0)	4 (20.0)	13 (65.0)	3 (15.0)	
Sex			0.129W					0.076 F
Female	120	13.5 (7.0-24.0)		4 (3.3)	27 (22.5)	69 (57.5)	20 (16.7)	
Male	129	11.0 (8.0-17.0)		10 (7.8)	21 (16.3)	86 (66.7)	12 (9.3)	
Mode of delivery			0.544 W					0.70 F
CS	155	12.0 (8.0-22.0)		7 (4.5)	29 (18.7)	100 (64.5)	19 (12.3)	
SVD/BBA/Vacuum	94	12.0 (6.0-19.0)		7 (7.4)	19 (20.2)	55 (58.5)	13 (13.8)	
Birthweight in grams: Median (IQR)				1918 (1600-2400)	1932 (1748-2140)	1480 (1300-1760)	1168 (1020-1380)	<0.001 K
Birthweight category			<0.001 K					<0.001 F
<1,000 grams	13	29.0 (25.0-38.0)		0 (0.0)	0 (0.0)	6 (46.2)	7 (53.8)	
1,000 to <1,500 grams	103	18.0 (12.0-27.0)		3 (2.9)	4 (3.9)	74 (71.8)	22 (21.4)	
1,500 to <2,499 grams	133	8.0 (6.0-13.0)		11 (8.3)	44 (33.1)	75 (56.4)	3 (2.3)	
Gestational age in weeks: Median (IQR)				34 (33-36)	34 (33-35)	33 (32-34)	30 (30-32)	<0.001 K
Gestational age at birth category			<0.001 K					<0.001
<32 weeks	64	23.0 (14.0-31.0)		0 (0.0)	5 (7.8)	38 (59.4)	21 (32.8)	
32-33 weeks	84	13.0 (8.5-21.0)		4 (4.8)	9 (10.7)	62 (73.8)	9 (10.7)	
34-36 weeks	101	8.0 (5.0-12.0)		10 (9.9)	34 (33.7)	55 (54.5)	2 (2.0)	
Day of initial breastfeeding			<0.001 K					<0.001 F
Day 1	58	7.0 (3.0-11.0)		11 (19.0)	19 (32.8)	26 (44.8)	2 (3.4)	
Day 2	83	10.0 (7.0-16.0)		2 (2.4)	20 (24.1)	53 (63.9)	8 (9.6)	
Day 3	52	14.0 (11.0-26.0)		0 (0.0)	5 (9.6)	38 (73.1)	9 (17.3)	
Day 4-7	48	17.0 (12.0-25.0)		1 (2.1)	4 (8.3)	35 (72.9)	8 (16.7)	
Day 8-14	8	32.5 (19.5-39.5)		0 (0.0)	0 (0.0)	3 (37.5)	5 (62.5)	
Type of Feeds			0.023 K					0.015 F
EBM	188	13.0 (8.0-23.0)		9 (4.8)	29 (15.4)	123 (65.4)	27 (14.4)	
Formula	34	8.5 (6.0-16.0)		4 (11.8)	10 (29.4)	20 (58.8)	0 (0.0)	
Mixed	27	12.0 (7.0-23.0)		1 (3.7)	9 (33.3)	12 (44.4)	5 (18.5)	
Age of attainment of full feeds			<0.001 K					<0.001 F
1-7 days	72	7.0 (5.0-10.0)		2 (2.8)	45 (62.5)	24 (33.3)	1 (1.4)	
8-14 days	100	13.0 (10.0-17.0)		0 (0.0)	0 (0.0)	93 (93.0)	7 (7.0)	
15-21 days	30	25.5 (19.0-29.0)		0 (0.0)	0 (0.0)	21 (70.0)	9 (30.0)	
>21 days	18	39.5 (29.0-48.0)		0 (0.0)	0 (0.0)	4 (22.2)	14 (77.8)	

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Table 3: Bivariate association between neonatal co-morbidities and length of stay in the NICU

		Number of days	Wilcoxon	Length of stay category				Fisher's
		Stayed in hospital	Rank sum	<3 days	3-7 days	8-28 days	>28 days	Exact
Neonatal co-morbidities	**N**	**Median (IQR)**	**P-value**	**n/N (%)**	**n/N (%)**	**n/N (%)**	**n/N (%)**	**P-value**
Neonatal jaundice			0.017					0.004
No	95	10.0 (5.0-19.0)		11 (11.6)	21 (22.1)	49 (51.6)	14 (14.7)	
Yes	154	13.0 (8.0-23.0)		3 (1.9)	27 (17.5)	106 (68.8)	18 (11.7)	
Neonatal sepsis + neonatal meningitis			<0.001					<0.001
No	128	9.0 (6.0-13.0)		13 (10.2)	39 (30.5)	73 (57.0)	3 (2.3)	
Yes	121	17.0 (12.0-28.0)		1 (0.8)	9 (7.4)	82 (67.8)	29 (24.0)	
Others			0.556					0.380
No	173	12.0 (8.0-22.0)		12 (6.9)	30 (17.3)	107 (61.8)	24 (13.9)	
Yes	76	11.5 (7.0-20.0)		2 (2.6)	18 (23.7)	48 (63.2)	8 (10.5)	
Respiratory distress syndrome			0.014					0.012
No	179	12.0 (7.0-18.0)		13 (7.3)	34 (19.0)	116 (64.8)	16 (8.9)	
Yes	70	14.0 (9.0-26.0)		1 (1.4)	14 (20.0)	39 (55.7)	16 (22.9)	
Intrauterine growth restriction			0.599					0.660
No	235	12.0 (7.0-21.0)		14 (6.0)	45 (19.1)	147 (62.6)	29 (12.3)	
Yes	14	12.5 (10.0-23.0)		0 (0.0)	3 (21.4)	8 (57.1)	3 (21.4)	
Retro-exposed			0.065					0.180
No	236	12.0 (7.0-19.5)		13 (5.5)	48 (20.3)	144 (61.0)	31 (13.1)	
Yes	13	23.0 (10.0-26.0)		1 (7.7)	0 (0.0)	11 (84.6)	1 (7.7)	
Probable necrotising enterocolitis			<0.001					0.042
No	240	12.0 (7.0-19.0)		14 (5.8)	48 (20.0)	150 (62.5)	28 (11.7)	
Yes	9	27.0 (25.0-48.0)		0 (0.0)	0 (0.0)	5 (55.6)	4 (44.4)	
Congenital heart disease			0.365					1.000
No	242	12.0 (7.0-21.0)		14 (5.8)	47 (19.4)	150 (62.0)	31 (12.8)	
Yes	7	17.0 (9.0-27.0)		0 (0.0)	1 (14.3)	5 (71.4)	1 (14.3)	
Neonatal infections other than NNS			0.123					0.084
No	243	12.0 (7.0-21.0)		14 (5.8)	47 (19.3)	153 (63.0)	29 (11.9)	
Yes	6	23.0 (11.0-46.0)		0 (0.0)	1 (16.7)	2 (33.3)	3 (50.0)	
Low birth weight			0.594					0.810
No	245	12.0 (7.0-21.0)		14 (5.7)	48 (19.6)	151 (61.6)	32 (13.1)	
Yes	4	10.0 (9.0-13.0)		0 (0.0)	0 (0.0)	4 (100.0)	0 (0.0)	
Neonatal encephalopathy			0.939					1.000
No	245	12.0 (8.0-21.0)		14 (5.7)	47 (19.2)	152 (62.0)	32 (13.1)	
Yes	4	13.5 (9.0-16.0)		0 (0.0)	1 (25.0)	3 (75.0)	0 (0.0)	
Transient tachypnoea of the new-born			0.323					0.420
No	245	12.0 (8.0-21.0)		14 (5.7)	46 (18.8)	153 (62.4)	32 (13.1)	
Yes	4	7.5 (7.0-13.5)		0 (0.0)	2 (50.0)	2 (50.0)	0 (0.0)	
Surgical conditions			0.802					0.380
No	246	12.0 (8.0-21.0)		14 (5.7)	47 (19.1)	154 (62.6)	31 (12.6)	
Yes	3	8.0 (5.0-48.0)		0 (0.0)	1 (33.3)	1 (33.3)	1 (33.3)	
Hepatitis B exposed			0.081					0.540
No	246	12.0 (7.0-21.0)		14 (5.7)	48 (19.5)	153 (62.2)	31 (12.6)	
Yes	3	20.0 (17.0-42.0)		0 (0.0)	0 (0.0)	2 (66.7)	1 (33.3)	
Risk factor for coagulopathy			0.144					0.610
No	247	12.0 (8.0-21.0)		14 (5.7)	47 (19.0)	154 (62.3)	32 (13.0)	
Yes	2	6.5 (5.0-8.0)		0 (0.0)	1 (50.0)	1 (50.0)	0 (0.0)	
Congenital anomalies			0.193					0.380
No	248	12.0 (8.0-21.0)		14 (5.6)	47 (19.0)	155 (62.5)	32 (12.9)	
Yes	1	5.0 (5.0-5.0)		0 (0.0)	1 (100.0)	0 (0.0)	0 (0.0)	
Infant of diabetic mother			0.686					1.000
No	248	12.0 (7.5-21.0)		14 (5.6)	48 (19.4)	154 (62.1)	32 (12.9)	
Yes	1	10.0 (10.0-10.0)		0 (0.0)	0 (0.0)	1 (100.0)	0 (0.0)	
Other respiratory disorders			0.098					0.180
No	248	12.0 (7.5-21.0)		14 (5.6)	48 (19.4)	155 (62.5)	31 (12.5)	
Yes	1	54.0 (54.0-54.0)		0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)	

%: Row percentages. F: P-value from Fishers exact test. W: p-value from the Wilcoxon rank sum test. K: p-value from the Kruskal Wallis test

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Table 4: Negative binomial regression models of factors associated with the length of stay in the hospital among preterm infants admitted at NICU, KBTH, Accra

	Negative binomial regression model of number of hospital days				
	Unadjusted model			Adjusted model	
Characteristics	**uβ [95% CI]**	**P-value**		**aβ [955 CI]**	**P-value**
Sex					
Female	0.00 [reference]			0.00 [reference]	
Male	-0.19 [-0.38, -0.01]	0.044		-0.11 [-0.23, 0.02]	0.088
Birth weight					
<1,500 grams	0.00 [reference]			0.00 [reference]	
1,500-2,499 grams	-0.81 [-0.97, -0.64]	<0.001		-0.39 [-0.54, -0.24]	<0.001
Gestational age					
<32 weeks	0.00 [reference]			0.00 [reference]	
32-33 weeks	-0.38 [-0.58, -0.17]	<0.001		-0.22 [-0.39, -0.05]	0.011
34-36 weeks	-0.93 [-1.12, -0.74]	<0.001		-0.42 [-0.60, -0.24]	<0.001
Breastfeeding initiation					
Day 1	0.00 [reference]			0.00 [reference]	
Day 2	0.33 [0.02, 0.65]	0.038		0.04 [-0.22, 0.30]	0.761
Day 3	0.73 [0.40, 1.06]	<0.001		0.20 [-0.08, 0.48]	0.155
Day 4+	0.82 [0.49, 1.14]	<0.001		0.31 [0.01, 0.60]	0.040
Type of feeds					
EBM only	-0.01 [-0.36, 0.34]	0.948		-0.17 [-0.41, 0.08]	0.179
Formula only	-0.47 [-0.87, -0.08]	0.019		-0.32 [-0.64, -0.01]	0.043
Mixed	0.00 [reference]			0.00 [reference]	
Neonatal comorbidities					
Neonatal jaundice	0.17 [-0.03, 0.38]	0.098		0.15 [0.02, 0.28]	0.023
Neonatal sepsis & meningitis	0.75 [0.59, 0.91]	<0.001		0.44 [0.30, 0.57]	<0.001
Respiratory distress syndrome	0.30 [0.10, 0.51]	0.004		0.06 [-0.07, 0.19]	0.339
Probable necrotising enterocolitis	0.85 [0.58, 1.12]	<0.001		0.37 [0.16, 0.58]	<0.001
Neonatal infections other than NNS	0.59 [0.03, 1.15]	0.040		0.32 [0.00, 0.63]	0.047

uβ: Unadjusted coefficient estimate. aβ: adjusted coefficient estimate. CI: Confidence interval

Discussion

The ability to predict the length of stay is very crucial in the clinical and administrative practices of a given facility as it provides the information for counselling of the parents and plan the day-to-day running of the institution. In this study, the median LOS was 12 days. This is similar to what was found by Aljohani and his team[13] in Saudi Arabia. However, this is prolonged compared to what Kanimozhi and team[14] found in India. This might be because our study population included only few extreme low birth weight infants who are known to stay in the NICU for a longer period. This is demonstrated in our study where preterm infants who were born at 32-36 weeks' gestation had shorter during of hospital stay compared to those born less than 32 weeks. There was also a similar trend concerning infants who weighed between 1500 and 2499g and those below 1500g, meaning the more advanced in age and in body weight the infant, the shorter the duration of stay.

In our study preterm infants who were exclusively formula-fed had on average shorter duration of hospital stay compared to those who were on mixed feeding and exclusive breastmilk feeding. Even though it is a common practice in this study centre to practice exclusive breastfeeding at birth, there are instances where preterm infants are fed with formula. For example, when there is a demise of a mother, or the mother is too ill to provide expressed breastmilk. Also, some parents of patients who are HIV-exposed do opt to formula-feed their babies. The finding in this study could be because the preterm formula has a higher protein content compared to the breastmilk[15] which contributes to adequate weight gain and as such the infants will meet the criteria for discharge earlier. This finding might be due to chance for that matter the authors advocate strongly that breastmilk feeding should be the primary option, and formula should be used in extreme circumstances such as stated above. The study found that preterm infants with co-morbidities like neonatal infections, neonatal jaundice and probable necrotising enterocolitis had prolonged stay. This is like findings by different authors from different geographical location.[2,16] These findings call for policies which will help reduce the frequent occurrences of these condition among this patient population. It is well-known that a simple activity like frequent handwashing goes a long way to preventing neonatal sepsis. It is also to be advocated that preterm infants should be fed with breastmilk to help curb the rate of necrotizing enterocolitis.

Maternal conditions as risk factors for LOS in the NICU is controversial.[2] None of the maternal conditions were associated with length of stay in the present study. This is contrary to finding in China by Zhang et al[7] who found that maternal hypertension, primigravida and caesarean section were associated with prolonged LOS.

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Limitation

For being a retrospective study, we were not able to verify the information that were on the EMR. Concerning the variable "age of attainment of full feed", there were 29 (11.6%) participants that we could not retrieve their data because they were not documented on the EMR.

Conclusion

Knowing the length of stay of the preterm infants in the NICU will help alleviate the emotional and economic burden on the family and the institution attending to these infants. The factors affecting the LOS in the study population are birth weight, gestational age, time to initiate breastfeeding, neonatal infection, probable necrotising enterocolitis and neonatal jaundice. Appropriate measures like hand hygiene, early initiation of breastfeeding and early diagnosis and treatment of neonatal jaundice and neonatal sepsis can go a long way to reducing the LOS in this centre.

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Authors Contributions

KAE: conceptualization, methodology, interpretation of the results, wrote the first draft of the manuscript. NOK: conceptualization, collection of data, reviewing and editing the manuscript. YA: methodology, analysis of the data, interpretation of the results, reviewed the manuscript.

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RELIGIOUS MANDATORY PREMARITAL HIV TESTING; ASSESSMENT OF PERCEPTIONS ON ETHICAL CONCERNS AMONG HEALTHCARE WORKERS IN KWAEBIBIREM

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Abstract

Objective: This cross-sectional survey describes healthcare workers' (HCWs') perceptions on religious mandatory premarital HIV testing- (RMPmHT) associated ethical concerns.

Methodology: An online survey was completed with an e-questionnaire, circulated via WhatsApp, (a freeware, centralized instant messaging cross-platform). This involved 530 participants and data were descriptively analyzed using Epi info 3.5.1.

Results: The findings illustrate that HCWs, mostly aged 30 or younger with a mean age of 30.4 (±7.2), were largely familiar with RMPmHT, (58.5%). Despite general acceptance, disclosing positive results to RO leadership was widely discouraged. HCWs considered RMPmHT non-intrusive, yet paradoxically believed it increased the risk of stigmatization. Despite an unclear ethical paradigm and state silence on RMPmHT, HCWs didn't see knowledge of a positive result as a 'right' for RO leadership. Policy frameworks for 'medico-legal' permission and result disclosure were seen as ambiguous. Concerns about fragile confidentiality structures persist, and the prohibition of marriages for HIV-positive or RMPmHT-dissenting couples was widely deprecated.

Conclusion: RMPmHT, tenably, infringes upon the right to marry and found a family, bodily integrity, privacy, and information as negative results may subtly be a precondition for marriage. Advocacy for the need to situate RMPmHT in a clear ethical paradigm remains imperative. Policy frameworks guiding documentation of consent processes, HIV couple discordancy, counselling, information, disclosure, data management and linking RMPmHT services to public health institutions should be engendered.

Key words: *Mandatory, premarital, HIV, testing, Ethics, religious*

Introduction

Religious organizations (RO) and governments in various countries have, over the years, implemented Mandatory Premarital HIV Testing (MPmHT) programs as part of their efforts to control HIV infection. It is a common practice to link positive test results with the prohibition of marriage[1]. Besides infringing upon the human rights of people living with HIV (PLHIV), this practice threatens three key principles of HIV testing: free consent, pre- and post-test counseling, and the confidentiality of test results[1]. Within the context of social determinants influencing HIV infection and the broader social impact of the pandemic, ethical questions, inherently interconnected, present numerous challenging complexities[2]. The four pillars of medical ethics—autonomy, non-maleficence, beneficence, and justice—constitute overarching principles that, nonetheless, permit interpretation and judgment in specific cases[2].

Mandatory HIV testing, frequently characterized by unclear pathways for voluntary consent and its imposition as a prerequisite for accessing civil or social benefits, is subtly discouraged by policies governing HIV control[2]. Current efforts to enhance the utilization of testing services are generating ethical concerns, notably stemming from the increasing emphasis on 'opt-out' approaches, which exhibit marginal yet notable distinctions from coercive methods [2]. MPmHT is globally promoted, notwithstanding its limited attention in the field of bioethics literature[3]. The expansion of testing opportunities is crucial for disease control, even in the presence of an ambiguous ethical framework. HIV testing is primarily provided before marriage, during childbirth, and during any hospital visit [3]. The relatively neglected subject of MPmHT, often characterized by undocumented procedures, exists within a realm of obscurity [3]. Civil rights groups have raised human rights concerns about prohibiting marriage for those with positive HIV test results.[3,4].

Understanding contextual distinctions between Premarital HIV Testing (PmHT) policies therefore remains essential[5]. The ambiguous use of the terms 'voluntary,' 'mandatory,' and 'compulsory' in reference to testing modalities often leads to an incomplete understanding of the distinctions between them, further blurring their individual ethical significance.[5]. The terms 'voluntary' and 'compulsory' pertain to the methods of offering testing, generating results, and disclosing those results. It's important to note that while testing itself can be voluntary, the possession of test results may be mandatory as a prerequisite for accessing certain civil or social benefits[5]. Voluntary Pre-marital

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HIV Testing (VPmHT), equivalent to Voluntary Counseling and Testing (VCT), includes various methods for testing individuals intending to marry. MPmHT, on the other hand, pertains to policies where a negative test result is *prerequisite* for accessing civil, social, and/or religious benefits, such as marriage, immigration, employment, etc.[5]. Mandatory' is therefore not synonymous with 'compulsory' testing. Both VPmHT and MPmHT involve diverse approaches to disclosing and maintaining the confidentiality of results. This survey examines the ethical concerns of MPmHT from the perspective of Healthcare Workers (HCWs), with a focus on religious MPmHT (RMPmHT).

Materials and Methods

Study Site and Design

This descriptive online survey involved the administration of a self-administered, structured, pretested electronic questionnaire (or e-questionnaire) to a total of 530 HCWs in the Kwaebibirem Municipal area of the Eastern administrative Region of Ghana. The preferred administration of e-questionnaires via WhatsApp, initially due to COVID-19 safety concerns, offered advantages like convenience, cost-effectiveness, data handling efficiency, eco-friendliness, and accessibility. This approach ensured data security, flexibility, and ease of data importation for analysis, making it a robust choice for this survey beyond pandemic-related considerations. The e-questionnaire was distributed as a link accessible on smartphones with internet connectivity. Participants were provided with comprehensive information about their right to participate or decline without coercion prior to accessing the e-questionnaire. The participant pool included HCWs from the Kwaebibirem Municipal area, covering the municipal hospital, four health centers, and twenty-nine CHPS compounds. Convenience sampling was used, allowing all willing HCWs to participate. This approach was preferred as the number of HCWs approximately matched the sample size. Including other districts for probability sampling was avoided to prevent administrative challenges.

The e-questionnaire, following pre-testing in the Upper West Akyem and Denkyembuor districts, was subsequently distributed to HCWs in Kwaebibirem via the WhatsApp smart mobile phone application. The contact information for HCWs was obtained from the administrative units of both the Kade Government Hospital and the Kwaebibirem Municipal Health Directorate. Before distributing the e-questionnaire link, prospective participants were individually contacted via phone by the principal investigator, who is also a HCW known to all. The calls began with a brief self-introduction by the principal investigator, followed by a concise explanation of the survey's purpose, objectives, and participation criteria. Participants were informed of their right to decline participation at any stage of the e-questionnaire process. A scanned letter emphasizing this right was sent with the e-questionnaire link to consenting HCWs. The e-questionnaire did not include personal information like names and residential addresses that could identify participants. Although all questionnaires were returned, the lack of uniform responses led to inconsistent subgroup totals in the subgroup analysis.

We utilized the Likert Scale to assess participants' agreement or disagreement levels with hypothetical scenarios related to RMPmHT. In this survey, the term 'healthcare workers (HCWs)' was operationally defined broadly to include all Ghana Health Service staff in Kwaebibirem working across different health facilities. However, specific categories of employees, including janitorial services, drivers, morgue attendants, and security guards, were excluded from the survey. This decision was grounded in the assumption that their educational backgrounds might pose challenges for self-administration of the e-questionnaire. Moreover, their exclusion aimed to mitigate potential researcher bias when interpreting questions for HCWs incapable of self-administration. This particular group of HCWs was also observed to be less active on the few WhatsApp groups to which they belong. The survey participants primarily comprised government hospital staff directly or indirectly involved in clinical service delivery. This included personnel from various clinical units, such as doctors, nurses, and midwives, as well as staff from pharmacy, administration, finance, records, National Health Insurance Vetting, and X-ray departments. Participants associated with the municipal health directorate included personnel from all lower-level health facilities. This included HCWs engaged in both clinical and preventive health service delivery, along with administrative staff at the municipal health directorate. The primary focus of the e-questionnaire was to gather information on participants' age, gender, and their general familiarity with RMPmHT. The e-questionnaire also incorporated hypothetical scenarios designed to solicit participants' opinions regarding their willingness to disclose positive results of PmHT to RO leadership. These scenarios aimed to assess HCWs' perspectives on linking PmHT results to marriage without obtaining prior full individual consent for testing. Additionally, the survey aimed to capture HCWs' opinions on the fundamental distinctions between coercion and mandatory testing.

Ethical Consideration

Approval for the execution of the study was obtained from the Ethical Review Committee of the Ghana Health Service – Research and Development Division (GHS-ERC:029/10/23).

Data Analysis

We performed descriptive data analysis using Epi Info version 3.5.1 to calculate the frequency and percentage distribution of all variables. The results, primarily expressed as proportions and arithmetic means with associated standard deviations, were presented in tabular formats.

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Results

The age distribution among HCWs spanned from 21 to 60 years. The mean age of the entire cohort was 30.4 years (±7.2), with a variance of 52.44. Predominantly, HCWs fell within the age range of 20-30 years, followed by those aged 31-40 years, and a notable minority comprising individuals aged 41 years and older. Marital status analysis revealed that the majority of HCWs were single, followed by those who were married or cohabiting, with a notable proportion being divorced. A substantial majority of HCWs expressed familiarity with RMPmHT, indicating it was consistently considered a prerequisite for marriage in their respective ROs. Most HCWs identified as Christian, while a minority adhered to Islam, and a smaller portion subscribed to other religions. Table 1

Table 1 Evaluation of demographic characteristics and awareness of religious mandatory premarital HIV testing among healthcare workers

Characteristic	Frequency – N (%)
Age group	
≤ 30 years	344 (65.6)
31-40 years	140 (26.7)
41-50 years	22 (4.2)
≥ 51 years	18 (3.4)
Marital status	
Married/cohabitation	209 (39.5)
Single	308 (58.2)
Divorced	12 (2.3)
Familiarity with RMPmHT	
Yes	307 (58.5)
No	218 (41.5)
Religion	
Christian	484 (92.0)
Muslim	40 (7.6)
Other	2 (0.4)

RMPmHT – Religious mandatory premarital HIV testing, RO – Religious Organization Source: ©Authors survey, 2024

The communication of a potentially positive RMPmHT result to Religious Organization (RO) leadership was largely discouraged. Despite an unclear ethical framework, the majority of respondents strongly advocated for the continuation of PmHT before marriage. RMPmHT was commonly characterized as inherently non-intrusive and non-coercive, subtly implying an endorsement for its promotion. The hypothetical assertion that RO leadership had the 'right' to be informed about a member's PmHT result was generally met with resistance. A modest majority indicated discomfort with the prospect of remaining in their RO of affiliation in the event of a positive RMPmHT result. National policy frameworks outlining the medico-legal permissions for conducting tests and accessing test results for Voluntary Counseling and Testing (VCT), Voluntary Pre-Marital Health Testing (VPmHT), Mandatory Pre-Marital Health Testing (MPmHT or RMPmHT) were perceived to be absent.

HCWs expressed a notable observation that the state maintained a conspicuous silence on matters related to RMPmHT. The vast majority voiced concerns, indicating that RO leadership's attitudes toward members with positive RMPmHT results could inadvertently lead to subtle or overt scorn, and technically, stigmatization. Moreover, respondents overwhelmingly believed that the eventual unauthorized disclosure of RMPmHT positive results by RO leadership to other RO members and/or non-members was likely to transpire over time. This suggested a perception that RO leadership might eventually fail to maintain confidentiality regarding a member's positive status, anticipating that it would inevitably become public knowledge at some point.Table 2

Table 2.0: Healthcare workers' general opinions on religious mandatory premarital HIV testing and preferred responses to a hypothetical positive test result

Characteristic	Frequency – N (%)	
	Yes	No
Positive test result - leaders should be informed	191 (36.0)	339 (64.0)
Should premarital HIV testing be discontinued	149 (29.9)	350 (70.1)
Test regardless of couple's willingness	359 (67.9)	170 (32.1)
Premarital HIV testing is coercion	211 (40.5)	310 (59.5)
Marriage should be permissible in the absence of testing	198 (37.9)	324 (62.1)
Information about results is a leaders' 'right"	120 (22.8)	406 (77.2)
Positive result - leadership's confidentiality assured	99 (18.9)	426 (81.1)
Positive result - Leadership will never stigmatize	90 (17.9)	412 (82.1)
Positive result - would still attend religious organization	291 (56.8)	221 (43.2)
Clear policy - permission to test/know results	127 (24.8)	386 (75.2)
Do you know who is permitted to test/know results?	193 (37.8)	318 (62.2)
Religious HIV testing is inconspicuous in Ghana	316 (63.2)	184 (36.8)
Preferred individual actions to a hypothetically positive religious mandatory premarital HIV test result		
Stay but no tell anyone	153 (28.9)	377 (71.1)
Leave the religious organization	58 (10.9)	472 (89.1)
Stay and tell the leadership	66 (12.5)	464 (87.5)
Loose interest in the marriage	101 (19.1)	429 (80.9)
Marry outside of the religious organization	92 (17.4)	438 (82.6)
Tell my partner	280 (52.8)	250 (47.2)
I don't know	27 (5.1)	503 (94.9)

Source: ©Authors survey, 2024

HCWs exhibited diverse individual reactions to the hypothetical scenario of a positive RMPmHT result, with the majority expressing their intention to inform

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their partners, irrespective of their partners' test results, among other potential responses. [Table 3.0]

A proclivity for a voluntary approach to PmHT is evident, juxtaposed against the current mandatory framework. HCWs posit that ROs should solicit the preferences of prospective couples regarding their inclination to undergo PmHT. It is emphasized that dissent, within a voluntary framework, expressed by either partner, should not precipitate impediments to the marriage approval process by the respective ROs. HCWs predominantly advocate for a delimited dissemination of RMPmHT results exclusively to the prospective marital couple, precluding disclosure to RO leadership. The prevailing recommendation underscores that ROs should ascertain the couples' voluntary willingness to partake in testing, with the resultant test outcomes reserved for the exclusive knowledge of the implicated individuals. Table 4

Table 3.0: Healthcare workers' perspectives on marriage officiation and confidentiality of religious mandatory premarital HIV test results

Characteristic	Frequency – N (%)	
	Marry irrespective of result	Only couple to know result
Strongly disagree	59 (11.7)	34 (6.8)
Somewhat disagree	18 (3.6)	11 (2.2)
Neither agree nor disagree	25 (4.9)	17 (3.4)
Somewhat agree	90 (17.8)	62 (12.3)
Strongly agree	314 (62.1)	379 (93.2)

Source: ©Authors survey, 2024

Table 4.0: Healthcare workers' perspectives on the efficacy and ethical implications of religious mandatory premarital HIV testing: 'effective for infection control' vs. 'fraught with ethical concerns

Characteristic	Frequency – N (%)
Efficacy of religious mandatory premarital HIV testing for HIV infection control – "it is good for infection control"	
Strongly Agree	368 (70.50)
Agree	95 (18.20)
Neutral	46 (8.80)
Disagree	4 (0.80)
No Opinion	9 (1.70)
Perspectives on the ethical implications of mandatory premarital HIV testing – "it is fraught with ethical concerns"	
Strongly disagree	209 (40.3)
Somewhat disagree	40 (7.7)
Neither agree nor disagree	25 (4.8)
Somewhat agree	98 (18.9)
Strongly agree	147 (28.3)

Source: ©Authors survey, 2024

The practice of RMPmHT was predominantly characterized as a commendable measure believed to hold the potential for augmenting HIV infection control. However, divergent viewpoints were expressed by some, indicating dissenting perspectives on the matter.

The majority of HCWs appraised RMPmHT as a routine procedure without notable ethical concerns. Consequently, in their evaluations, they commonly regarded it as both 'acceptable' and 'necessary.

Discussion

The promotion and extensive adoption of MPmHT by RO or RMPmHT, persist, notwithstanding its limited scrutiny within the bioethics literature[3-5]. Although these policies may appear to enhance the utilization of HIV services, they are commonly instituted in areas where HIV/AIDS is highly stigmatized, leading to significant ethical considerations that are subject to extensive debate[5]. MPmHT is implemented and sanctioned in Bahrain, Guinea, the United Arab Emirates, and Saudi Arabia, within the framework of both moral principles and legal provisions[6]. Local governments and legislatures oversee its implementation in five Indian states, specific regions of China, and designated areas of Ethiopia. In Uzbekistan, premarital consultation is mandatory, while PmHT remains optional[6]. Although national health guidelines in numerous countries advocate for voluntary HIV testing, churches in African nations like Burundi, the Democratic Republic of Congo, Ghana, Kenya, Nigeria, Tanzania, and Uganda have instituted MPmHT. Notably, in Ghana, the national government stands as the sole entity among these nations to have achieved successful collaboration with local RO in the promotion of PmHT. Nevertheless, data from Ghana highlights the persistent de facto compulsory nature of PmHT[6].

The age characteristics of HCWs in this survey exhibited a correlation with the results of a cross-sectional survey conducted among health professionals in Ghana. The latter survey focused on assessing health service activity standards and standard workloads for primary healthcare[7]. HCWs predominantly conveyed their disapproval regarding the hypothetical disclosure of positive results from RMPmHT to RO leadership. Their reservations were grounded in perceptions of fragile confidentiality structures. Existing literature further highlights concerns about the efficacy of RMPmHT in ensuring informed consent, safeguarding result confidentiality, and delivering sufficient counseling and information[6]. International guidelines on HIV/AIDS and human rights categorize breaches of confidentiality as violations of fundamental human rights, encompassing bodily integrity, privacy, and the right to information. These guidelines underscore obligations to uphold physical privacy, secure informed consent, and guarantee the confidentiality of an individual's HIV status information. HCWs notably expressed a preference for RMPmHT results to be disclosed exclusively between prospective marriage partners, rather than to RO leadership. Their preference aligns with a scenario wherein couples would be asked about their comfort with sharing results exclusively

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between themselves, without divulging them to RO leadership.

In the hypothetical scenario of testing positive for HIV during RMPmHT, HCWs expressed a preference to maintain distance from their affiliated RO. This inclination arose from concerns related to the perceived fragility and lack of clarity in mechanisms for maintaining confidentiality. Varied RMPmHT practices exist, with some prioritizing the disclosure of test results by health professionals directly to RO marriage committees, while others opt for disclosure to RO leadership or state authorities for the purpose of issuing marriage licenses[8]. In this context, HCWs voiced disagreement with the hypothetical assertion that RO leadership inherently possess the 'right' to access RMPmHT results. Ghana's National HIV/AIDS policy emphasizes the necessity of offering universally available, easily accessible, high-quality, and confidential VCT services[9]. The legal and ethical guidelines that govern the disclosure of HIV test results specify that health and social welfare workers are prohibited from divulging any confidential information to any third party without the explicit consent of the client[9]. Disclosure is permitted under certain circumstances when, guided by the professional's informed judgment, it is either authorized by the law or deemed to be in the best interests of the client, their spouse, other supportive family members, or another individual involved in the client's care[9].

The National Workplace HIV/AIDS Policy (2004) unequivocally upholds the principles of privacy and confidentiality, explicitly guarding against disclosure without informed consent unless mandated by the law. This exception notably extends to disclosure to HCWs directly involved in the provision of care, where knowledge of the individual's HIV status is deemed essential for informed clinical decision-making[10, 11]. The disclosure modalities of RMPmHT results demonstrate variation. In Burundi, couples typically undergo testing together and share their results with each other, consistently avoiding disclosure to RO leadership. These practices align with the preferences of HCWs in this survey. In specific regions of the Democratic Republic of Congo (DRC) and Uganda, the results of RMPmHT are transmitted to the RO leadership before being shared with the couples. In Malaysia, where RMPmHT is mandated by the state government's religious department, the results are jointly disclosed to couples. Meanwhile, the disclosure practices in Kenya remain unclear[6]. In this survey, RMPmHT was generally not perceived as intrusive or coercive by HCWs.

MPmHT policies are also seen as potential instruments for empowering women by ensuring equal testing opportunities. In specific instances, such as Senegal in 2003, women's groups endorsed PmHT for women to ascertain their prospective husbands' HIV statuses. However, these policies, while theoretically fair and empowering, may still lead to practical unfairness due to their interaction with existing social inequalities[6]. This stance indirectly underscores a potential lack of awareness regarding the imperative to eradicate all forms of coercion from PmHT. The Ghana National HIV/AIDS policy (2019) explicitly opposes the imposition of mandatory medical services as a prerequisite for employment, enrollment into educational institutions, or marriage[9]. The World Health Organization (WHO) and UNAIDS strongly condemn coercive and intrusive methods for HIV testing, emphasizing that the decision to undergo testing should be an individual choice rather than one influenced by doctors, partners/spouses, family members, employers, or other external parties[12-14]. In this survey, HCWs consistently viewed RMPmHT as an 'acceptable' practice. This aligns with a study examining attitudes toward RMPmHT among unmarried youths in Ibadan Northwest Local Government Area, Nigeria. Furthermore, it corresponds with a news report on the BBC that shed light on instances where Nigerian ROs appeared to exert pressure on individuals to disclose their RMPmHT results to RO leadership[15, 16].

HCWs expressed the view that national policy frameworks governing the authorization to request, conduct, and access HIV test results were deficient. They also noted a prevailing silence on matters related to RMPmHT in state policies. Although legal regulations for HIV testing may be relatively inconspicuous, the 2019 Ghana National HIV and AIDS Policy, aimed at achieving universal access to prevention, treatment, and care, and the 2013 Ghana National HIV and AIDS, STI Policy, exemplify restrictions on the disclosure of test results[9,17]. The unregulated acquisition or utilization of test kits, as emphasized in contemporary literature, substantiates the alleged policy gap in HCWs ethical considerations. This underscores the need for additional scrutiny and discussion within the realm of bioethical discourse[18,19]. The overarching concerns expressed by HCWs indicated that divulging RMPmHT results to RO leadership might lead to subtle or overt 'scorn' from the ROs. This aligns with existing evidence suggesting that positive MPmHT results amplify the risk of stigmatization[5]. Despite the ethical ambiguities surrounding RMPmHT, the majority of HCWs categorized it as a 'best practice' for HIV control. However, contemporary evidence challenges the effectiveness of RMPmHT in HIV control, characterizing it as 'vacillating' primarily due to its significant independence from collaboration with public health institutions[5]. The practice additionally reinforces religious prohibitions and echoes intuitive claims of its effectiveness, as it is often implemented with minimal evaluation and monitoring mechanisms in place to measure their impact [5].

HCWs strongly advocated for a reevaluation of RMPmHT, proposing its separation from the disclosure of results to RO leadership and from marriage considerations. In 2004, Albania contemplated a draft amendment to its Family Code, which would have

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mandated PmHT and barred individuals with HIV/AIDS from marrying. Despite facing opposition from legal and humanitarian organizations, the amendment did not pass. It is noteworthy that the lack of practical 'opt-out' avenues render RMPmHT de facto compulsory[5]. Any PmHT service that makes negative results a prerequisite for accessing civil, social, or religious benefits infringes upon internationally guaranteed inalienable human rights. RMPmHT, characterized by fragile structures for informed consent, confidentiality, and inadequate access to counseling and information, arguably encroaches upon rights such as the right to marry and found a family, bodily integrity, privacy, and information[6,9]. Inference drawn from this suggests that a comprehensive, participatory, and objective review of PmHT, including R/MPmHT, is imperative. This review should be conducted with a robust understanding that anti-retroviral medications play a crucial role in predicting a high quality of life[20].

Conclusion

The widespread promotion of RMPmHT in various countries, with limited scrutiny in bioethics literature, requires further evaluation. These policies, aiming to boost HIV service utilization, are implemented in stigmatized areas, raising ethical concerns. HCWs express reservations about RMPmHT's impact on confidentiality, informed consent, and individual rights. They disapprove of disclosing positive results to RO leadership, citing confidentiality concerns. Despite ambiguities, HCWs generally find RMPmHT 'acceptable,' aligning with attitudes in other studies. Concerns about stigmatization, coercion, and human rights violations emphasize the need for a comprehensive review of all PmHT services, including RMPmHT. The complexity and challenges associated with RMPmHT, along with its ethical implications, highlight the need for careful consideration.

Recommendations

Bioethical research on all PmHT services, with larger sample sizes, should be prioritized. Public awareness of inalienable fundamental human rights such as the right to marry and found a family, bodily integrity, privacy, and information should be promoted. The formulation of clear policy frameworks, comprehensively guiding and linking all PmHT procedures to public health services, should be strengthened.

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PREVALENCE AND PREDICTORS OF COMPLEMENTARY AND ALTERNATIVE MEDICINE USE AMONG CHILDREN ATTENDING AN ASTHMA CLINIC IN A TERTIARY HOSPITAL IN GHANA

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Abstract

Objective: The objectives of this study were to determine the prevalence and type of CAMs, and predictive factors among Ghanaian children with asthma.

Methodology: A cross-sectional study involving 110 children with physician-diagnosed asthma attending the Asthma Clinic of the Department of Child Health (DCH), Korle Bu Teaching Hospital (KBTH), Accra were consecutively recruited between February 2018 to May 2019. Data were collected with a semi-structured, pre-tested, investigator-administered questionnaire.

Results: Out of the 110 participants, forty-nine (44.5%) had used CAM within the last 12 months. The three most frequently used remedies as stand-alone or in combination were honey (80.0%), garlic (34.2%) and lemon/lime (26.3%%). In the multivariable logistic regression analysis, CAM use among children aged 10--13 years was over 4 times the use among those aged 5--9 years (AOR=4.45, 95% CI: 1.32-14.98, p=0.016), 71% less among female children (AOR: 0.29, 95% CI: 0.10-0.80, p=0.017) and 85% less among mothers in middle occupation class relative to the low occupation class (AOR: 0.15, 95% CI: 0.15, 95% CI: 0.03-0.77, p=0.023).

Conclusion: There was high prevalence of CAM use among the children attending the asthma clinic, KBTH. Adolescents and children from low occupational class are more likely to use CAM, while the female child was less likely.

Key words: *Complementary and alternative medicine, asthma, occupational class*

Introduction

Complementary and Alternative medicine (CAM) is "a group of diverse medical and healthcare systems, practices, and products that are not generally considered part of conventional medicine."[1] Complementary medicine is used concurrently with mainstream medicine (e.g., herbal preparations), while alternative medicine is purposefully used to replace conventional medicine (e.g., Ayurveda, chiropractic, homeopathy, naturopathy, and acupuncture).[2] CAM has widespread use among children living with chronic diseases such as asthma, especially in low-and-middle-income countries (LMICs), like Ghana.[3,4] The World Health Organization estimates that about 80% of the world population accesses healthcare through non-orthodox healthcare systems.[5] Globally, CAM therapies such as herbal medicine, acupuncture, homoeopathy, yoga, massage therapy, traditional Chinese medicine and Ayurveda medicine are patronised as treatment for asthma,[1,6] especially in resource-poor settings.[3] Among children with asthma, the use of herbal preparations such as teas, cough syrup, camphor, oil and menthol as well as honey and prayers are common in high income countries.[7] These are also reported in LMIC like Nigeria, [3] where due to poverty and lack of access to mainstream healthcare systems and the high cost of guideline specific medications like the inhaled corticosteroids (ICS) patients seek to the use of CAM for the treatment of their disease.[3,8] In Ghana, Goka *et al* [4] reported that most parents (80%) of 69 children with asthma considered herbal medicine to be an important therapy for asthma, even though only 36.4% of those with that belief admitted to administering herbal preparations to their wards. Other therapies considered important were lime/lemon and honey combination (20%), while only 1.5% of the parents mentioned prayers as an important treatment option.

There are several reasons why people would use CAM. Some of the reasons reported are affordability, accessibility, dissatisfaction with western medicine, no known side effect with CAM, fear of adverse drug reactions with conventional medicine, and the need for more individual attention.[2] Other reasons attributed to CAM use include its complementary nature with orthodox medicine in disease management and the perceived belief that CAM treats the causes of the ailment and does not merely relieve symptoms. Additionally, CAM has a natural and holistic appeal, i.e., CAM use improves the whole person: body, mind and soul.[9] In Nigeria, Oshikoya *et al*[3] reported in a prospective study that parents use CAM for their children with asthma as a form of direct cure, to improve the physical condition of their children or to relieve symptoms of the disease.

Contrary to the popular belief that CAM users are uneducated, several studies in high-income countries

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like the United States of America (USA) found that parents of these children are well educated.[7,9] In a study by Oshikayo *et al*,[3] in Nigeria, parents of the children who consumed CAM had secondary level education or higher (67%). However, the use of CAM among the well-educated is said to be associated with the consumption of dietary supplements, vitamins, massage, acupuncture and chiropractic medicine. In contrast, the use of folk medicine, defined as a "range of remedies including prayer, healing touch or laying on of hands, charms, herbal teas or tinctures, magic rituals" was found to be of higher use among the minority (blacks and Hispanic) and the poor in society in the 2002 National Health Interview Survey in the USA.[7] Similarly, this has been reported in a systematic review of studies from sub-Sahara Africa,[8] though the study was not only on asthma.

Parents of CAM users either do not discuss with their regular health care providers, albeit they were eager to do so,[3] or only a few discuss the use of CAM with their asthma healthcare team, because many of them believe that it is not important or not within the professional capability of their orthodox health care provider.[10,11] In Africa, patients refuse to disclose the use of CAM to their health care practitioner for fear of being attended to poorly and the apparent negative attitude of the health care personnel towards the user of CAM.[8] It is also reported that healthcare practitioners do not enquire about the use of CAM among their patients even when they are willing to tell them.[3] This might have been due to high workload, forgetfulness or lack of knowledge or interest from the health personnel. This might not be different in Ghana, and this may have negative consequences on those users of CAM as there could be the possibility of drug-drug interactions and possible consumption of poisonous substances. Furthermore, CAM users are likely to stop taking their orthodox medications which would put them at risk for poor asthma symptom control and acute exacerbations. For example, the use of herbal products was found to be associated with decreased inhaled corticosteroids (ICS) adherence and patients who were using CAM were more likely to have been hospitalised or intubated for asthma compared to those who did not use.[12] It is therefore of paramount importance for the asthma care practitioner to enquire about the use of CAM and initiate discussion with the view of finding the reasons for their use in a non-judgemental manner.

There is a gap in data in Ghana concerning the use of CAM among children with asthma. Specifically, there is lack of knowledge on the prevalence of CAM use among this group of patients, as well as the socio-demographic and clinical factors associated with CAM usage. This needs to be explored to provide evidence, based on which asthma care practitioners can modify their approach to asthma management education taking the use of CAM by patients into account. The evidence from this study could help in reducing CAM use among children with asthma.

It may contribute to public education, policy formulation and may guide future research into CAM use in Ghana.

The aim of this study was to determine the prevalence of CAM use among children with asthma aged 5-13 years who attend the Asthma Clinic of the Department of Child Health (DCH), Korle Bu Teaching Hospital (KBTH), Accra, identify the most commonly used type of CAM, determine the characteristics of the children with asthma who patronise CAM and determine the factors associated with the use of CAM among these children.

Materials and Methods

Study Design

The study was originally designed as a hospital-based 1:1 sex and age matched case-control study to determine factors associated with frequent emergency department (ED) visits by children attending asthma clinic in Korle Bu Teaching Hospital, Accra. The study recruited a total of 110 study participants, 55 controls and 55 cases. Cases were defined as patients who visited the ED at least two times within the preceding 12 months of being interviewed and controls were children who had at most one visits to the ED. For the objective which sought to assess the factors associated with CAM use among children attending the asthma clinic, the analysis considered the data as a cross-sectional study since the outcome, CAM use, was not considered as a matching variable at any point of sampling the children into the database.

Study Settings

The study was conducted among children with physician-diagnosed bronchial asthma who were attending the weekly asthma clinic of the department of child health, Korle Bu Teaching Hospital, Accra from February 2018 to May 2019. The annual clinic attendance is about 630 patients. Thus, on average, about 13 patients are seen at the clinic weekly with about five of them being new cases.

Sample Size and Power Analysis

Given that the study was not originally designed as a cross-sectional study, the power analysis is conducted to assess the precision of using a sample size of 110. Using a sample size of 110, and CAM use among the controls of 34.6% from this study, at 0.05 level of significance and 80% power, the study is powered to detect a difference in prevalence of at least 26.4%.

Inclusion Criteria

The inclusion criteria were children aged 5-13 years and enrolled at the asthma clinic with physician--diagnosed asthma for at least one-year, with no evidence of acute exacerbation at the time of recruitment, and whose parents had consented to take part in the study. Informed assent was sought from participants who were aged 8 years and above.

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Exclusion Criteria

Patients were excluded if they were outside this age category, if they had any congenital or acquired lung or heart disease. Also excluded were patients who had other chronic conditions such as sickle cell disease, Human Immunodeficiency virus/Acquire Immunodeficiency Syndrome (HIV/AIDS) as well as those whose parents refused to consent.

Data Collection

The eligible patients and their parents were approached by the researchers. The purpose of the study was explained in the language that was most comfortable for the participants and written informed consent was sought from those who were voluntarily willing to participate**.** English was the primary language used. A pre-tested, semi-structured, interviewer-administered and face validated questionnaire was used to collect the data. The questionnaire contained information on socio-demographic characteristics of the child (sex, age, birth order) and the parents (age, educational level, occupational classification according to the United Kingdom Registrar General Classification/Social Class Based on Occupation).[13] Data was also collected on the type of housing and the source of energy for cooking.

Information on the frequency of emergency department (ED) visit in the past 12 months was obtained. The participants were classified into frequent ED visits (participants who had had two or more ED admissions in the preceding 12 months to relieve bronchospasm by nebulisation),[14] and no frequent ED visits (participant who had less than two ED admissions in the preceding 12 months to relieve bronchospasm by nebulisation).[14] Parents were asked *"Has your child used complementary and alternative medicine to treat his or her asthma in the past 12 months? If yes, please state the type…a) herbal remedies; b) faith-based; c) chiropractic; d) folk medicine*. Assessment of asthma symptom control was done using the modified consensus-based GINA assessment guideline of asthma control.[15] which categorises patients as well-controlled, partially controlled, or uncontrolled.

The dependent variable was CAM use within the last 12 months. Independent variables were the sex of the child, parents' educational level, occupational class, type of housing, source of energy for cooking, level of asthma control and frequency of emergency department (ED) visits.

Ethical Considerations

Ethical clearance was approved by the Institutional Review Board (IRB) of the Korle Bu Teaching Hospital, Accra (Reference No: KBTH IRB/0077/2017). Approval was sought from the head of department of DCH, KBTH.

Data Management and Analysis

All data were entered into Microsoft Excel 2010 and imported into Stata IC version 15 (Stata Corp, College station, TX, USA). Descriptive statistics (frequency and percentage) was used for the analysis of participants' socio-demographic information and other categorical variables. Measured continuous variables were analysed as median (lower quartile, upper quartile). Association between socio-demographic characteristics, frequency of ED visits, level of asthma symptom control and the use of CAM was determined using chi-square tests or Fisher's exact test where appropriate. All the variables were used as candidate sets for the univariable and multivariable conditional binary logistic regression analysis. The univariable binary logistic regression was employed to determine the predictors of CAM use based on the crude odds ratio (COR) at a 95% confidence interval (p-values < 0.05). Adjusted odds ratio (AOR) with 95% confidence interval was employed to assess the strength and direction of the association, while P-value <0.05 was used to determine statistical significance in the multivariable binary logistic regression analysis.

Results

The socio-demographic and the clinical characteristics of the study's population are shown in Table 1. A total of 110 participants were included in the analysis. There was a male preponderance, with a male to female ratio of 1.4:1. The median (IQR) age of the participants was 7 (6,10) years. Majority of the mothers 85 (77.3%) and the fathers 98 (89.1%) of the children involved in the study had received secondary education or higher. Most of the mothers 59 (53.6%) as well as the fathers 69 (62.7%) were in the higher occupational classes. Most of the study participants 67 (60.9%) had poorly controlled asthma (partially controlled and uncontrolled). The types of CAM used by the participants are shown in Table 2. Forty-nine (44.5%) of the study population had used one form of CAM or the other. Thirty-eight (38/49, 77.5%) of these used different combinations of herbal remedies while 10/49 (20.4%) reported to have used faith-based therapy as CAM. The three most frequently used remedies as standalone or in combination were honey (n=30/38, 80.0%), garlic (n=13/38, 34.2%) and lemon/lime (n=10/49, 26.3%) (Table 2).

Bivariate association between socio-demographic and clinical characteristics and the use of CAM

Table 3 shows the association between socio-demographic and clinical characteristics and CAM use. The following factors were significantly associated with the use of CAM; age of the participant (p=0.049), sex (p=0.033), mothers educational level (p<0.001), fathers educational level (p=0.005), mothers occupational class (p<0.001), fathers occupational class (p=0.025), housing characteristics (p=0.004), source of fuel for cooking (p=0.031) and frequency of ED visits (p=0.035).

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Table 1: Frequency distribution of socio-demographic and clinical characteristics of the participants and their parents

Variable	Total (N=110) n (%)
Age of child in years, median (IQR)	7 (6,10)
Age group	
5-9 years	80 (72.7)
10-13 years	30 (27.3)
Sex	
Male	64 (58.2)
Female	46 (41.8)
Mother's education	
Basic	25 (22.7)
Secondary	29 (26.4)
Tertiary	56 (50.9)
Father's education	
Basic	12 (10.9)
Secondary	29 (26.4)
Tertiary	69 (62.7)
Mother's occupational class	
Class I&II	59 (53.6)
Class III	23 (20.9)
Class IV&V	25 (22.7)
Missing	3 (2.7)
Father's occupational class	
Class I&II	69 (62.7)
Class III	26 (23.6)
Class IV&V	12 (10.9)
Missing	3 (2.7)
Housing	
Compound	28 (25.5)
Self-contained	82 (74.5)
Source of energy for cooking	
Firewood/charcoal	8 (7.3)
Liquefied petroleum Gas (LPG)	79 (71.8)
Firewood & LPG	23 (20.9)
Levels of asthma control	
Well controlled	42 (38.2)
Partially controlled	38 (34.5)
Uncontrolled	29 (26.4)
Missing	1 (0.9)
Frequency of ED visit in the past 12 months	
Two or more	55 (50.0)
One or no visit	55 (50.0)
Ever used CAM in the last 12 months	
Yes	49 (44.5)
No	61 (55.5)

Interquartile range: (IQR), n: frequency. %: column percentage

Table 2: Frequency distribution of the types of CAM used and the different combination of herbal remedies used by the studied population

Alternate medicine used	Total n (%)
Coconut and egg	1(2.0)
Garlic and lemon	1(2.0)
Garlic	1(2.0)
Garlic & honey	6 (12.2)
Honey	12 (25.0)
Honey, lime	4 (8.2)
Honey and herbal medicine	1(2.0)
Honey, cinnamon powder	3 (6.1)
Honey, garlic, Grains of selim (xylopia aethiopica (hwentia)]	1(2.0)
Lime, honey, ginger, garlic	3 (6.1)
Lime	1(2.0)
Onion, garlic, honey	1(2.0)
[Aidan fruit [tetrapleura tetraptera (Prekese)], grains of selim (xylopia aethiopica)	1(2.0)
Warm water, lime, honey	1(2.0)
Faith based	10(20.4)
Combination of faith and herbal remedies	1(2.0)
Mother didn't know the name	1(2.0)
Total	**49**

Binary logistic regression model of factors associated with the use of CAM among children with asthma

Table 4 shows the univariable and multivariable binary logistic regression analysis of the predictors of CAM use among the children aged 5-13 years with asthma in DCH, KBTH, Accra. The current study showed in the univariable logistic regression analysis that the female sex (COR=0.43, 95% CI: 0.19 - 0.94, p=0.035), participants whose mothers had tertiary education (COR=0.14, 95% CI: 0.05-0.41, p<0.001), participants who lived in self-contained houses (COR=0.27, 95% CI:0.11-0.68, p=0.005), and participants who had frequent ED visits (COR=0.44, 95% CI: 0.2-0.95, p=0.037) were protective against CAM use. After adjusting for maternal educational level, maternal occupational class, paternal education, paternal occupational class, housing characteristics, source of energy for cooking, asthma control level, and frequency of ED visits, CAM use was over 4 times high among children aged 10-13 years (AOR=4.45, 95% CI: 1.32-14.98, p=0.016) and 71% less among the female children (AOR=0.29, 95% CI: 0.10-0.80, p=0.017) compared to their male counterparts and 85% less among children whose mothers were in the middle occupation class (Class III) compared to mothers in the lowest occupation class (AOR=0.15, 95% CI: 0.03-0.77, p=0.023). (Table 4)

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Table 3: Association between Socio-demographic and clinical characteristics of study respondents and the use of CAM

		Use of alternate medicine		Chi-square value	P-value
Variables	**Total**	**Yes (%)**	**No (%)**		
Age group of child				3.99	0.049
5-9 years	80	31 (38.8)	49 (61.3)		
10-13 years	30	18 (60.0)	12 (40.0)		
Sex				4.56	0.033
Male	64	34 (53.1)	30 (46.9)		
Female	46	15 (32.6)	31 (67.4)		
Mother's education				16.10	<0.001
Basic	25	18 (72.0)	7 (28.0)		
Secondary	29	16 (55.2)	13 (44.8)		
Tertiary	56	15 (26.8)	41 (73.2)		
Father's education				10.66	0.005
Basic	12	6 (50.0)	6 (50.0)		
Secondary	29	20 (69.0)	9 (31.0)		
Tertiary	69	23 (33.3)	46 (66.7)		
Mother's occupation				15.12	0.001
Class I&II	59	18 (30.5)	41 (69.5)		
Class III	23	12 (52.2)	11 (47.8)		
Class IV&V	25	19 (76.0)	6 (24.0)		
Father's occupation				7.38	0.025
Class I&II	69	24 (34.8)	45 (65.2)		
Class III	26	17 (65.4)	9 (34.6)		
Class IV&V	12	6 (50.0)	6 (50.0)		
House				8.26	0.004
Compound house	28	19 (67.9)	9 (32.1)		
Self-contained house/	82	30 (36.6)	52 (63.4)		
Level of asthma				3.46	0.063
Controlled	42	14 (33.3)	28 (66.7)		
Poorly controlled	68	35 (51.5)	33 (48.5)		
Source of fuel				F	0.031
Firewood only	8	7 (87.5)	1 (12.5)		
Gas only	79	31 (39.2)	48 (60.8)		
Firewood & Gas	23	11 (47.8)	12 (52.2)		
Frequency of ED visits in the past 12 months				4.45	0.035
Two or more	55	30 (54.6)	25 (45.4)		
One or no visit	55	19 (34.6)	36 (65.4)		

F: P-value from the Fisher's exact test. All other p-values are from the Pearson's chi-square test.

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Table 4: Univariable and multivariable logistic regression model of factors predicting the use of CAM

	Simple Binary Logistic Regression Model			Multiple Binary Logistic Regression Model	
Variable	**COR [95% CI]**	**P-value**		**AOR [95% CI]**	**P-value**
Age group					
5-9 years	1.00 [reference]			1.00 [reference]	
10-13 years	2.37 [1.00, 5.61]	0.050		4.45 [1.32, 14.98]	0.016
Sex					
Male	1.00 [reference]			1.00 [reference]	
Female	0.43 [0.19 - 0.94]	0.035		0.29 [0.10, 0.80]	0.017
Mother's education					
Basic	1.00 [reference]			1.00 [reference]	
Secondary	0.48 [0.15 - 1.5]	0.207		3.25 [0.60, 17.50]	0.170
Tertiary	0.14 [0.05 - 0.41]	<0.001		0.22 [0.01, 3.67]	0.289
Father's education					
Basic	1.00 [reference]			1.00 [reference]	
Secondary	2.22 [0.56 - 8.87]	0.258		2.31 [0.21, 25.92]	0.497
Tertiary	0.5 [0.14 - 1.73]	0.274		1.07 [0.09, 13.21]	0.957
Mother's occupational class					
Class I&II	0.14 [0.05, 0.41]	<0.001		0.79 [0.04, 15.38]	0.878
Class III	0.34 [0.10, 1.18]	0.091		0.15 [0.03, 0.77]	0.023
Class IV&V	1.00 [reference]			1.00 [reference]	
Father's occupational class					
Class I&II	0.53 [0.15, 1.85]	0.321		8.21 [0.96, 70.44]	0.055
Class III	1.89 [0.47, 7.64]	0.372		10.41 [0.98, 111.14]	0.052
Class IV&V	1.00 [reference]			1.00 [reference]	
Housing					
Compound house	1.00 [reference]			1.00 [reference]	
Self-contained house/	0.27 [0.11 - 0.68]	0.005		0.41 [0.12, 1.38]	0.148
Level of asthma					
Controlled	1.00 [reference]			1.00 [reference]	
Poorly controlled	2.12 [0.95, 4.73]	0.066		1.50 [0.52, 4.31]	0.454
Source of energy for cooking					
Firewood only/ with Gas	1.00 [reference]			1.00 [reference]	
Gas only	0.47 [0.20, 1.09]	0.078		0.70 [0.19, 2.55]	0.585
Frequency of ED visits					
Two or more	1.00 [reference]			1.00 [reference]	
One or no visit	0.44 [0.2 - 0.95]	0.037		0.72 [0.27, 1.90]	0.503

COR: crude odds ratio. AOR: adjusted odds ratio. CI: confidence interval.

Discussion

Complementary and alternative medicine use among children with asthma who attend asthma clinics is not one of the main topics that are addressed by the health care provider. This has been attributed to the fact that patients are not willing to share such information due to the perception that they might upset the health care professional.[3] On the other hand, the health care provider might not enquire about the use of CAM and so it does not get to be discussed.[3] The current study sought to find the prevalence, socio-demographic and clinical characteristics and factors associated with CAM use among children with asthma aged 5-13 years who attend the asthma clinic, DCH, KBTH, Accra, who use CAM.

Our study showed a high prevalence (44.5%) use of CAM among the study population. The most frequently used CAM were honey, garlic and lime. Kalaci *et al*[10] reported 76.4% of CAM use by children with asthma in Canada. Humidifiers, air purifiers and multivitamins were the most common modalities in their study. In Turkey, Hacaoglu *et al* [17] found 66% of children with asthma used CAM, with herbal medicine, honey and

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grape syrup being the most frequently used CAM. An earlier study conducted in our facility showed that 29% of the study's population were using CAM, with lime and honey being the most commonly used modalities.[4] Oshikoya *et al*[3] in Nigeria reported in 2008, a significant but lower prevalence (25%) of CAM use among children with asthma. Similarly, they also found that the commonest CAM were the herbal remedies. The higher prevalence in our study could reflect an increasing trend in the use of CAM globally.[18] The wide diversity in the prevalence among different countries may be due to differences in the definition of CAM, socio-demographic characteristics, culture, beliefs of the people involved in the study, and different types of products considered as CAM by different group of people.[19]

Our study revealed that the female child with asthma is less likely to use CAM compared to the male. This is contrary to a previous study in Norway which showed that male teenagers have reduced odds of using CAM for various diseases.[20] The reasons for gender disparities in asthma are not well understood but have been linked to hormonal and immunological factors as well as differences in gender-related responses to environmental factors.[21,22] While females may be at a higher risk of disease severity, acute exacerbations, hospitalizations and death compared to their male counterparts, boys up to 14 years of age, are at a higher risk of asthma-related outpatient department (OPD) and emergency room visits and hospitalizations.[23–25] This has been buttressed by the fact that young boys have smaller airway diameter in relation to their lung volume compared to their female counterparts, consequently, putting them at risk of airway obstructions.[26,27] Based on this assertion we speculate that because young females are less likely to visit the ED for acute asthma care, their caregivers are unlikely to resort to using CAM with the hope of curing their ailment.

The current study found that children aged 10-13 years are over four times more likely to use CAM compared to those aged 5-9 years. Findings are varied in the literature; while some studies[20,28] suggest that the adolescent population, including the age group of 10-13 years, are at increased risk of CAM use, there are other findings where younger age group, less than 6 years are said to be associated with the use of CAM.[29–31] The reason behind this variation is not well understood. However, adolescents with asthma are known to have poor adherence to their prescribed medications and like experimenting or taking risk with other treatment options.[32] The finding may also be a reflection of parents being more cautious about the use of CAM when their children are younger.

Our data revealed that children whose mothers had received tertiary education and children who lived in self-contained houses had significantly reduced risk of using CAM in the univariable logistic regression analysis. This significance was lost when they were adjusted for other socio-demographic characteristics.

However, these factors are indicators of people from higher socio-economic background. Our data showed that children from middle and high occupational class had reduced odds of CAM use compared to those from the lower occupational classes. Patients of higher socio-economic status would be able to afford the cost of the orthodox medications like the ICS, as such, may not resort to CAM. They are also more likely to be well educated and therefore can understand the teachings that are carried out by the asthma care providers and as such might not use CAM for the treatment of their asthma. The current finding is consistent with studies conducted in Nigeria[3] and other Sub-Saharan African countries.[8] This is contrary to studies which have reported that parents of children who use CAM have higher education level.[9,33] Our study found that children who had either visited the ED once or did not visit the ED in the preceding 12 months had 56% reduced risk of CAM use compared to those who had visited the ED two or more times in that same period. This might be due to the fact that these patients might have well controlled asthma and so had no need to try other non-orthodox medications.[34] The use of herbal products was found to be associated with decreased ICS adherence, consequently leading to increased hospitalization or even intubation for asthma attacks.[12] The evidence suggests that there is the need for asthma care providers to encourage conversation on CAM use with their patients, especially those of lower socio-economic background. CAM use should be discussed in a non-judgemental manner with the caregivers of the patients attending the asthma clinic. This would provide the opportunity to discuss their specific beliefs, dispel myths and reduce the likelihood that they are relied upon in preference to prescribed medications.

The current study did not explore the reasons for the use of CAM. However, several studies have reported reasons why parents may give CAM to their children with asthma. Most have stated the natural and holistic nature of CAM, complementary role and for symptom relief. In other studies, the respondents stated lack of side effects of CAM.[3] It would be revealing to find out the reasons for the use of CAM by the children attending the asthma clinic, KBTH, as this may differ from the aforementioned.

Limitations

The original study design and sample size is not adequately powered to detect the conventional 5% difference in prevalence of binary outcomes studies, in this case, CAM use among children with asthma. Nonetheless, due to the dearth of studies in CAM use among children with asthma in Ghana, this study can serve as a basis for a larger study that is powered to further investigate the phenomenon. Furthermore, the study may be subject to recall bias as participants were asked to provide the answer to the question *"has your ward ever used CAM in the past 12 months".* There was no way to authenticate their response. The study did not

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seek to find the reason for the use of CAM by these patients; this information could potentially influence the development of guidelines for asthma care.

Conclusion

In conclusion, CAM use was highly prevalent among children attending the asthma clinic in KBTH with honey, lime/lemon and garlic being the most frequently used remedies. The adolescent age group was strongly associated with CAM use, and children from lower socio-economic background were more likely to use CAM. Female sex may be a protective factor against the use of CAM among the children attending the asthma clinic. The asthma care team at the asthma clinic, KBTH should initiate discussions on CAM use with the parents and adolescent children in a non-judgemental manner so they can be counselled appropriately on the need to adhere to prescribed effective medication for good control of their asthma and prevention of potential complications. A larger study on the use and effects of CAM among children with asthma in Ghana is needed.

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COMMENTARY

TRAINING AND DEVELOPING PHYSICIAN-SCIENTIST CAREERS TO ENHANCE MEDICAL RESEARCH IN GHANA

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Summary

A physician-scientist is a medical doctor who combines clinical practice with research. They often work in academic medical centers, research institutions, or hospitals, where they split their time between treating patients and conducting research to advance medical knowledge, develop new treatments, and improve public health. Their work is well recognized as they are reported to constitute 37% of Nobel Prize winners in Physiology or Medicine, and several prize winners in Chemistry. However, regardless of how inherently fulfilling this may be, in Ghana and many other regions of the world, increasingly fewer doctors aspire to become physician-scientists. Currently, there is a lack of clarity regarding the path to becoming a physician-scientist in Ghana and other African nations. So, for the young doctor of today who wishes to embark on a research career, there are more questions than answers. The authors emphasize the need for structured programs, early commitment, and resource allocation to nurture the next generation of physician-scientists. They also examine the potential of integrating research-focused training into existing medical programs and the role of various stakeholders, such as universities and the Ministry of Health, in supporting these initiatives. The authors call for innovative approaches and strategic planning to enhance the capacity of Ghanaian doctors to pursue careers in medical research, ultimately contributing to global scientific advancement and improving healthcare in low and middle-income countries. They conclude that more needs to be done to develop more physician-scientists.

Introduction

Recent global events, notably the COVID-19 pandemic, have demonstrated the astounding outcomes that years of medical research can produce.[1] Research enhanced pandemic control through the rapid development of vaccines, diagnostic equipment and therapeutic agents. Today, low and middle-income countries like Ghana are building capacity to become proficient in vaccine development and production. Undoubtedly, this will require the experience of seasoned research scientists such as physician-scientists. Ghana, like many developing countries, is also experiencing both a demographic transition as well as an epidemiologic transition creating a need to train more physician-scientists to tackle this challenge. The contribution of physician-scientists to science is well recognized as they are reported to constitute 37% of Nobel Prize winners in Physiology or Medicine, and several prize winners in Chemistry.[2]

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Postgraduate medical training through the Medical Colleges in Ghana and other West African countries has been the main source of training for physician-scientists and to a lesser extent the research units of the Ghana Health Service. The physician-scientist does two jobs, research and clinical work.[1,3,4] Nonetheless, no matter how intrinsically rewarding this might be, in Ghana and many parts of the world, increasingly fewer doctors aspire to become physician-scientists and much less, Nobel Prize winners.[2,4,6] This has been attributed to several factors militating against developing a research career such as lack of mentorship, the cost of research, inadequate technical skills and skills in grantology; lack of incentives in a climate of better salary structures in competing jobs such as clinical practice; lack of fulfillment from translating research into practice, not achieving a work-life balance, among others.[2,4-7] Notwithstanding these issues, experience from the US indicates that innovative approaches and thoughtful planning with stakeholders can re-ignite interest.[5,6,9] However, it requires a clear pathway, structured programmes, early commitment, resources, effective mentorship, diversity and stakeholder engagement as

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well as some knowledge of the current priorities in research[2,5-9, 10].

Current Situation / Literature Review

Training of Physician-Scientists Globally

Physician-scientists are doctors who hold a Medical degree and perform medical research as their primary professional activity.[11] They engage in biomedical, clinical research, translational research and population-based research.[11,12] These graduates currently work in academic institutions, research institutions and industries such as the pharmaceutical industry.[7,9,11] While the majority have only medical degrees, many have second degrees such as PhD, MPH and MBA. [11, 12] They constitute a unique group of investigators because their clinical experience through patient care shapes their approach to research enabling them to contribute to biomedical research and translate the results of their scientific work into clinical practice.[4,7, 9] They operate from "bench to bedside" and "bedside to bench", they determine disease mechanisms, discover vaccines, new drugs and devices for treating patients, engage in health disparities research, and study the epidemiology of disease, among others.[1,2,12,13,14] Physician-scientists also play technical, advisory networks and consultancy roles at national level. This was evident during the COVID-19 pandemic.[1] Their work also informs policy.[2]

The increasing complexity of clinical research led to calls for more formal training and mentoring in research from medical school to residency, and career development planning for young doctors interested in research careers.[2,6,7] This was because early exposure to research in medical school and as a young doctor was reported to influence the decision to choose a career in medical research, therefore, calls to incorporate research into medical school curricula and the training of young doctors have been made to promote succession.[2, 7, 12, 15] At the time, most German doctors, for instance, were reported to conduct research and produce a thesis as part of their training to be doctors.[15] Medical Students in Ghana also wrote a dissertation as part of their medical degree[3] In the UK, several institutions offer intercalated courses that enable medical students to interrupt their medical training and pursue a second degree usually with a strong research component.[15]

Clinical Fellowship schemes have also been instrumental in training young doctors and those in established post-graduate training programmes to become physician-scientists'[16, 17, 18] They may be formal and well-structured or informal.[17,18] Nuttal et al, describe a well-structured and sponsored Research Fellowship Scheme of the Royal College of Surgeons of England which gave surgical trainees training in research and an opportunity to conduct research.[18] A total of 531 publications were produced from the project and a third of the fellows who became consultants had some form of academic positions afterward. In addition to having indirect benefits to patients, half of the participants went on to receive funding for additional research. Courses on various aspects also contribute to the professional development.

In the United States, MD-PhD programs were introduced in the 1950's to provide scientific training in research early and to enhance the translation of scientific research into clinical care [9, 14]. This became necessary because of the increasing length and sophistication of the training to become a clinician or an independent scientist, thus, it sought to combine the two and start the training early to reduce the training time[14]. In 1964, the Medical Scientist Training Programme (MSTP) was started by the National Institute of General Medical Sciences (NIGMS) and the National Institute of Health to fund the MD-PhD programmes.[9,14] Another approach adopted by some institutions in the US was to add an additional year for research to the training programme during the MD programme, at which time, the resident does no clinical work or the training may be MD only with structured training in research during the preclinical years along a longitudinal fashion[19].

Training of a Physician-Scientist in Ghana

Currently, in Ghana and other African countries, the path to becoming a physician-scientist is not so well-defined.[4] Though undergraduate research programmes are well developed and linked to the curriculum, programmes for young doctors are mostly informal until they enter residency training.[3] For instance, a young doctor who was about to complete the second year of his house job in the Eastern Region of Ghana informed one of the authors that he was now certain he wanted to embark on a research career and wanted to know what his next step should be. This doctor had previously demonstrated his interest in research after completing medical school by volunteering his services and participating in a research internship while waiting for his posting for a house job.[3] He wanted to know this, amidst the uncertain climate of, competing job opportunities with greater financial incentives from private clinical practice, and an extended postgraduate training programme of at least 11 years from graduation to fellowship qualification for Ghana College of Physicians and Surgeons training and its sponsorship challenges; counting 2 years of housemanship, 2 years of being a medical officer to qualify for sponsorship, 3 years of membership training, 2 years of district service and 2 years to complete the Fellowship training. Eventually, this doctor's next posting to a district hospital came through, and while he was working there as a medical officer, he considered enrolling in a Master of Public Health (MPH) programme in Ghana. Rather, he chose to invest his energies into getting a research program in the USA so he could move there to further this career.

So, for the young doctor of today who wishes to embark on a research career, what were the options available to him after completing his house job? What additional research training can he obtain during the next two years of compulsory district rotation as a

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medical officer? Who will supervise him if he wishes to do some research? What seed grants are available to him? Will the government pay him a salary and allow him to be attached to a research centre while waiting to join the post-graduate training programme? Does he then do a PhD in the basic sciences or start his fellowship training in the Clinical Sciences? After all there are many clinicians with excellent research careers who have not done a PhD. Who will pay him a salary if he opts for a PhD as he is not eligible to join the University without a PhD or completion of his residency training? Is the exposure to research during the several years of preparation and residency training sufficient for timely progression through a research career to retirement? In reality, most doctors in Ghana become physician-scientists after completing the Ghana College or West African College of Physicians or Surgeons residency training programmes and a dissertation that can yield several publications, which become the basis of their future research. Further opportunities for research productivity during these years are available but require planning, mentorship and working in environments that integrate research with clinical work.[5] These considerations are not unique to would-be medical researchers in Ghana alone, they occur globally.[2,4-9]

The Universities are the highest employers of physician-scientists in Ghana but until the recent start of a PhD programme, they generally do not offer special programmes tailored to their needs. Presently, there is a rising trend among young doctors in Ghana to do an MPH privately at a local School of Public Health and leave the country afterward. Some also do the course abroad. So is it time for the medical schools to offer comprehensive courses in clinical, laboratory and public health research such as a Master's course linked to the final year course in medical school and give a dual degree, e.g. MBChB-MPH during the gap of 6-8 months while newly qualified doctors are waiting for house job posting; re-introduce intercalated courses, or start MD/MBChB-PhD programmes as has been recommended?[4,5,7,9] How can these programmes and research the students do to be funded? Is there also a need for some advocacy with the Ministry of Health or Ghana Health Service to provide and advertise a separate training track for research or academic track doctors and employ clinical research fellows?

The Ministry of Health through the Ghana Health Service is the highest employer of doctors in Ghana. It is responsible for employing housemen and medical officers and sponsors residency training. It has a health research directorate with research units in Kintampo, Dodowa, and Navrongo and is also supported by a research unit at Hohoe and Agogo Hospital, a Christian Health Association (CHAG) facility. These research units monitor populations linked to demographic surveillance systems that create the enabling environment for intervention studies, vaccines and drug trials. Eminent physician-scientists trained in these units have gone on to become seasoned researchers. Even though these physician-scientists start their research career earlier, once they join the research unit, they also have an obligation to undertake clinical practice and are not posted there to do research full-time but they work like clinical fellows. In addition, they are granted study leaves with pay to pursue PhD programmes if they have served the requisite number of years thus gaining research experience at the postgraduate level, similar to MD-PhD graduates but lacking clinical specialisation [5,9] It is not so for doctors in clinical practice who desire a PhD. This option was discussed with the young man, however, a clear pathway to access this choice was not presented as an option during the selection of his next rotation, and neither did he go out of his way to explore it. Eventually, he found a research programme with a training position in the US and left the country.

In recent times, a third alternative has emerged. The College of Health Sciences, University of Ghana has recently initiated a PhD programme in Clinical Sciences for doctors to create a focus on research in the clinical sciences. What is unclear is whether these efforts will yield physician-scientists actively engaged in research at a time when academic positions are not readily available, or they will be lured into clinical positions without research. Furthermore, integrating this with residency training needs to be considered as the MD-PhD programmes have done so the training time in both sciences can be combined and shortened. Thus, it needs monitoring. Research careers can be developed at any point along the training continuum, and opportunities for clinical research are available in some academic centres, regional and district hospitals through projects, and junior doctors, residents and early career researchers have participated in some of these projects.[3] Figure 1 outlines the options for formal training available to medical graduates who wish to become physician-scientists in Ghana.

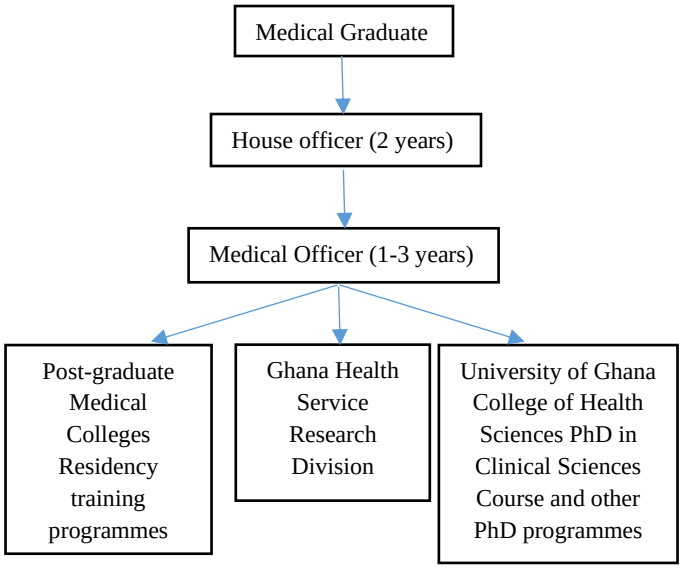

Figure 1: Pathways for formal training of physician-scientists in Ghana

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Discussion

In spite of establishing MD-PhD programmes across the US, in the 1980's and 1990's a decline in the number of physician-scientist in the US and their grant applications to the NIH was noted.[9, 14] This led to an investigation of the barriers that confront researchers in the clinical sciences.[14] Their findings showed that trainees not in MD-PhD programmes were saddled with student debts after the training period; and it seemed more lucrative to enter clinical practice; training time to gain clinical competence and the time required to transition into an independent researcher had increased, and finding a work-life balance seemed challenging for younger colleagues, while NIH funding also decreased. There were also other additional demands on one's time and energy. Besides this, decline in the funding of academic centres in the US and increasing demand for revenue from clinical practice were reported to have led to increasing clinical care loads of academic physicians restricting the time for research.[5,6] This highlighted the need for protected time for clinical research and more efficient use of the time dedicated to patient care[6]. Measures were taken to address the challenges and the numbers have stabilized[9]. However, the challenge now is how to prevent attrition and retain these doctors in research given the lower salaries in academic research compared to private practice.[9]

A four-pronged approach to tackle the problem of physician-scientists has been suggested.[5] This included having research-focused postgraduate training or residency programmes for physician-scientists that integrate medical and research training using lessons learned from MD-PhD programmes; a reduction in the time from training to an independent research position by five years; and promotion of an increase in the numbers and diversity of trainees. Additionally, a centralized mentoring and oversight process facilitated by creating institutional career development offices has been advocated to reduce attrition. The Ghana College of Physicians and Surgeons (GCPS) has also restructured its formal training in research as others have suggested to deal with some of these challenges.[4,7,6] The college is in the process of establishing a PhD/Fellowship track for its residents interested in pursuing academic/research careers as occurs in other settings.[4,5,9] The curriculum has been designed and presented at two (2) state universities. The discussion is currently at the level of the Academic Board of these institutions, awaiting approval. The West African Colleges have similar arrangements with universities in Nigeria. Some doctors are pursuing MPH programmes after school, MPhil and PhD programmes in basic sciences subjects such as Medical Microbiology and Physiology. What is lacking is opportunities for research degrees in the clinical sciences.

Availability of funds is an important determinant of the capacity to carry out research [4-5,14]. In the US apart from the funds from the Medical Scientist Training Programme, other support for MD–PhD programmes are obtained from institutions, training grants, individual fellowships, and research grants [9]. Researchers in Africa find it more difficult to access funding for research owing to the limited research funds provided by the governments of these countries including Ghana.[4] Furthermore, only a few researchers can access global funds dedicated to research due to unsuccessful applications, lack of training in grantology, and resolve to make an application[4]. Thus, training in grantology should be an essential component of the training of physician-scientists. In addition, training programs must establish links with funding institutions and form international collaborations to attract fellowships and grants for multicenter studies. These funding challenges can also be tackled by lobbying government, industry and other funders within the country.[6]

Mentorship in research is crucial for professional development and personal achievement.[5,20,21] It involves a nurturing relationship between a mentor, usually a successful or experienced researcher and a mentee, or student, during which the changing needs of the mentee are identified and met over time through guidance, problem-solving, networking, critical thinking and advice[5,20]. Good mentorship ensures the mentee's goals are met through action plans set to achieve them and that there are opportunities for review, critical reflection, problem-solving and research productivity through developing research proposals, grant applications, publications and presentations at conferences [5,20]. Mentorship can also be used as a tool to address issues peculiar to minorities such as females in research and ethnic minorities [21]

Collaboration with academic institutions such as the Noguchi Memorial Institute of Medical Research, the Department of Medical Microbiology of the Medical School and other basic and clinical science units of universities, can provide mentors for biomedical research. Exchange programmes to expose trainees and physician-scientists to best practice environments and international mentors are also relevant. Additionally, creating centres of excellence in clinical research within the country can provide leadership, best practice experience and cutting-edge research; it can also stimulate innovation and support training in a focused area to promote scientific ventures that are not feasible within conventional funding from other sources [22]. They can also provide the infrastructure to support clinical trials, and longitudinal studies and address research priorities linked to international goals like the sustainable development goals (SDGs) as well as in-country research priorities.[10]

Additional uncertainties remain at the stakeholder level such as the need for the classification of grades of doctors by the MOH/GHS so that clinicians with academic degrees such as a PhD can be better placed and be adequately remunerated. Thus, uniform or near-uniform remuneration for physicians who join academic institutions with proper equivalences should be established concurrently to encourage more doctors to

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go into research, though one may have to demonstrate additional workload.[6] Government and other stakeholder support to meet funding needs can also be an incentive to retain these researchers. Other incentives such as research support for physicians while in training at all levels of the Health System in the form of infrastructure, mentorship and protected time should also be made available as others have suggested.[4,5,7]
Exemption from some district rotations may be considered to shorten the duration of fellowship training and the time to scientific independence. These exemptions are currently only being offered in specialties with limited residents such as Psychiatry, Radiology and Anaesthesia and need to be diversified. At the same time, posting to some district hospitals, particularly those linked to the research units or districts integrate research with clinical work can be designated as places where mentorship and research experience can be gained by doctors on the physician scientist track and offered as clinical fellowships for 1-2 years.

Conclusion

Doctors desiring a career path in clinical research need clear pathways and structured programmes to develop their skills. Mentorship, funding and infrastructure are also needed. It is important that training in both clinical work and research roles commences early to boost productivity and set those desiring university tenure on a path to professorship. When mentored by physician-scientists and other seasoned researchers, these doctors can be instrumental in transforming wherever they work into centres for cutting-edge research so that research questions useful for clinical care can be generated, answered and translated into better patient outcomes. They can also assist with recruiting patients to make up the numbers for large international clinical trials, identifying patients with rare diseases for surveillance, and monitor and develop treatments. Just as field epidemiology graduates trained by the Centre for Disease Control have made a major impact on the control of epidemics in Africa [10], these doctors can have a similar impact on the research front and a steady stream could pave the way for large longitudinal studies which are limited in Africa and perhaps, win Nobel prizes in the sciences from Ghana.

Recommendation

We recommend that academic institutions and the Ministry of Health collaborate with other stakeholders to define a clear pathway for training of physician-scientists, their career progression and ensure that this information is made available to doctors requiring postings. Furthermore, academic institutions, and the postgraduate medical colleges should offer courses tailored to the needs of doctors desiring research career in either public health, biomedical sciences and the clinical sciences. This should include research-focused postgraduate training and residency programmes for physician-scientists and provide technical skills including skills in grantology. The Ministry of Health can offer scholarships for training, sponsor mentorship programmes, research fellowships, and provide competitive salary structures that are near or comparable with those of their colleagues who go into clinical practice/service delivery or incentives for pursuing a career in health research. Additionally, the Ministry of Health should provide funds for research and an environment where research findings can be translated into policy, including the establishment of clinical research centres of excellence. We also recommend that the length of training to become a physician scientist be examined and shortened where possible. Finally, we recommend that, the challenges with training these professionals be addressed so that they can contribute to research on issues emanating from national policies such as the National Universal Health Care roadmap and National Health Policy and strategy as well as the control of communicable and non-communicable diseases, diseases of nutrition and lifestyle, pollution, and reproductive and child health issues.

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REVIEW ARTICLE

MICROBIAL DYSBIOSIS AND IMMUNOPATHOGENESIS OF ORAL MICROBIOME IN THE DEVELOPMENT AND PROGRESSION OF ORAL SQUAMOUS CELL CARCINOMA: SYSTEMATIC REVIEW

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Summary

Objective: The purpose of this review is to evaluate the specific bacterial species and their association with oral cancer, particularly in oral squamous cell carcinoma (OSCC)

Methodology: A literature search was done through PubMed, Scopus, and Web of Science databases, and data were extracted according to inclusion criteria. Original studies of 20 articles were included in this review.

Results: A total of 20 articles and 961 samples were included in this review. The mean age was 60.12 ± 7.63, with a significantly higher male predilection (M: F – 2:1) ratio. 16S rRNA sequencing was found to be the most commonly used detection method. Alteration in the oral microbiome was seen with varying degrees of epithelial dysplasia, early & late stages of oral cancer. In OSCC patients, there was an increased abundance of specific microbiomes *like Fusobacterium species, Porphyromonas gingivalis*, and *Prevotella* compared to other species.

Conclusion: From this systematic review, it has been found that the changes in diversity of oral microbiome in cancerous patients than that of healthy patients. In OSCC there is an increased abundance of specific species such as *Fusobacterium* species, *Porphyromonas gingivalis*, and *Prevotella* species.

Key words: *Oral microbiome, Oral cancer, Microbiota, Metagenomics, Systematic review*

Introduction

Oral squamous cell carcinoma (OSCC) is the most prevalent malignant tumor in the head and neck region. It is the sixth most common tumor worldwide and its prognosis and survival rates are poor, the 5 year survival rate is less than 50% [1]. Nowadays, the incidence and mortality rate of oral cancer is increasing among both men and women due to changes in lifestyle and habits.

The etiology of OSCC is multifactorial; tobacco use and alcohol, are the most prevalent risk factors for OSCC, other contributing risk factors are oncogenic viruses, especially Human papillomavirus (HPV), oral microbiota, genetic factors, chronic irritation, poor oral hygiene, and nutritional deficiencies[2]. The development of oral cancer has been potentially influenced by genetic alteration associated with the activation of oncogenes and inactivation of tumor suppressor gene signaling, resulting in uncontrolled proliferation of OSCC cells[3].

Oral microbiome is defined as the collective genome of microorganisms that exist in the oral cavity. Oral cavity is home to a variety of diverse microbiomes, comprising more than 700 species which include bacteria, viruses, fungi, protozoa, and archaea[4].

The oral microbiome plays a role in maintaining a symbiotic relationship with the host, essential for various physiological processes. Dysbiosis or disturbance in homeostasis, has a significant effect on the host immune system, eventually resulting in both local and systemic disorders[5]. The prolonged and persistent colonization and survival of pathogenic microbiota can lead to functional alteration of oral microbial diversity and translocation, which is the initial mechanism for the development of distant carcinomas[6].

Recent studies suggest that bacteria play an important role in the pathogenesis of cancer by the following three mechanisms, chronic inflammation, preventing apoptosis, and production of carcinogenic substances[7]. Microbiome's role in causing cancer has been ignored for a long time until the studies in the early 1990s observed that gastric cancer was caused by *Helicobacter pylori (H. pylori)*[8] .

Followed by other bacteria such as *Salmonella enterica* in colon carcinoma, *Salmonella typhi* in gallbladder carcinoma, *Chlamydia trachomatis* in carcinoma of the cervix and ovaries[9]. *Fusobacterium nucleatum (F. nucleatum),* and *Porphyromonas gingivalis (P. gingivalis*) are the two most common oral bacteria that play an important role in causing oral cancer[10]. These bacteria are classified as Group -1 human carcinogen by 'The International Agency for Research on Cancer and the 'World Health Organization[10].

This systematic review is based on the updated evidence from recent studies published between January 2022 to December 2023, compiles the relationship between the oral microbiome and oral squamous cell carcinoma (OSCC), and also focuses on different

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bacterial genera and their pathogenesis in oral cancers, and also highlights the increased and decreased abundance of certain bacterial species in oral cancer compared to normal samples.

Materials and Methods

Protocol

A systematic literature search was conducted independently and the Preferred Reporting Items for Systematic Reviews and Meta-analyses "PRISMA" guidelines were followed in this systematic review[11].

Research Question

The research question was designed based on the PICO format: "Does OSCC patient have alteration in salivary microbial composition?"

Population

Patients with oral squamous cell carcinoma (OSCC).

Intervention

Microbiome alteration.

Comparison

Healthy individuals or patients without OSCC.

Outcome

Changes in the oral microbiome composition in OSCC patient.

Data Sources And Search Strategy

Records were identified through a literature search in PubMed, SCOPUS, and Web of Science databases. For the search strategy, combining MeSH terms and free text words using Boolean operators such as: Microbiota AND ((oral cancer) OR (Squamous Cell Carcinoma of Head and Neck) OR (oral carcinoma)), "((Carcinoma) OR (Squamous Cell), "OR "(Head and Neck Neoplasms)"AND "(Metagenomics)","(Microbiota)," AND "(Mouth Neoplasms)," OR "(Squamous Cell Carcinoma of the Head and Neck)" were used in articles published from January 2022 to December 2023.

Eligibility Criteria

The inclusion criteria for selection of the article were:

1. Human studies
2. Articles published in English
3. Articles with (minimum of 10 patients or?)10 or more than 10 patients in the study group
4. Clinically and histopathologically diagnosed cases of oral squamous cell carcinoma with well–defined staging and grading

The Exclusion Criteria

1. Narrator review or systematic reviews, meta-analyses, case reports, and series; in vitro studies; in animal studies
2. Studies with less than 10 patients
3. Analysis of oral microbiome in patients affected by OSCC, during or after cancer therapy
4. Studies which are not clinically and histopathologically diagnosed

Literature Screening

A two-step procedure was performed in this literature screening. First, all the recognized citations' titles and abstracts were extracted and preliminarily screened for inclusion in the full-text review. Second, the inclusion and exclusion criteria indicated above were used to determine if entire texts were eligible. The PRISMA flowchart depicts an overview of the literature search and screening processes given in Figure 1.

1. Data Extraction
2. Data extracted from the literature search were: author, country, year, mean age, gender, type of study, study population, cancer stage, risk factor, samples collected, detection method, associated microbiome, α and β diversity, and results.

Statistical Analysis

Statistical Package for the Social Sciences (SPSS) software was used for analyzing the data.

Results

Literature Search And Study Selection

In the preliminary search, 360 articles (PubMed – 180, Web of Science = 60 and Scopus = 120) were selected. 250 articles were screened after the removal of duplication. Of these, 133 articles were removed by reviewing titles or abstracts and 117 articles were eligible for full-text view. Papers not in English (n =11), not relevant to the topic (n = 17), Narrative or systematic review, meta-analysis, case report, and series (n = 23), Studies with less than 10 patients (n=7), not clinically and histopathologically diagnosed cases of OSCC (n = 18), no well-defined classification (n =10), insufficient data (n = 10) were excluded, thus a total of 20 articles were finally included in the review. (Figure 1)

Aspects of Included Studies

In total, 20 articles were included in this review published from January 2022 to December 2023. Of this one article was a retrospective study and 19 were prospective studies (including case-control (n =10), cross-sectional (n= 7), and observational study (n = 2) *(Supplementary Table 1).*

Socioeconomic Details

Of the 20 articles, nine were from China, four were from the USA, three were from India, two were from Japan, and one each from Australia and Finland. The overall sample size ranged from 12 to 112 which included 961 cases. The mean age was 60.12 ± 7.63, and in these 656 (68%) were male and 461 (48%) were females. Eighteen studies showed male predilection, whereas in two studies females predominated. Collectively, there was significantly higher male predilection than females leading to a 2: 1 of M: F ratio.

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Among 961 cases, 352 (36.6%) were stage I & II, 258 (26.8%) were stage III & IV, and for 351 (36.6%) the

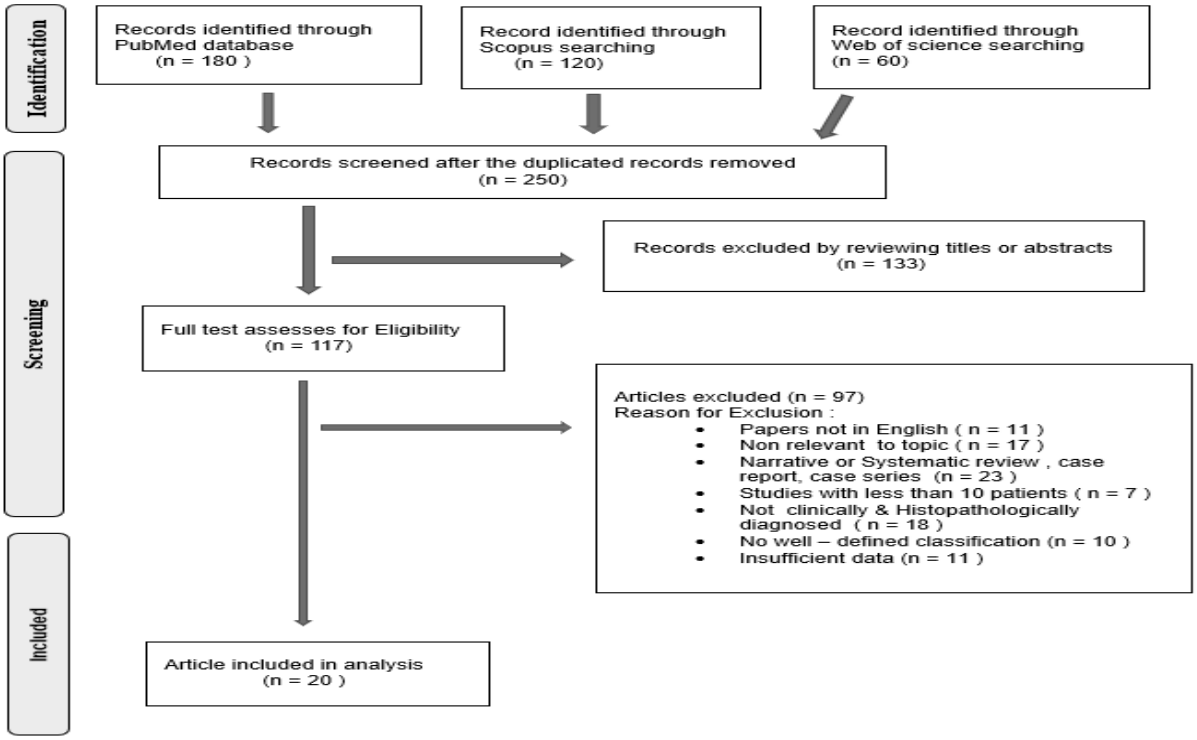

Figure 1: PRISMA figure depicting an overview of the literature search and screening processes

stages were not mentioned. The most commonly involved site was the tongue (n= ,50%), followed by the buccal mucosa (n=,30%), the gingiva (n=,15%), the floor of the mouth (n=, 10%), followed by (5%) each in other sites like the alveolar ridge, hard palate, faucial pillars, and retromolar areas and cancer site was not mentioned in 4 articles (table- 1).

Risk Factors

Major risk factors for oral cancer include alcohol, smoking, tobacco, and betel nut habits. In this review of 961 cases, 438 (45%) had a history of alcohol, 356 (37%) smoking, and 24 (2.49%) used tobacco. For 5 articles, 167 (17.3%) cases the habit history was not mentioned.

Samples and Detection Method

To observe changes in the oral microbiome in oral cancer patients, different types of samples were collected which included, 11 (55%) saliva samples, 8 (40%) tumor tissue samples, 6 (30%) oral swab samples, 2 (10%) tongue, and dental plaque samples. Numerous methods and commercial kits were available for the detection of microbiomes from the samples. In this review, we observed that out of 20 articles, 13 (65%) articles used the 16 S rRNA - V4 sequencing detection method, which is a principal method for microbiome investigation, followed by 9 (25%) articles that used DNA extraction method, other methods like 16 S rDNA sequencing, library construction, amplification, FISH Immunostaining,

Table 1 General characteristics of included OSCC cases

Characteristics	n (%)
Age (mean ± S.D)	**60.12 ±7.63**
Sex	
Male	656 (68.26%)
Female	461 (47.97 %)
Type of Study	
Prospective study -	
Case-control study	10 (50%)
Cross-sectional study	7 (35%)
Observational study	2 (10%)
Retrospective study	1 (5 %)
Cancer stage	
Stage – I	129 (13.42 %)
Stage - II	134 (13.94 %)
Stage - III	52 (5.41 %)
Stage – IV	93 (9.67 %)
Stage – I/II	89 (9.26 %)
Stage – III/IV	79 (8.2 %)
Not mentioned	351 (36.5 %)
Risk factor	
Alcohol	438 (45.57 %)
Tobacco	24 (2.49 %)
Smoking	356 (37.04 %)
Not analysed	5 (0.52 %)
Site	
Buccal Mucosa	10 (50 %)
Tongue	8 (40 %)
Gingiva	15 (75 %)

610(63.5%

Floor of Mouth	7 (35 %)
Alveolar ridge	3 (15 %)
Hard palate	3 (15 %)
Retromolar Trigone ,	1(5%)
Faucial pillars	4 (20 %)
Not mentioned	

PCR each were used in 2 (10%) articles and also shotgun sequencing, gel electrophoresis, whole exome sequencing (WES), whole genome sequencing (WGS), metagenomic sequencing each was used in 1 (5%) article given in table -2.

Table 2 Different samples, detection method, and diversity of included cases

Characteristics	n (%)
Samples examined	
Saliva samples	11 (55 %)
Tissue samples	8 (40 %)
Oral swab	6 (30 %)
Tongue Plaque	2 (10 %)
Dental plaque	2 (10 %)
Detection Method	
16S rRNA Sequencing	13 (65 %)
16 S rDNA Sequencing	3 (15 %)
DNA Extraction	9 (45 %)
RNA Extraction	1 (5 %)
FISH	2 (10 %)
PCR	2 (10 %)
Whole – exome sequencing (WES)	2 (10 %)
Whole genome sequencing (WGS)	1 (5 %)
Shotgun Sequencing	1 (5 %)
Gel Electrophoresis	1 (5 %)
Metagenomic Sequencing	1 (5 %)
Library Construction	2 (10 %)
Diversity	
α – diversity	7 (35 %)
β - diversity	6 (30 %)
Both diversity	3 (15 %)
Not mentioned	2 (10 %)

Microbial Diversity

Diversity was calculated in two ways, namely alpha and beta diversity. Alpha diversity is the diversity occurring within a particular area or ecosystem. In contrast, beta diversity is the comparison of diversity between ecosystems, usually measured as the number of species changes between the ecosystems. In our review, 16 (80%) articles reported a change in diversity between diseased and healthy controls, in 2 (10%) articles there were no significant differences in diversity between the groups[12,13] and in the other 2 (10%) articles diversity between groups was not analyzed.[14,15] Out of 16 articles, 7 reported alpha diversity, 6 articles reported beta diversity and the remaining 4 articles showed changes in both alpha and beta diversity in cancerous samples.[16.17,18,19] Overall, In alpha diversity, 5 articles showed increased richness[20,21,22,23,24], and 4 articles showed decreased richness.[16,19.25,26] Eight articles showed significant changes in beta diversity in cancerous samples.[16,18,19,27,28,29,30,31]

Microbial Abundance

We observed that there was a significant difference in microbial composition between cancerous and non-cancerous patients. Out of 20 articles, 2 articles reported only with *fusobacterium species*, 1 with *prevotella*,1 with *fusobacterium, Actinobacteria*, 1 with *streptococcus and Gamella*, 3 with *streptococcus, Neisseria, Rothia* and *Capnocytophagia*, 12 with other microbiome species such as *Fusobacterium, prevotella, Porphyromonas, streptococcus, Bacteroides, Treponema, Filifactor, Rothia Aggregobacterium, Campylobacter, Leptotrichia, Pasteurellaceae, Velionella.* After combining the result,14 (70%) reported with a higher abundance of *Fusobacterium* at the species level, 8 (40%) of *Prevotella*, 6 (30%) of *Porphyromonas gingivalis*, 4 (20%) of *Peptostreptococcus*, 3 (15%) of *Bacteroides, Parvimonas, Capnocytophagia*, and 5% reported with others bacteria like *Actinobacteria, Treponema, Carnobacterium, Tanerella, Filifactor, Abiotrophia defective, Selemonas, Peptoanaerobacter, Gamella species, Ralstonia, Pedobacter, Aggregobacterium, Campylobacter, Leptotrichia, Pasteurellaceae, Velionella* which showed increased abundance in cancerous patient (figure 2).

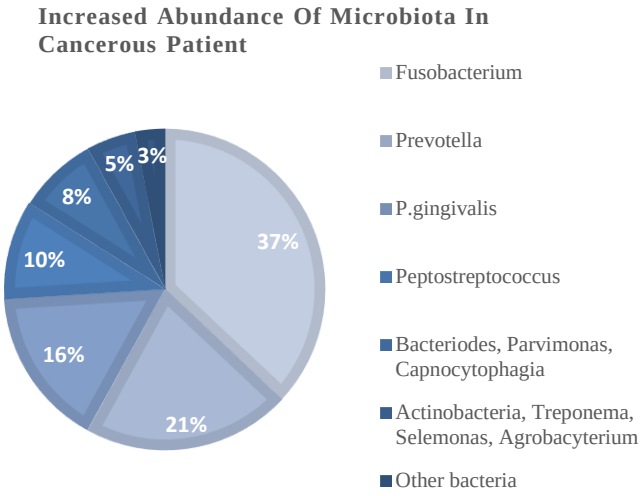

Figure 2: Increased Abundance of Microbiota in the sample of Cancerous patient

Out of 20 articles, 8 (40%) of *Streptococcus* species, 5 (25%) of *Neisseria*, 4 (20%) of *Firmicutes*, and 2 (10%) of *Rothia* showed increased abundance in healthy controls than in oral cancer patients.

Based on the evidence from this review, we observed a quantitatively increased abundance of salivary microbial composition in cancerous patients than in non-cancerous patients. Higher microbial abundance was seen with varying degrees of epithelial dysplasia, early & late stages of cancer, and also in patients with smoking, alcohol, and tobacco habits. *Fusobacterium, P.gingivalis*, and *Prevotella* were the most common

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species that showed higher abundance in all cancerous patients. *Capnocytophagia* gingivalis played an important role in OSCC by promoting OSCC invasion and metastasis. This study shows that OSCC significantly alters the dynamic balance between the host and the resident oral microflora of the oral cavity.

Discussion

Oral squamous cell carcinoma (OSCC) is one of the most common malignancies in the head and neck region. Recent researchers suggest that the oral microbiome plays an important role in the development of oral cancer, particularly OSCC. The oral cavity harbors about 500 - 700 diverse species of microorganisms.[32] The oral microbiome plays a role in maintaining a symbiotic relationship with the host; alteration in the microbial diversity and host - microbial interactions has been reported to be associated with the oral squamous cell carcinoma[5]. However, in this systematic review, our objective was to evaluate the specific bacterial species and their impact on oral cancer, particularly in oral squamous cell carcinoma (OSCC). In the overall comparison of results, the diversity and richness between healthy and tumor tissue showed variations.[33] In our review, changes in microbial diversity were more obvious when comparing cancerous patients with healthy patients.

In the 20 articles reviewed, different samples were collected such as saliva, tissue, oral swabs, and plaques. The type of sample collected may affect the result in evaluating the relationship between oral microbiota and cancer. Salivary samples and oral swabs may have colonizing microbiota from the superficial surface, whereas tissue samples may reveal more significant potential microbiota from a deeper surface.[34] Various factors such as salivary pH, redox potential, and oral hygiene status may influence surface microbial communities. Saliva is the optimal sampling site for acquiring oral microbiota DNA for analysis as it represents the microbiota found in all oral sites and their related diseases, and it is also used for exploring different biomarkers. There is no significant difference in stimulated, unstimulated, and mouth rinses given by Ryutaro et al.[35] Mouth rinse is the most reliable sample for detection in specific patients with low saliva flow and in elderly patients.

The reliability of microbial investigations is primarily dependent on molecular biology techniques. In our review, 16S rRNA gene sequencing and amplification is the principal detection method used. It is cost-effective and it provides gene-level taxonomic classification.[36] In the 16S rRNA technique, V3-V4 regions were the most commonly sequenced region. Along with 16S rRNA gene sequencing other detection techniques such as DNA extraction, 16S rDNA sequencing, shotgun sequencing, FISH Immunostaining, PCR, RNA extraction, gel electrophoresis, whole exome sequencing (WES), whole genome sequencing (WGS), library construction, amplification, metagenomic sequencing were also used.

Oral microbiota such as *Fusobacteria, Firmicutes*, and *Bacteroidetes* were predominant in cancer patients in several studies.[37] From this review, *Fusobacterium, Porphyromonas gingivalis, prevotella,* and *Peptostreptococcus* showed greater abundance in oral cancer patients compared to other bacterial species. Dysbiosis or disturbance in homeostasis, has a significant effect on the host immune system, and eventually results in local and systemic cancer[38]. Various research studies on colorectal and breast cancer focused mainly on *Fusobacterium species.* Recently, the presence of *fusobacterium* has been identified in oesophageal cancer (ESCC).[39] Studies show that it promotes tumor growth, and metastasis, and alters host immune responses. In *fusobacterium* infection, there is chronic inflammation and it also alters the antiapoptotic pathways by inducing NF-kB signaling. It activates β-catenin signaling via IL 6, STAT3, binding to E-cadherin and also through LPS. The wnt transcriptional activity is increased with activation of pro-inflammatory cytokines. FadA is the virulent factor of *fusobacterium* that causes methylation of cyclin-dependent kinase inhibitor 2A (CDKN2A) promoter and alters macrophage infiltration in cancer cells. In addition, it activates p38, resulting in the secretion of Cyclin D1, MMP-9, MMP-13, and the expression of c-myc oncogenes which are involved in tumor invasion and metastasis.[40]

Porphyromonas gingivalis has a malignant potential in oesophageal, gastric, and pancreatic cancer.[41] It is a common oral commensal, proved to be found in OSCC sites. Studies showed that it undergoes chronic inflammation, apoptosis, epithelial-mesenchymal transition (EMT), cell proliferation, and tumor invasion. *Porphyromonas gingivalis* secrete an anti-apoptotic enzyme NDK (Nucleoside diphosphate kinase), modulates ATP / P2X7 – signaling, and produces ROS (Reactive oxygen species). ROS is a key mediator, associated with chronic inflammation and tumor development. *Porphyromonas gingivalis* is NF-B-dependent and produces cysteine proteinases called gingipains, it cleaves the MMP-9 pro-enzyme and activates MMP-9 which promotes tumor cell migration and invasion. In the anti-apoptotic pathway, it inactivates Bad (pro-apoptotic) through Akt / Jak 1 / Stat3 signaling. It also alters the cyclin / CDK (cyclin-dependent kinase) activity by inactivating the p53 tumor suppressor gene.[42]

In this review, other anaerobic bacteria such as *Peptostreptococcus, prevotella, Aggregatibacter*, and *Bacteroides* were also highly abundant in OSCC samples. On the other hand, *Streptococcus, Neisseria, firmicutes*, and *Rothia* showed decreased abundance in OSCC samples when compared to other species. Apart from carcinogenic bacteria, there is insufficient data on the involvement of viruses, parasites, and fungi in oral cancer [6]. There is evidence that the presence of periodontal disease is one of the high-risk factors for the development of OSCC[43]. Inflammation is the link

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between periodontitis and cancer and it is considered to be the seventh hallmark for cancer. In periodontitis, there is an increased release of inflammatory mediators such as cytokines which may promote damage in DNA, thereby causing tumorigenesis.[44] From this review, we additionally found that microbiome can vary according to the degree of dysplasia and stages of cancer. Oral microbiota is comparatively low in mild and moderate dysplasia when compared to severe dysplasia. In the early stage, there is a decreased abundance of microbiota when compared to the late stage of cancer. Increased abundance of microbiota was seen in severe dysplasia and advanced-stage cancer.

Analyzing the results, the oral microbiome in cancerous patients differs from that of healthy patients, and the microbiome may also play an important role in the progression, differentiation, invasion, and metastasis of cancer[45].

Conclusion

Based on the current evidence, we conclude that there is a significant dysbiosis in the oral microbiome which leads to changes in oral microbial diversity in cancer patients and healthy controls. This shows that the oral microbiome plays a significant role in the development and progression of OSCC. This review also highlights that the *Fusobacterium, Porphyromonas gingivalis, Prevotella*, and *Peptosptreptococcus* species showed increased abundance in OSCC than other bacterial species, this microbiome represents a valuable prognostic factor for OSCC.

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CASE REPORT

A DISTURBING EMERGING TREND OF ALCOHOL-BASED HAND SANITIZER BURNS IN NORTHERN GHANA: A CASE SERIES

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Abstract

Introduction: During the COVID-19 pandemic and in the aftermath of it, there was a surge in the use of alcohol-based hand sanitizer (ABHS). This was because the Center for Disease Control and Prevention and the World Health Organization recommended it as an essential commodity for hand hygiene and the reduction of infection transmission. However, alcohol is flammable and has the potential to cause burns if ignited. There are few reports of ABHS-related burns in literature. We aim to report 8 cases of ABHS burns in Northern Ghana and sound a clarion call to stakeholders on a disturbing emerging trend.

Case Presentation: About 62.5% of the victims were children and 75% were female with a male-to-female ratio of 1:3. The mean age of victims was 13.25 years while the mean total burn surface area was 29.8%. All victims in this study sustained their injuries because of an attempt by either them or their collaborators to use ABHS as fuel to light a fire for domestic purposes. Most of the burns sustained were second-degree (75%). The case fatality rate of ABHS burns was 25%.

Conclusion: Alcohol-based hand sanitizer, though effective for hand hygiene, is flammable and can cause burns when used injudiciously. ABHS burn is an emerging public health problem. There is a need for public education to curb this emerging trend and forestall future incidents. The Food and Drugs Authority (FDA) should consider the addition of warning labels for flammability on the containers and instruction manuals of sanitizers.

Keywords: *Alcohol-based hand sanitizer, Burns, Northern Ghana*

Introduction

In the wake of the COVID-19 pandemic, there was a surge in the use of alcohol-based hand sanitizers (ABHS) among people. It was a recommendation by the World Health Organization (WHO) and the Center for Disease Control and Prevention (CDC) to wash hands with soap and use ABHS for effective hand hygiene to prevent the transmission of COVID-19[1,2]. ABHS on the market are formulated either in liquid or gel form. A key component of these products is alcohol. The CDC guidelines for the production of ABHS are to use at least 70% of isopropanol or 60% of ethanol[2]. ABHS is effective for hand hygiene, albeit notable complications such as contact dermatitis, burns, ocular irritations, etc[3–6]. ABHS is highly flammable, more so in the liquid form than the gel form, and thus can cause burns if used injudiciously7. There are few reports of ABHS-related burns in the literature[6,8].

We aim to report a series of 8 cases of ABHS burns that presented to the Plastics and Reconstructive Unit of Tamale Teaching Hospital for management. We also wish to sound a clarion call to stakeholders on an emerging trend of burns that has the potential to impact an already burdened healthcare system.

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Conflict of Interest: None Declared

Cases Presentation

Case 1

A 27-year-old female igniting charcoal using ABHS burst into flames causing second-degree burns on the left upper limb with a total burn surface (TBSA) area of 9%. She learned from her siblings that sanitizers could be used to light a fire. She had in stock lots of donated ABHS during the COVID-19 pandemic (**Figure 2**), which was about to expire, so she decided to put it to use. She was a first-time user. She spent 9 days in the hospital and was managed expectantly.

Case 2

A 15-year-old female sustained 22% second-degree burns to the face, upper limbs, and trunk (**Figures 1b and 1c**) while attempting to light up charcoal using ABHS and match sticks. She presented 4 days after the incident and was admitted for 7 days and managed expectantly. She had learned from her peers at school that ABHS was a quicker and better agent for lighting a fire than the usual paper or kerosine. Since then, she had used ABHS to light up fire multiple times before this incident.

Case 3

A 5-year-old girl was sitting beside her mother who was cooking in an open kitchen. Her mother attempted

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lighting a fire using ABHS which resulted in an explosion and her clothes caught fire resulting in about 10% second-degree flame burns on the face and upper limbs. She was admitted for 7 days and managed conservatively. The mother did not sustain any burns. The mother had seen her co-tenants and neighbors use ABHS to light a fire and she decided to try it also. She attributes the explosion to pouring a lot of the sanitizer over the charcoal.

Case 4

A 2-year-old girl sustained 26% second-degree burns from naked flames when her mother tried to light up some charcoal using a matchstick and ABHS. It exploded and burnt her. She was admitted and managed conservatively for 14 days. The mother is a multiple-time user of ABHS to light fires and had learned this from her peers at work. She used her COVID-19-donated ABHS for this act.

Case 5

A 25-year-old mother was lighting up charcoal using match sticks and ABHS. It resulted in an explosion that caused burns in her and her 1-year-old baby who was sitting beside her. She sustained 54% mixed-thickness flame burns affecting the face, upper limbs, and trunk (**Figure 1a**). She was admitted and counseled for skin coverage with skin grafting but she did not consent to surgery. She developed sepsis and succumbed to it after 48 days of admission. She too was a multiple-time user of ABHS to light fires. She had learned this from her peers at work. She was using her expired stock of COVID-19 donated ABHS to light fire multiple times before this incident. Both the mother and baby sustained burns.

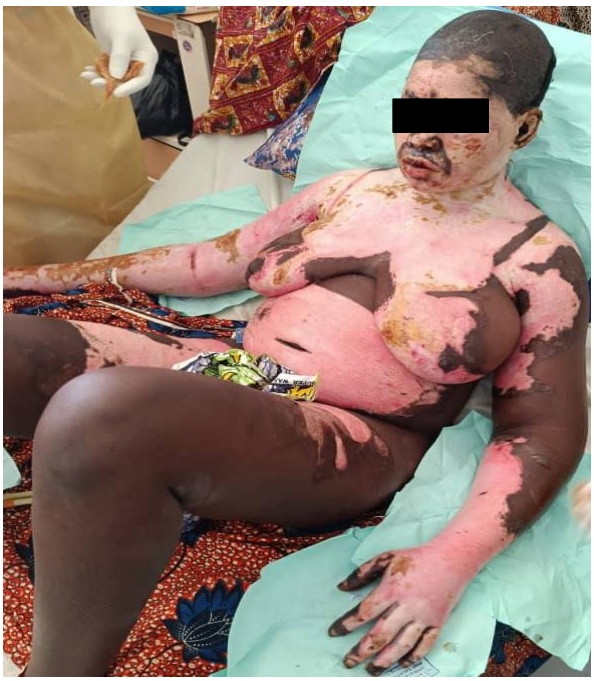

Figure 1a: Mixed thickness burns on face, trunk, and limbs

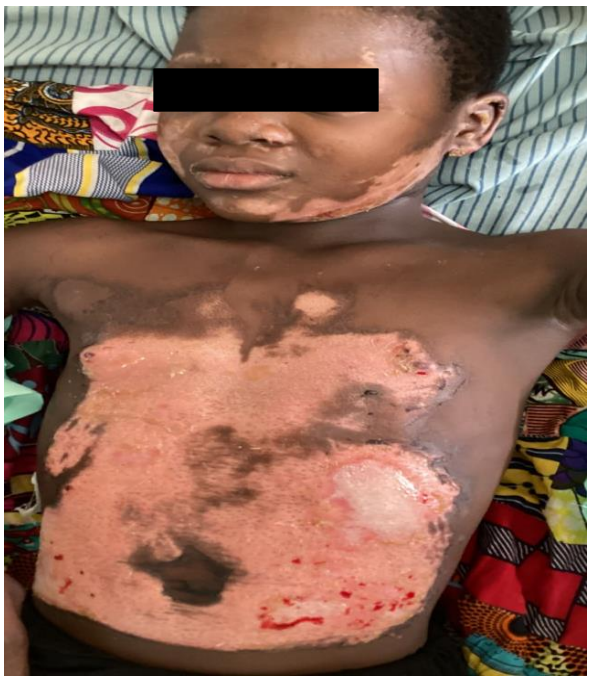

Figure 1b: Second-degree burns on face, trunk, and upper limb

Figure 1c: Second-degree burns on face, trunk, and upper limb

Case 6

A 1-year-old boy was a collateral victim of case 5. He sustained 10% second-degree flash burns to the face and upper limbs. He was admitted and managed expectantly for 17 days.

Case 7

A 5-year-old boy was standing closer to the mother who was trying to light up some charcoal using ABHS and match sticks. It exploded causing about 37%

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second-degree burns to the face, upper limbs, and trunk. He was admitted for 18 days and managed expectantly. The mother escaped unhurt. The mother had been using her expired sanitizer stock to light fire. She learned the behavior from her neighbors. She attested that ABHS was a quicker and better agent for lighting up a fire than her usual kerosine.

Figure 2: Different types of alcohol-based hand sanitizers

Case 8

A 26-year-old female attempted to ignite charcoal for cooking using ABHS and a matchstick. It exploded and her long straight nylon dress caught on fire. She sustained about 70% mixed-thickness flame burns. She was brought to Tamale Teaching Hospital where the initial resuscitation and wound dressing was done and then referred to Komfo Anokye Teaching Hospital for admission into a burn intensive care unit. She succumbed to her injuries 3 days later due to multiple organ dysfunction. She was also a multiple-time user of ABHS to light fires. She learned this from her peers and ever since had been using her stock of expired ABHS donated to her during the COVID-19 pandemic.

Discussion

During the COVID-19 pandemic and in the aftermath of it, the CDC and WHO recommended both hand washing with soap and ABHS rubs as effective methods of reducing the transmission of infections. These hand hygiene techniques were made available at entry and exit points in public and private places to enable usage[1]. While both are effective hand hygiene techniques, ABHS is relatively easier to use and less time-consuming, hence an increase in the compliance of usage. They can also be used in places where there is no portable water. ABHS contain moisturizers and emollients which make them less allogenic when compared to handwashing with soap[5]. They have become a household commodity even in the aftermath of the COVID-19 pandemic and are carried around for sanitary hand rubs. Ethanol, isopropanol, and n-propanol are the commonly used alcohols in clinical practice. They have a wide antimicrobial coverage which makes them effective in infection prevention. They are bactericidal, fungicidal and viricidal[9]. They are used in varied proportions in ABHS. The CDC and WHO recommend greater than 70% isopropanol (isopropyl) and at least 60% ethanol (ethyl alcohol) to be used in ABHS for maximum antimicrobial activity[1,2]. It has been established that effective bactericidal activity can be achieved with about 15 seconds of ABHS hand rubs[10]. Alcohol for medical use is highly flammable and therefore must be used with utmost precautions[7,11]. In our setting, there were a lot of donations of ABHS to communities, individuals, and hospitals by both governmental and non-governmental organizations. To date, most of these products are still in use in most households. During the COVID-19 pandemic, most ABHS in Ghana were produced by local manufacturers with little or no supervision or certification by the Food and Drugs Authority (FDA). A lot more of the locally produced ABHS did not meet the minimum standard requirements of CDC or WHO. These products were put to judicious use during the COVID-19 pandemic. However, in the aftermath of the pandemic, a lot of these ABHS have expired, and people have large volumes in stock. The emerging trend therefore appears to be an alternative use that has been discovered to put these expired sanitizers to use.

In this study, more than 75% of the victims were female with a male-to-female ratio of 1:3. About 62.5% of the victims were children. The mean age of victims was 13.25 years. This is at variance with available literature where most of the victims of ABHS burns are adults and males[6,8]. A significantly higher mean age of victims (33.2±17.9 years) was reported in an Iranian study[6]. Thus, most of the studies report adults as the predominant victims which is contrary to this study. The TBSA in this study ranged from 9-54% with a mean TBSA of 29.8%. All but 2 of the cases sustained second-degree burns (75%). All the patients in this study were admitted. The mean length of hospital stay was 15.9 days. The case fatality rate of ABHS burns was 25%. The available literature on ABHS burns is scanty globally. This may be because it is an emerging trend of burns which is a sequela of the pandemic. Dahmardehei et al (2021) in an Iranian study reported about 76 cases of ABHS burns with most of them being males (75%) as compared to more females (75%) in the present study. Their mean TBSA was significantly lower (6.1±6.5 years) compared to our study[6]. This means that most of the burns sustained in their study were minor burns. Their mean length of hospital stay (11.7±8.6 days) was also comparable to the present study. Their study did not record a mortality[6]. Gupta and More (2021) in a study in India also recorded a case fatality of 25% which is similar to the present study[8]. To the best of our literature search, there were no reports of ABHS burns in Sub-Saharan Africa (SSA). In Ghana, there were also no reports of ABHS burns in literature even though

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colleagues from some tertiary hospitals have managed a case or two of such. All the cases in this study resulted from imprudent use of ABHS. In all the cases described, there was an attempt to light up charcoal for domestic purposes using ABHS as the fuel. This resulted in an explosion because of the highly flammable nature of ethanol and isopropanol. ABHS burns could be accidental or intentional. There are reported reports of the use of ABHS burns for homicidal and suicidal purposes[8]. However, the majority of ABHS burns are accidental from injudicious use of the products. All 8 cases in this study could have been avoided if the ABHS had been used for its intended purpose. This emerging behavioral trend needs to be modified through public health education to prevent future casualties. Considering the old medical adage, "prevention is the best medicine", we strongly recommend that the public refrain from using alcohol-based hand sanitizers to light fires. This will prevent needless injuries and avoidable deaths. We also recommend that the Food and Drugs Authority consider the addition of warning labels for flammability on hand sanitizer containers and their instruction manuals. However, if one must use ABHS to light a fire, then it must be done using the following safety precautions. A small amount of the ABHS should be used to avoid an explosion when the fire is lit. It should be done in an open space that is less windy to prevent flash or flame burns. One must not wear long and loose clothing while using ABHS to light a fire. Before lighting the fire with ABHS, one must rub their hands to make sure the sanitizer dries before the act.

Conclusions

Alcohol-based hand sanitizer (ABHS) is a useful commodity that is effective for hand hygiene and infection prevention. It is also flammable and can result in burns with imprudent use. There is a need for public education by key stakeholders to curb this emerging trend and forestall future incidents. The Food and Drugs Authority (FDA) should consider the addition of warning labels for flammability on the containers and instruction manuals of sanitizers.

Consent

All patients and caregivers consent to the use of their medical data and images for academic and research purposes.

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Authors' Contribution

ASS and EI conceived the study and AIL and AAA gathered the data for the study. ASS wrote the first draft. All authors reviewed and approved of the final draft.

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COMPLETE PENTALOGY OF CANTRELL: CASE REPORT AND REVIEW OF LITERATURE

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Abstract

Introduction: Pentalogy of Cantrell (POC) is a rare congenital anomaly with two sub-categories: complete or partial. Complete has all five defects (anterior diaphragmatic defect, ventral abdominal wall defect, pericardial defect, intracardiac anomalies, and lower sternal defect). The first documented case was described by Cantrell et al. in 1958. Both sporadic and genetic causes have been proposed for POC, with a reported incidence of 5 - 10 cases per one million live births and various clinical presentations. The prognosis of POC depends on the severity of the defects and the associated cardiac anomalies. This case report seeks to increase awareness of this condition, emphasize the need for appropriate counselling in our environment, and review the literature on previous reported cases' outcomes.

Case Presentation: A 5-hour-old term female neonate was referred to our Children Emergency Center with multiple defects (ectopia cordis, sternal cleft, omphalocele, and limb abnormalities) with dysmorphic facies. A diagnosis of POC was made, and multidisciplinary management was instituted. The eviscerated heart and epigastric omphalocele were dressed and evaluated for palliative surgical care. However, she developed complications with sepsis and electrolyte derangements and died from multi-organ failure before any surgical intervention could be carried out.

Conclusion: Though rare, the Pentalogy of Cantrell in its classical form does occur in our environment. The presence of extracardiac and limb deformities worsens the outcome. Based on poor outcomes, there is a need to emphasize appropriate antenatal and postnatal assessments to provide effective counselling on termination, neonatal palliative care, and surgical repairs as appropriate.

Keywords: *Pentalogy of Cantrell; Birth defect; Ectopia cordis; Congenital anomaly*

Introduction

Pentalogy of Cantrell (POC) is a medical condition with five defects affecting the heart, pericardium, diaphragm, sternum, and abdominal wall. Not too many cases have been documented in the literature. The cases are mostly sporadic. Some familial cases have been reported, suggesting that genetic factors may play a role in the development of this disorder.[1] Ideally, Pentalogy of Cantrell [2] should be detected during an antenatal ultrasound scan rather than the first presentation at birth. A male predominance of 1.35 to 1 has been reported. [3] Though of multifactorial etiology, Cantrell et al. attributed it to a developmental failure of a segment of the lateral mesoderm at about the 14th to 18th days of intrauterine life, with subsequent failure in the development of the transverse septum of the diaphragm and the failure in the ventromedial migration of the paired mesodermal folds of the upper abdomen.[2] Through this gap, the heart and the abdominal viscera protrude, causing ectopia cordis and Gastroschisis or omphalocele**.**

Initial management usually addresses the lack of skin overlying the heart and abdominal viscus. Death may occur early in life, usually from infection, cardiac failure, or hypoxemia. [4] Surgical therapy for neonates without overwhelmingly severe cardiac anomalies consists of covering the heart with skin without compromising venous return or ventricular ejection. Repair or palliation of associated defects is also necessary.

This case report seeks to create awareness of this condition, emphasize the need for appropriate counselling in our environment, and also review the literature on the outcome of previously reported cases.

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Conflict of Interest: None Declared

Cases Presentation

Baby I.B., a 5-hour-old term female neonate, presented at the Children Emergency Center of our facility following a referral from another facility on account of an exposed heart (ectopia cordis) with multiple congenital abnormalities noticed at birth. The baby was delivered to a 41-year-old P4+1 (4A) mother via emergency cesarean section on account of antepartum hemorrhage. Mother had several episodes of antepartum hemorrhage due to a low-lying placenta, which was diagnosed at 4-month gestation and managed

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conservatively. There was no history of smoking, use of herbal concoctions or unprescribed medications. There was no family history of cardiac disease, congenital anomalies, or known genetic disorder, and exposure to irradiation was ruled out. Mother had a positive history of miscarriage in the immediate preceding pregnancy. At delivery, baby cried well at birth. Birth weight was 2,100g. She was referred on account of the multiple anomalies.

Clinical Findings

On examination at presentation, she had a lower sternal cleft, ectopia cordis, anterior diaphragmatic hernia, an epigastric omphalocele, limb abnormalities, and dysmorphic facies (flat nasal bridge and low set ears - Fig. 1). Limb abnormalities noted were an absence of the right midleg and foot (stump with a blind-ended sinus), hypoplastic left first toe, and syndactyly of the 2nd and 3rd digits of the left hand. She was tachypnoeic with a respiratory rate of 75 cycles per minute and a peripheral oxygen saturation of 91%. She was placed on intra-nasal oxygen. Other examination findings were not remarkable. She was subsequently admitted into the neonatal intensive care unit, and the eviscerated heart and omphalocele were dressed in normal saline-moistened gauze and sofra-tulle, respectively.

Diagnostic Assessment

A complete blood count and serum procalcitonin were suggestive of sepsis. She also developed hyponatremia (120 mmol/L), hypokalemia (2.5 mmol/L), and moderately elevated hyperbilirubinemia while on admission. Imaging studies, such as a thoracoabdominal computed tomography (CT) scan and echocardiography, were requested but were not done before her demise due to severe financial constraints.

Interventions Given and Outcome

The eviscerated heart was dressed three times daily with gauze moistened with normal saline, while the omphalocele was cleaned daily and dressed with sofra-tulle. She was also placed on antibiotics. Her management was multidisciplinary. Pediatric cardiologists, cardiothoracic, orthopedic, and pediatric surgeons reviewed her. The hyponatremia, hypokalemia, and neonatal jaundice were corrected with appropriate fluids and treated with phototherapy, respectively. Her parents were extensively counseled on the condition, the possible developmental failure, treatment options, and our palliative line of management which would include covering the exposed heart with skin flaps, and the likely prognosis. As the patient was unable to afford echocardiography before demise we were not able to counsel on any corrective cardiac surgery options. The baby died on the 9th day of life before the palliative surgical intervention could take place. Post-mortem reported both cardiac and extra-cardiac defects, which include ectopic heart on the anterior chest wall, absent pericardium, ventricular septal defect (0.9cm in diameter) with overriding aorta, and absence of part of the anterior diaphragm amongst other anomalies. Atelectasis and cerebral edema which were likely complications of mediastinal injuries, sepsis, and electrolyte imbalance were also reported.

Figure 1. Pentalogy of Cantrell: Clinical photographs of the patient

Discussion

POC is a very rare structural congenital syndrome presenting with five classic features, and the index patient had all five features.[5,6] The condition may be diagnosed at the first-trimester ultrasound. The prenatal diagnosis allows families to make informed decisions regarding further pregnancy management. Additionally, a definitive intervention can also be planned with this information.[7] Antenatal diagnosis was never made in our patient, though the mother had several antenatal ultrasounds. The accuracy of antenatal diagnosis for POC may depend on the level of expertise of the sonographer. After birth, a chest X-ray can reveal diaphragmatic hernia and dextrocardia. The association of ectopia cordis and omphalocele is the best diagnostic clue for this syndrome, which was present in our patient. She was a complete variant and had other structural defects; limb abnormalities, and dysmorphic facies. Other important differentials to POC are the limb body wall complex, body stalk anomaly, and the amniotic band syndrome. Unlike POC these other anomalies are more associated with the involvement of the anomalies of the face, central nervous system, and the limbs.[3]

Craniofacial defects and limb-body wall anomalies have been associated with severe and fatal variants.[7] Reported findings in the limb body wall complex include a short umbilical cord, craniofacial defects, and amniotic band anomalies. [8] Also, majority of the cases described in the literature underwent fetal demise. [8] Our patient had no obvious craniofacial abnormality and had the classical components of POC.

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Postnatal investigations in POC should include imaging studies to evaluate the extent of the respective defects to aid in planning for surgical corrective procedures. Though our patient could not access these imaging studies due to financial difficulties, a CT scan and echocardiography are necessary for the evaluation. The treatment of the POC is tailored towards the respective defects and their extent. Reconstructive repairs can be single or multi-staged and require an interprofessional team approach.[3] Surgical management of cardiac, diaphragmatic, and other defects is crucial and initially involves covering the defects.[3] Our patient remained unstable till her unfortunate demise and could not undergo the surgical interventions.

The survival rate of patients with this condition is around 37%.[9] The prognosis of POC depends on the severity of intra and extra-cardiac defects, pulmonary hypoplasia, the extent of abdominal wall defect, cerebral anomalies, and diaphragmatic herniation. The mean survival rate without any interventional surgery is about 36 hours.[10] Studies showed that even with care monitoring in professional centers and multiple corrective surgeries, they had high morbidity and mortality rates,[7] and the long-term prognosis was poor.[11] Additionally, the involvement of facial dysmorphism and limb-wall complexes confer poor prognosis.

Counselling is an important aspect of managing infants with congenital anomalies as the affected families are usually anxious and distressed. [12] Many perceive it as a calamity that had befallen them. Multi-stage counselling may be considered like in our patient. Giving too much negative information at once may tip the caregivers into losing hope or worse, abandonment of the baby in our environment. [13] However, to make progress in doing what is best for the affected child, ensuring the caregivers understand the diagnosis, and treatment options cannot be overemphasized.

Conclusions

Though rare, POC can occur in our environment. The index patient presented with the classical features in addition to limb-wall anomalies. The morbidity course and fatal outcome supported previous findings that the severity of extra and intracardiac defects leads to worse outcomes. Based on documented poor neonatal outcomes, there is a need to emphasize appropriate antenatal and postnatal assessment to provide effective counselling on termination, neonatal palliative care, and surgical repairs as appropriate.

Author Contribution

All authors contributed to the management of the patient and made significant contributions to the writing of the manuscript. BNE, FO, and OM conceived the idea of the manuscript and its design. BNE, FO, FA, IA, AOA, and SIO did the literature search, collected data, and drafted the manuscript. IBF and VCE Supervised the work. All authors reviewed the manuscript, provided critical feedback, and helped shape the final draft. All authors read and approved the final manuscript submitted

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ULNAR ARTERY PSEUDO-ANEURYSM IN A YOUNG ADULT MALE DUE TO PENETRATING TRAUMA

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Abstract

Introduction: We present a young adult male who developed a proximal left ulnar artery pseudo-aneurysm that resulted from a penetrating stab wound after a period of 10 years.
Case Presentation: A 28years old male was referred to our facility with a history of an expanding left forearm swelling. He was initially diagnosed as a case of haematoma. A clinical diagnosis of pseudoaneurysm was confirmed by computed tomography angiography and resection done with ligation of the proximal ulnar artery and the distal branches.
Conclusion: Proximal ulnar artery pseudo-aneurysm is very rare and may be associated with dire consequences in cases of delayed or missed diagnosis. Operative intervention remains the mainstay of treatment.

Keywords: *Proximal ulnar artery, Pseudo-aneurysm, Penetrating stab wound*

Introduction

Ulnar artery aneurysm may arise from infection, trauma and atherosclerosis involving the artery. Distal ulnar artery aneurysms have been well described in adults, although uncommon. Most cases are part of clinical finding in Hypothenar Hammer Syndrome. True aneurysms have a sac, which is formed by dilatation of the whole arterial wall and contain elements of internal elastic or muscular fibers whereas false aneurysm does not have all the component of the arterial wall.[1,2]. Pseudo-aneurysms of the proximal ulnar artery are very rare (1%). The true natural incidence is unknown. However, it was reported to develop in 0.1% of patients following endovascular intervention requiring arterial puncture.[16]. To the best of our knowledge, it has not been reported in Ghana although other peripheral arteries false aneurysm has been reported. Subfascial arteries of the upper limb are more affected by pseudoaneurysm compared to the perifascial arteries.

Cases Presentation

A 28years old male presented at our facility with a fifteen-month history of an expanding left forearm swelling. He was stabbed with a knife at the site of the swelling more than 10 years ago during a cultural festival. The wound was successfully managed at a community health facility. However, he observed an increasing swelling of 15months duration at the previous wound site and reported back to the same health facility where he was initially treated. Following evaluation, he was diagnosed of haematoma and referred to us. There was no other swelling elsewhere in his body and no significant or relevant family and other past medical history. On physical examination, he was not pale, anicteric, afebrile (temperature was 36.6C) with a respiratory rate of 15cycles/minute. Radial pulse was 86bpm, regular and normal volume.

A round (8x9cm), firm, pulsatile and expansile mass located in the medial left forearm 3cm distal to the cubital fossa was evident. It was covered by a normal skin but with a visible central scar, not warm to touch, non-tender, relatively mobile and no lymphadenopathy. The radial artery pulse was palpable, regular, normal volume and rate. The ulnar artery pulse was not palpable, had a very low pitch with handheld vascular Doppler. Allen's test was normal. The motor and sensory functions of distal left forearm and hand were normal.

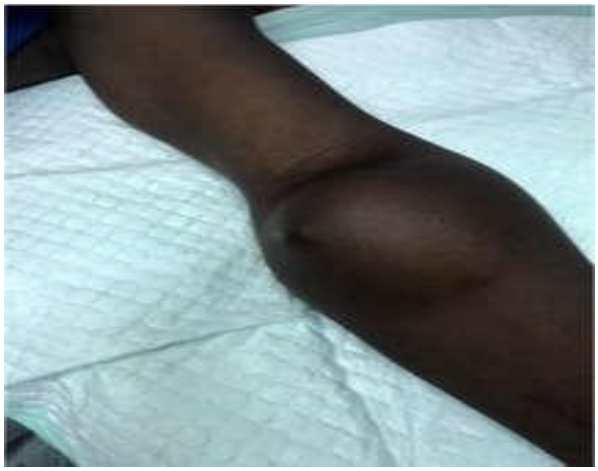

Figure 1: Other systemic examination was normal.

Laboratory investigations revealed that haemoglobin was 12.6g/dL, white blood cell count was 9,500/µL and platelet count was 315,000/ µL. Based on the history of a stab wound to the left forearm and subsequent swelling as

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well as physical examination finding of a pulsatile(expansile) mass, a diagnosis of pseudo-aneurysm of the proximal left forearm was made. The clinical diagnosis was confirmed by Computed Tomography Angiography (CTA) which also showed a thrombus within the sack. (Fig. 2).

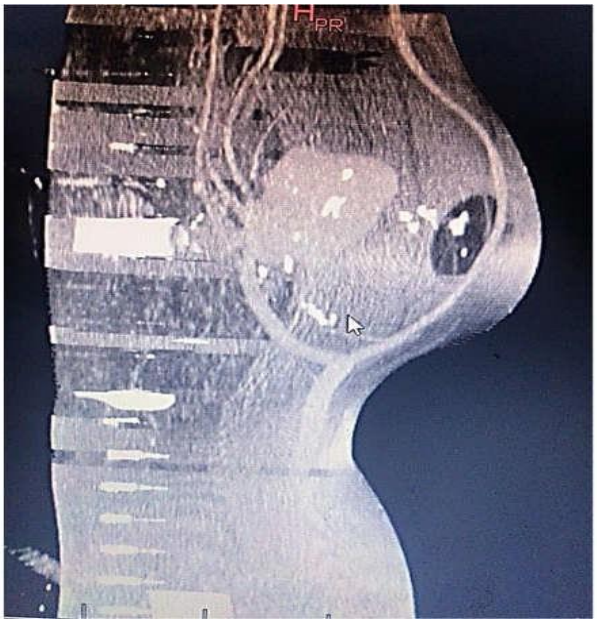

Figure 2: CT Angiogram of the left ulnar artery pseudo-aneurysm: showing a saccular dilatation of the proximal aspect of the left ulnar artery with a filling defect.

Operative Details

Under endotracheal general anaesthesia patient was placed supine on the operating couch with the left upper limb almost at right angle to the chest with pressure points appropriately padded. Intravenous (2g) Ceftriazone was given as a prophylactic antibiotics. The left upper limb was prepped a draped. A multiple lazy -S skin marking was placed over the swelling. A tourniquet was applied to the left arm and was inflated to limb occlusion pressure. Incision was made through the marking with extensive dissection to expose the aneurysm (saccular, measures 7x8cm). Other findings include five (5) arteries of equal caliber (<0.5mm) were seen leaving the distal end of the aneurysm. The ulnar and median were isolated and preserved. Following proximal and distal control of blood flow to the mass with vascular clamps, tourniquet was deflated and the mass was resected, incised and shows blood, extensive thrombus and multiple septa within its cavity. The distal arteries show evidence of good back flow. They were all ligated including the proximal ulnar artery with vicryl 2/0.Following aneurysmal resection, the radial artery pulse was clinically re-evaluated by palpation and revealed a regular, normal pulse rate(92bpm) with a good volume. In addition, the hand appeared pink with normal capillary refill time of less than 2seconds. Wound bed was irrigated with normal saline using a 50cc syringe with moderate pressure and wound was closed in layers. Immediate post -operative period was uneventful and patient was discharged home on post-op day seven. Patient follow up for one year has so far shown no significant problem.

Figure 3a: Appearance of the UAP before skin incision.

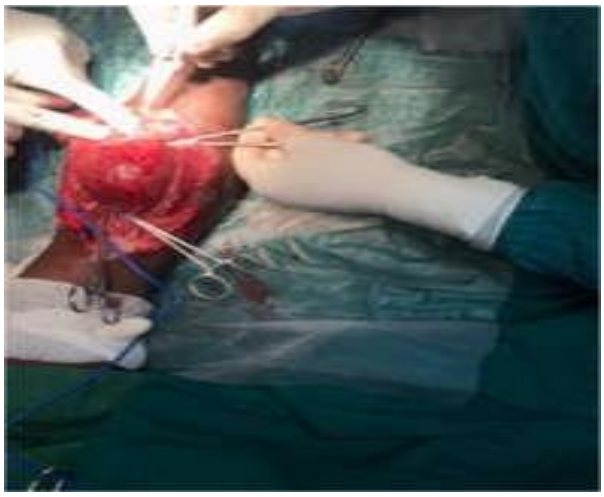

Figure 3b: Surgical exposure of the UAP

Figure 3c: Excised UAP

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Figure 3d: Dead space closure following aneurysmal resection.

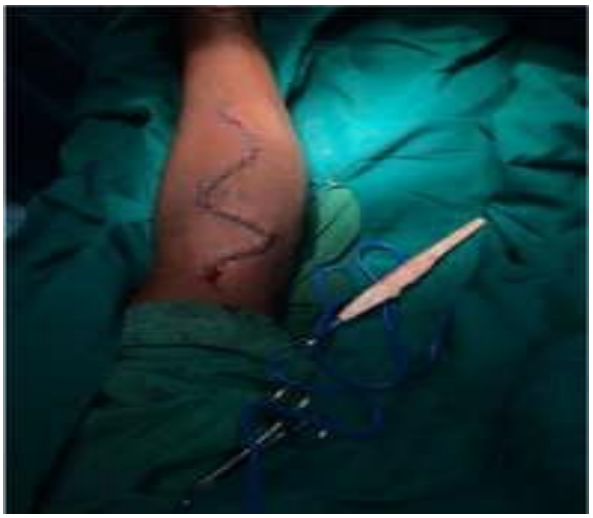

Figure 3e-skin closure

Discussion

My current case is supported by reported cases of proximal ulnar artery pseudoaneurysm following tension band wiring and non-traumatic pseudoaneurysm associated with eosinophilia. However, there has been one reported case related to penetrating trauma[10] confirming the rarity of ulnar artery pseudoaneurysm (UAP). Pseudo-aneurysms are usually caused by break in the continuity of endothelium as a result of trauma (blunt or penetrating) with subsequent perivascular formation of blood clot, reorganization of the hematoma and recanalization of the vasculature through a newly formed false lumen[1]. There is absence of internal elastic lamina on histopathology evaluation. Complication of ulnar artery false aneurysm may include rupture, thrombosis, distal emboli and neurovascular compromise as a result of compression of the surrounding structures. Imaging modalities for the diagnosis of (UAP) include selective upper extremity arteriography, ultrasonography,magnetic resonance imaging(MRI), and CTA. Ultrasound scan features include a hypoechoic saccular cystic formation demonstrating turbulent luminal blood flow and arising from the adjacent ulnar artery[11]. The typical finding on Doppler ultrasound is the "yin- yang" sign (a swirl of colours caused by the bidirectional flow within the aneurysm)[3]. The most specific sign of a pseudoaneurysm is the "to and fro" waveform on duplex ultrasound, seen due to the communicating channel between the artery and the pseudoaneurysmal sac[12].

However, ultrasonography may still have a limitation of being operator-dependent. MRI is advantageously highly sensitive and specific, but is precluded from being a routine imaging option because of its time-intensive and expensive nature. Interestingly, Kehara et al. have described a case of nontraumatic UAP that resembled a soft tissue swelling on CT and MRI due to atypical imaging characteristics of the UAP[13].

In our case, CTA provided evidence of a UAP with a filling defect likely thrombosis. CTA is an extremely valuable tool in the evaluation of UAP, when available, it is highly specific and sensitive. It can detect active extravasation, and assists in surgical planning[3,12]. It is becoming more favored compared to selective upper extremity arteriography (accepted gold standard investigation for diagnosis)[14]. Nevertheless, although catheter arteriography is becoming less and less common as the initial diagnostic imaging of choice, it is a useful tool when CTA findings are inconclusive or when endovascular intervention is due to be performed[15].The management approach to pseudo-aneurysms may be conservative or surgical. Conservative care is indicated for smaller leision without local mass effect (neurovascular compression), compartment syndrome and local infection[16]. Surgical intervention is indicated when the pseudo-aneurysm is associated with neurovascular compromise due to compression, infection and failure of conservative treatment. Options for surgery include (a.)excision of the pseudo-aneurysm with ligation of the ulnar artery (b.) microsurgical technique of ulnar artery re-anastomosis or an interposition vein graft following the excision of the pseudo- aneurysm[4,5]. Conservative treatment of ulnar artery pseudo-aneurysm comprise of ultra sound – guided compression, thrombin injection and endoluminal procedure[5].Thrombin injection of small vessel pseudo-aneurysm, may be associated intravascular thrombosis, distal ischemia and the risks of systemic thrombin administration[5]. In our case, excision of the UAP/proximal and distal ligation of the ulnar artery and multiple branches was executed because of its progressive expansion and possibility of compressive neuropathy and rupture in the presence of adequate distal forearm and hand perfusion. The option of venous graft interposition was jettison because of the multiple arterial branches distal to the aneurysm as it was difficult to identify the main distal continuation of the ulnar artery.

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Conclusions

Proximal ulnar artery pseudo-aneurysm is rare and may be associated with dire consequences in cases of delayed or missed diagnosis. Early diagnosis and treatment is crucial in preventing long-term morbidity. Operative intervention remains the mainstay of treatment. Intraoperative angiography helps in choosing the surgical approach.

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TWO STAGE FLEXOR TENDON RECONSTRUCTION AFTER OVER FIVE DECADES OF DISABILITY USING SILICONE FOLEY

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Abstract

Introduction: Surgical reconstruction of flexor tendon injuries, particularly old injuries, in the digital flexor sheath area (Zone II) are very difficult to perform, presenting significant challenges to both patients and treating surgeons. The healing tendons tend to adhere to the fibro-osseous canal, the proximal and distal ends of tendons are mostly retracted, and in worst cases, the fibro-osseous canal is already collapsed.

Case Presentation: We report in detail how we employed the silicone foley catheter SFC instead of Hunter's rod, to achieve a magnificent functional outcome in a two-staged reconstruction of a five-decade old flexor tendon injury in Zone II of the right ring finger (RRF).

Conclusion: Surgical correction is still an option for flexor tendon injury even decades after injury. The utility of one's hand can still be restored regardless of the age of the patient and the period of injury.

Keywords: *hand injuries, two-stage tendon reconstruction, Silicon Foleys Catheter, Tendon graft*

Introduction

Surgical reconstruction of flexor tendon injuries, particularly old injuries, in the digital flexor sheath area (Zone II) are very difficult to perform, presenting significant challenges to both patients and treating surgeons.[1–5] The healing tendons tend to adhere to the fibro-osseous canal, the proximal and distal ends of tendons are mostly retracted, and in worst cases, the fibro-osseous canal is already collapsed.[4,6,7]

We report in detail, how we employed the SFC instead of Hunter's rod, to achieve a magnificent functional outcome in a two-staged reconstruction of a five-decade old flexor tendon injury in Zone II of the right ring finger (RRF).

Cases Presentation

Our patient is a 63year old Ghanaian female, MAA, with no known chronic illness or family illness. At the age of 10years she suffered an accidental cutlass injury to the right hand by Her elder sister. Resulting In a deep laceration of the palmar aspect of her RRF and an amputation of her right little finger at Zone II. Her wounds were cleaned and sutured and managed on antibiotics, tetanus prophylaxis and analgesics at a peripheral center. The injury left her right hand with only three functioning digits and a flexion deficient RRF. Being right-handed, she temporarily lost the ability to write, which greatly deterred her education.

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Conflict of Interest: None Declared

50years following her injury, she reported to our team. We examined a stable middle-aged woman with a healed amputation site of the fifth finger. She was unable to flex her right ring finger, RRF, Figure 1. A diagnosis of flexor tendon injury of the RRF was made.

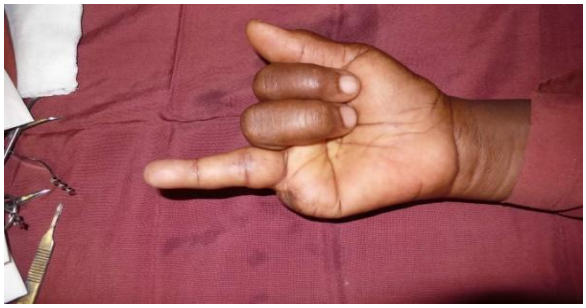

Figure 1

She consented to a staged reconstruction. The patient was positioned supine, with her right upper limb placed supine on a working table, after regional anaesthesia and sterile preparation. Access was through Bruner zigzag incision was made on the palmar side of the right ring finger, extending into the proximal palmar crease. Subcutaneous tissues and fibrosis dissected, Figure 2.

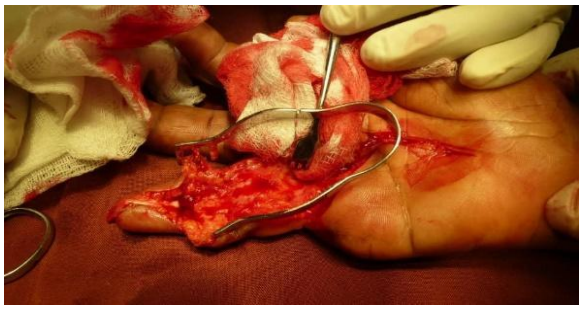

Figure 2

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A new fibro-osseous canal created and a 14fr SFC, implanted, Figure 3.

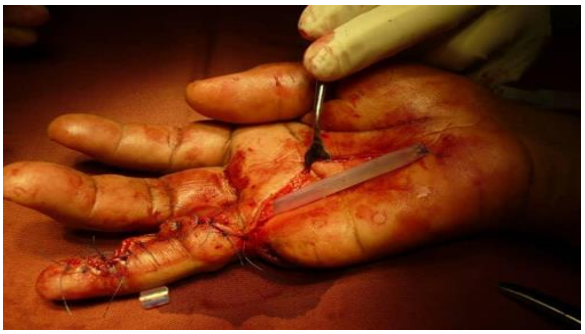

Figure 3

An artificial finger pulley system was then constructed over the silicone implant. Finger closed in layers, embedding the implant, in situ. Figure 4

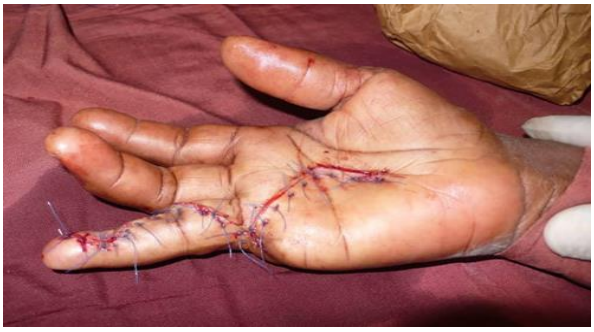

Figure 4

Two weeks after the initial surgery, the patient developed a septic reaction to the foreign body, Figure 5.

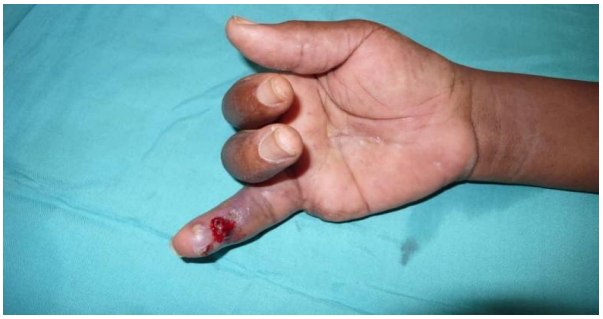

Figure 5

This was treated with antibiotics and analgesics. The infective process resolved, patient recovered remarkably and the rest of the recovery period was uneventful.

Ten weeks post first stage surgery, the second stage was performed. Anaesthesia, sterile preparations and patient positioning was just as the first stage surgery. A 4cm oblique palmer incision was made over the middle phalanx of the right middle finger (RMF). The middle finger's flexor Digitorium superficialis (FDS) tendon was harvested from its insertion at the middle phalanx. 5cm 'V' shaped palmer incision was then made just above the distal palmer crease straddling the right middle and ring fingers. The FDS tendons of the RMF was harvested from its insertion at the. The FDS tendon was extruded from this new incision. Figure 6

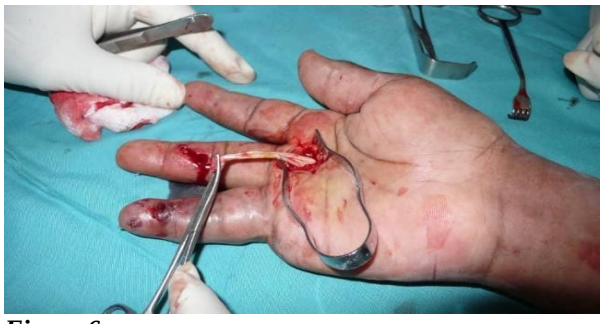

Figure 6

The SFC was extracted partially, through the foreign body reaction wound at the distal phalangeal region of the ring finger, to deliver its proximal part into the incised wound, Figure 7.

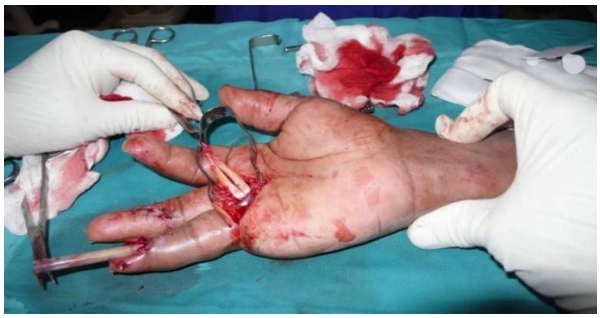

Figure 7

The distal tip of the harvested FDS tendon was then sutured to the proximal part of the SFC. The extraction of the SFC is completed ushering along the tendons of the FDS of the middle finger, thus transferring the FDS tendons through the pseudo sheath of the RRF. Using the modified Kessler technique, the transferred FDS tendon was then sutured through the periosteum of the distal phalanx with a non-absorbable suture. A tuft of gauze was placed between the finger and a button to serve as a cushion and the knot was tied over the button, Figure 8.

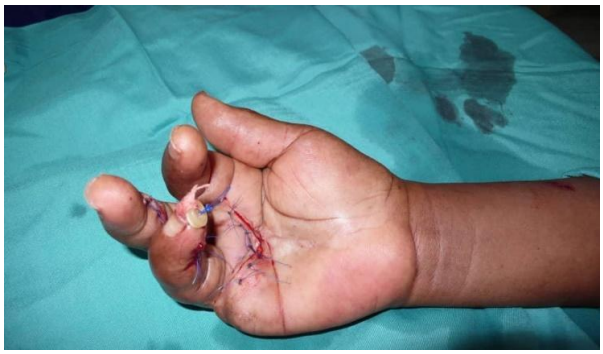

Figure 8

Physiotherapy commenced on the second day post-surgery. This involved controlled passive flexion and active extension exercises, throughout the day. Two

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weeks post-surgery review, the patient regained full flexion of the RRF, Figure9.

Figure 9

Incision wounds sutures were removed at two weeks but the button was removed at 6weeks, when tendon attachment was achieved, Figure 10.

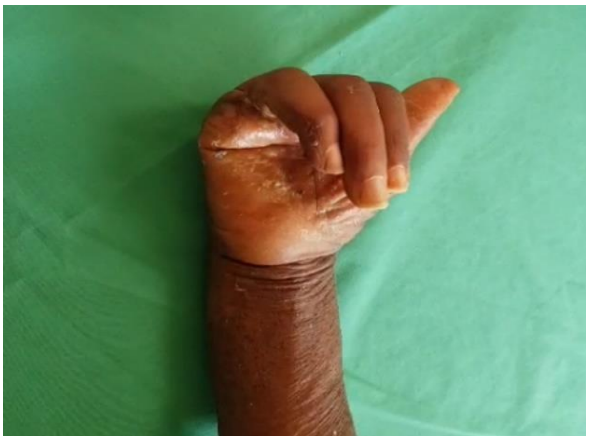

Figure 10

The patient's right hand over the past three years has shown marked increase on function, with no sign of decline. The patient was very satisfied with the outcome, aesthetically and functionally, Figure 11.

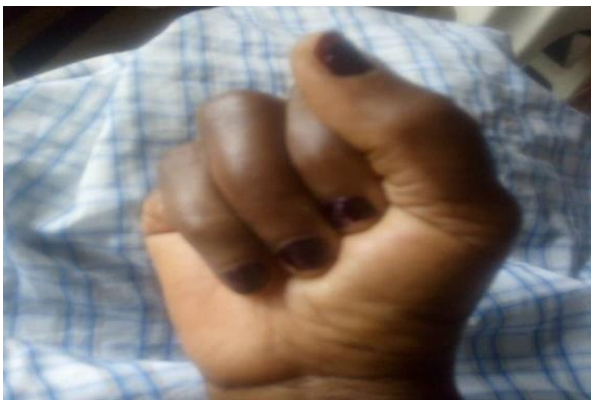

Figure 11

Discussion

The concept of tendon reconstruction using implantation was first published by hunter in 1965. Paired with Salisbury in 1971, they published a decade of experience with staged Flexor Tendon reconstruction using an implant reinforced with silicone and Dacron. This has led to remarkable advancement in the restoration of flexor function in severely scarred fingers.

The primary surgery involves finger exploration, including debridement, release of contractures, removal of scar tissues and adhesiolysis.[8] In addition, a silicone rod is implanted in the same surgery to reconstruct the pulleys and allow the formation of a pseudo sheath around it. The second surgery as described by Hunter and Salisbury, entails tendon grafting through the pseudosheath, six to twelve weeks after the primary surgery.[6,8,9]

The uniqueness of our case report stems from the fact that we did not come across any report of this surgery done for a patient after five decades of injury. A myriad of plaques tends to occur with lengthening of injury to repair duration such as; poor muscle compliance, fibrosis, retraction of both proximal and distal ends of the tendons, atrophy of the tendons and muscle and collapse of the fibro-osseous canal.[4,6,7] Longstanding disabilities affects not only the physical appearance of the patient but also the mental and socioeconomical wellbeing of the patient. The lives of the people around the patient are also dented.[10–12]

We performed two key steps differently from the described staged surgery. A SFC was used instead of a hunter's rod and a tendon transfer instead of a tendon graft. The Hunter's rod is expensive and not readily available,[6] worse so in Ghana. In 2006, Ahmad T, Bashir SA, Zaroo MI, Wani AH, Rashid S and Jan S concluded from their study that, SFC is an effective alternate to the Hunter's rod.[6] Due to the effects of the longstanding nature of our patient's injury, a tendon graft of any nature would have been extremely ambitious. There would not be any significant remnant of the FDS or FDP tendons or muscles of the RRF to attach a graft to. To counter this, the FDS tendon of the RMF was transferred to be used as the FDP of the RRF. This was permissible because whereas the FDS flexes the finger with the exception of the distal inter phalangeal joints, the FDP by its attachment to the distal phalanx, flexes the entire finger. Hence while the RRF gains flexion the RMF does not loss flexion either.

After the index surgery, our patient suffered a surgical site infection with a rupture at the distal end at the finger. While this was an undesired outcome, it is a recognized post first stage complication.[5,7] Resolution was attained with antibiotics, analgesics, wound care and rest. Employing a tendon transfer also enabled early physiotherapy, hence reducing recovery time. Post Stage II surgery, recovery was free of complications. The patient was followed till three years post-surgery, Function and cosmetic value has since been fully restored without evidence of deterioration.

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Prognostically our patient favored poorly.[7] The success of the surgery was dependent on the two staged FTR and making modifications to suit our patient.

Conclusions

Surgical correction is still an option for flexor tendon injury even decades after injury. The utility of one's hand can still be restored regardless of the age of the patient and the period of injury.

Informed Consent

Written Informed consent was obtained from the patient before writing of this report.

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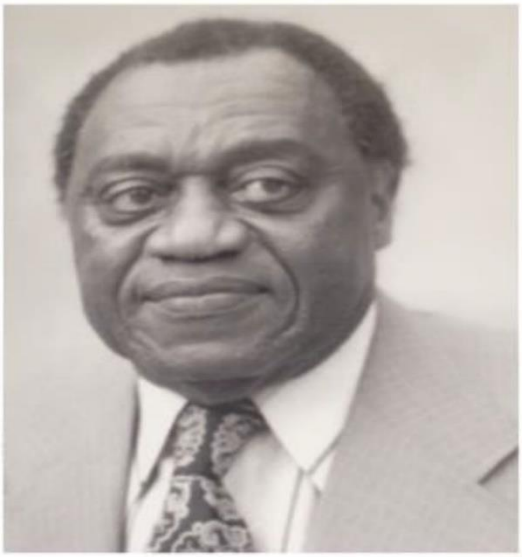

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EXAMPLES

Article

McLendon WW. A historical perspective as a compass for the future of Pathology. *Arch Pathol Lab Med* 1986; 110: 284-288.

Book

Talbot CH. Medicine in Medieval England. Oldbourne, London. 1926 p 120-136.

Book Chapter

Philips SJ, Whisnan JP. Hypertension and stroke. In: Laragh JH, Bremner BM, editors, Hypertension: pathophysiology, diagnosis and management. 2nd Ed. New York: Raven Press, 1995, p465-478.

Website references

Doe J, Phils MR. A client's guide to rational emotive behaviour therapy. Conseil. 2017: https://www.conseil.com/

Special identification items like digital object identifiers (DOI) will be allowed inclusion to end text references, aside this, all references should be arranged as stated in the instructions.

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