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Theme

MAINTENANCE OF HEALTH IN A CHALLENGING GLOBAL ECONOMY: POLICY AND PRACTICE IMPLICATIONS

Dates

5/12/2022 - Pre-Conference
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EDITORIAL

IMPROVING OUR EXAMINATION METHODS USING OSCE AND CBT

An 'Objective Structured Clinical Examination' (OSCE) is a brief, simulated clinical scenario whose purpose is to evaluate the clinical skills and knowledge of candidates who present themselves for the examinations. In Ghana the OSCE is conducted for many undergraduate and postgraduate exams whether formative or summative. The faculties of the Ghana College of Physicians and surgeons have adopted the OSCE.

The OSCE, a rather radical method of examination was first proposed in 1975 by R.M. Harden in the UK. It has gone global with varying degrees of modifications. His intention was to find one way of providing the assessment of clinical competence in a more objective manner to the satisfaction of the examiners, candidates and institutions. In an OSCE examination candidates move through a number of stations which provide short clinical scenarios. In these stations the candidates are exposed to a range of situations which are meant to place emphasis on specific topics and specific clinical skills. A blueprint for an undergraduate examination could be history taking, abdominal examination, pelvic examination, insertion of an IUCD, a communication station and a picture station. This can be contrasted with the traditional clinical examination where in the long case the candidate would take a history and examine a patient before the candidate faces the examiners. He then presents to the examiners with the history and a provisional diagnosis. Further discussion would involve the examination, laboratory investigations including imaging techniques and then the treatment.

In his original article, Harden found that the OSCE results had a far better correlation with the written results of the students than the traditional approach. A reason adduced was that the patient (usually simulated) was the same for all students. Also, the examiners had a standard scoring sheet, and their assessment was both clear and reproducible and unbiased. Since its introduction the OSCE has become a widely used examination tool for both undergraduate medical student and postgraduate specialist examinations for the West Africa College of Surgeons and the Ghana College of Physicians and Surgeons. It is currently a key component of the examination process in Obstetrics and Gynaecology at our institutions in Ghana. OSCE does not replace the need for written examinations to test purely factual knowledge.

It assesses a different range of practical skills. Aspects of clinical practice that can be assessed at the postgraduate/residency level in an OSCE ranges from taking a patient's history, general or focused, explaining investigations, abdominal examinations including Obstetric exams, pelvic examinations and interpretations, demonstration of managing of emergencies such shoulder dystocia and birth asphyxia, abnormal Pap smear interpretation, CTG, and the communication of bad outcomes.

CBT and SBAs

The computer-based tests (CBT) and single best answer (SBA) enable examinations to be held simultaneously in many centres in one or many countries. SBAs are widely used in undergraduate and postgraduates. A question stem describes a clinical vignette followed by a lead in question about the described scenario such as the likely diagnosis or the next step in the management plan. There are a set of answers, and the candidate chooses the best one. It is reliable and ideal for machine marking. Validity is the problem since medicine is not limited making the SBA inherently flawed. Wrong options quality, ability of students to learn cues and signposts may enable the candidates to pass the exams even when they lack adequate knowledge.

The OSCE and CBT both require heavy capital investment in the acquisition of the logistics such as manikins and computers which are efficiently networked to carry out the assignment. Training of examiners is necessary in the OSCE since most are used to the traditional type of questions. Often there is inertia on the part of the older lecturers and the change has to be efficiently managed.

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Prof JD SEFFAH
Editor-in -Chief

COMMENTARY

CHRONIC PAIN: MULTIFACETED DISEASE REQUIRING HOLISTIC MANAGEMENT

The International Association for the Study of Pain (IASP) definition of pain as an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage. Chronic pain is that which is persistent or recurrent lasting longer than 3 months[1]. The global burden of pain is enormous and has been increasing. The prevalence among adults worldwide is estimated as 20%. Pain is the commonest reason people seek medical attention and 1 in 10 patients are diagnosed with chronic pain annually[2,3].

Low back and neck pain have featured consistently as major causes of disability globally, with other chronic pain conditions prominent among the top 10 causes of disability[4]. Chronic pain is associated with the prevalence of chronic comorbidity such as cardiovascular disease, chronic pulmonary disease and mood disorder. It has also been identified as an independent risk factor for all-cause mortality in such patients with comorbidities. The direct health care costs for chronic pain has been estimated to be up to €32 billion in Europe, $300 billion in the United States and CAD$ 17.2 billion in Canada. The indirect annual societal costs are estimated to be even higher[5,6]. These factors provide justification for the cogent call for chronic pain to be viewed as a public health priority.

Pain is an experience and not just physiological nociception (perception of a noxious stimuli). Neither should chronic pain be viewed also as an acute pain with an extended duration. The pathophysiology for chronic pain is different from that of acute pain and involves peripheral and central sensitization, altered pain modulation, microglial activation, neuroimmune signalling and neuroplasticity. Genetic, environmental, physiological, psychological and socio-cultural factors determine the risk, degree and time-course of chronification of pain[7]. Chronic pain affects several facets of the patient's life. It is associated with anger, frustration, fatigue, depression, anxiety, poor-quality or nonrestorative sleep, reduced libido, excessive alcohol and drug use which may put a stain on relationships with spouse, family and friends. Chronic pain is also associated with kinesiophobia (an excessive, irrational, and debilitating fear of physical movement and activity) and catastrophizing (an exaggerated negative orientation toward actual or anticipated pain experiences) which leads to decreases in physical activity resulting in impaired work performance and reduced productivity which negatively impacts on finances. The relationship between pain the mental health is likely bi-directional with anxiety, depression, and catastrophizing beliefs being associated with poor prognosis[8].

Acute pain is easily assessed using unidimensional tools whilst chronic pain due to its multi-facet effects on patients is best assessed using multi-dimensional tools which explore the impact of chronic pain on various aspects of the patient's life including but not limited to general activity, ability to work / economic impact, mood, inter-personal relationships, sleep, enjoyment / quality of life[9]. A dynamic integration among physiological, psychological, and social factors that reciprocally influence one another can be used to describe chronic pain and its associated disabilities. The biopsychosocial model has been used and proven to be the best model for the management of chronic pain. The diversity of its aetiology and the ramification of the effects of chronic pain makes it impossible for one specialist to adequately manage it.

Multidisciplinary teams are required for the appropriate management of chronic pain. Members of the multidisciplinary team may include Neurologists and Neurosurgeons, Orthopaedists and Orthopaedic surgeons, Anaesthesiologists, Oncologists, Physiatrists, Nurses, Physical therapists, Occupational therapists, Psychologists/Psychiatrists, Palliative specialists, Social workers, Religious leaders among others[10].

Due to the complex nature of chronic pain, single treatment modalities usually are inadequate for pain management. Successful treatment regimens often involve pharmacotherapy, non-pharmacological / complimentary methods, interventional pain procedures (Nerve /Regional Anaesthetic blocks, myofascial injections, intra-articular injections, neuro-modulation, spinal cord stimulation) and surgery. Pharmacotherapy may involve the use of traditional analgesics, antidepressants, anti-convulsants, N-methyl D-Aspartate inhibitors, cannabinoids among others. Non-pharmacological complimentary modalities include physical therapy, occupational therapy, psychotherapy, acupuncture,

Transcutaneous Electrical Nerve Stimulation (TENS), hypnosis and relaxation techniques[11]. Chronic Pain is no longer viewed only as a symptom of a disease but as a recognised disease entity codified in the 11th version of the International Classification of Diseases (ICD-11)[12]. The high prevalence of chronic pain and its profound negative socio-economic impact not just on patients but the community and nation as a whole calls for designing of effective and efficient chronic pain management services13. The utilization of comprehensive multidisciplinary teams employing a variety of strategies and specialist treatments, has been shown to be a more clinically effective and cost-efficient to management by a single-discipline[14].

It is thus gratifying to note that the Faculty of Anaesthesia of the Ghana College of Physicians and Surgeons has begun a fellowship programme in Regional Anaesthesia and Interventional Pain Management and the first fellow will be graduating this year. This is the first locally trained pain specialist in the sub-region, an important milestone. Presently only the Komfo Anokye and Korle-bu Teaching Hospitals run properly organised and human resourced pain clinics. It is however, hoped that the Ghanaian health system and institutions will quickly adopt the multidisciplinary approach to the management of chronic pain, facilitate the training of the required specialists, encourage the formation of appropriate teams and establish chronic pain clinics and centre of excellence in chronic pain management.

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ORIGINAL ARTICLES

CAUSES OF ASCITES AND ITS CORRELATION WITH SERUM-ASCITES ALBUMIN GRADIENT IN PATIENTS ADMITTED AT MEDICAL WARDS IN A TERTIARY HOSPITAL IN GHANA.

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Abstract

Objective: Ascites can be classified depending on whether it results from portal hypertension (PH) or non-portal hypertension (NPH) causes. This classification is relevant because the modes of evaluation and management are different for these two groups. Serum-ascites albumin gradient (SAAG) has been proposed in many studies to categorise ascites better than ascetic fluid total protein. This has not been determined in Ghanaian patients with ascites. The aim of this study was to determine the aetiology of ascites and to assess the performance of SAAG in the classification of portal versus non-portal hypertension ascites among patients admitted to a tertiary hospital in Ghana.

Methodology: A cross-sectional study was conducted at the Korle-Bu Teaching hospital, where 140 patients with ascites were recruited within the study period. Data on socio-demography, clinical features, and results of relevant laboratory investigations and imaging studies were collected using pretested questionnaires

Results: The mean age of patients was 44.7±13.2 years. Chronic liver disease (CLD) was the major cause of ascites in this study representing 73.57%. SAAG had a sensitivity of 91.59%, positive predictive value of 95.15% and diagnostic accuracy of 90.0% in classifying ascites as due to a PH or NPH.

Conclusion: CLD was the major cause of ascites in Ghanaian patients. SAAG has satisfactory diagnostic accuracy in differentiating ascites related to PH from NPH causes. This could be used as a first line investigation in the aetiological diagnosis of ascites for initiation of prompt treatment.

Key words: *ascites, serum-ascites albumin gradient, portal hypertension, non-portal hypertension.*

Introduction

Ascites is defined as the pathological accumulation of fluid in the peritoneal cavity and may occur as a result of various causes.[1] Ascites can develop due to conditions which either directly involve the peritoneum (infection, malignancy), or occur remote from the peritoneum (liver disease, heart failure, hypoproteinaemia, kidney disease). Its causes have been well described in Western countries. Cirrhosis is the commonest cause of ascites in the Western world (75%), followed by peritoneal malignancy (12%), cardiac failure (5%) and peritoneal tuberculosis (2%).[2] In sub-Saharan Africa especially Ghana, ascites is a common symptom for which patients seek medical attention in internal medicine departments, however data pertaining to admissions as a result of ascites and its associated causes remains under documented.

Previous studies from sub-Saharan Africa countries described the prevalence of ascites in internal medicine departments to be between 3.6 to 10.8%.[3-5] Ascites causes significant discomfort for patients, particularly those with severe ascites due to difficulty in mobility and in carrying out activities of daily living, as well as social stigma associated with the condition. Successful treatment depends on accurate diagnosis of its cause, which may broadly be classified into PH and NPH causes. This is important because the mode of evaluation and management has some variation based on this classification. In the past, PH ascites was

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distinguished from the NPH causes by determining whether the ascitic fluid is a transudate or an exudate, by the estimation of the ascitic fluid total protein (AFTP). Ascites with AFTP of ≥25gm/L was considered to be exudative and <25gm/L as transudative.[6-8] This classification is however unable to correctly identify the aetiological factors responsible for its causation and has been challenged on various occasions in different clinical conditions especially in cirrhotic patients on prolonged diuretic therapy, cardiac ascites, patients of malignant ascites, spontaneous bacterial peritonitis, and sometimes even in patients with normal ascitic fluid parameters.[9] Moreover, it offers little insight to the pathophysiology of ascitic fluid formation.[9]

A more meaningful system has been developed, on the basis of the amount of albumin in the ascitic fluid in comparison to the serum albumin level. This system is called the serum-ascites albumin gradient or SAAG. Ascites due to PH has a SAAG value generally greater than 11gm/l. On the other hand, the SAAG value for ascites that is not related to portal hypertension has a value lower than 11gm/l. The SAAG is accurate in 96.7% cases even in the presence of diuretic and intravenous infusions of albumin.[8] However, it is inaccurate in cases of mixed ascites. There is a dearth of knowledge about the causes of ascites and its relation to SAAG in Ghana. This study was therefore to determine the causes of ascites among patients admitted to a tertiary hospital in Ghana, and to assess the performance of SAAG in the classification of portal versus non-portal hypertension ascites in the Ghanaian context.

Materials and Method

Study design

A formal approval of this study was obtained from the Ethical and Protocol Committee of the University of Ghana medical School. This study was conducted in accordance with the Helsinki Declaration. The research design was a cross-sectional hospital-based study, carried out at the Department of Medicine, Korle-Bu Teaching Hospital (KBTH), Accra, from 25th March 2016 to 25th November, 2016. One hundred and fourty (140) patients with ascites admitted to the medical block of KBTH were consecutively recruited. All adult patients above 18 years with ascites who provided informed consent were included. Diagnosis of ascites was made based on the clinical features of abdominal distension, the presence of shifting dullness and/or positive fluid thrill. This was subsequently confirmed by diagnostic paracentesis or an abdominal ultrasound scan**.**

Data Collection and Measurements

The study focused on socio-demographic data and clinical history by trained research personnel. Patients' medical records were additionally reviewed. Physical examination for clinical features of liver cirrhosis, congestive heart failure, nephrotic syndrome, lymphoma, abdominal tuberculosis, chronic kidney disease, and other causes of ascites prevalent in our setting was performed. Ascites was graded as mild (detectable only on ultrasound), moderate (visible moderate symmetrical abdominal distension), or severe (marked abdominal distension). A sample of 15mls of venous blood was taken for haematological, biochemical and serological investigations. Hematological and biochemical workup included full blood count, liver chemistry and function test blood urea and electrolyte and urine routine examination. All patients were tested for Hepatitis B surface antigen (HBsAg) and anti-bodies to hepatitis C virus (anti HCV-Ab) to determine the causes of liver cirrhosis. Abdominal paracentesis was performed using an aseptic technique at the right or left iliac fossa, 3cm above and 3cm medial to the anterior superior iliac spine. Approximately 10mls of ascitic fluid was collected using a sterile syringe and 5mls was inoculated into a sterile ethylenediaminetetraacetate (EDTA) bottle and sent to the laboratory for cell count and differentials, albumin and protein. Further tests were performed on the ascitic fluid if there was a need for further evidence of the cause of ascites including adenosine deaminase, lactate dehydrogenase, serum amylase, PH, acid fast bacilli and cytology. Ultrasound Scan: All patients underwent an abdominal ultrasound scan and the following details were recorded: maximum vertical span of the liver; nodularity of liver surface; spleen size (length of its longest axis); and presence of ascites. The size of the kidneys and the presence or absence of corticomedullary differentiation were also determined. Enlarged abdominal lymph nodes and any other masses seen were also noted. Additional investigations: Participants underwent further diagnostic investigations to ascertain the cause of ascites. These included but were not limited to chest x-ray (heart failure, lymphoma, TB), electrocardiography and echocardiography (heart failure), abdominal CT scan (malignancy), sputum for acid fast bacilli and Gene Xpert (TB).

Statistical Analysis

Data were entered, compiled, and analyzed using statistical package for the social sciences (SPSS) 16. Descriptive statistics were generated on patient demographics, clinical features and causes of ascites. Chi square was used to determine the level of association. A p-value less than 0.05 was considered significant. The diagnostic accuracy of the tests used in this study was calculated as the sum of true positive

plus true negative results divided by the total number of cases.[10]

Results

A total of 140 patients with ascites were recruited for the study with a mean age of 44.7±13.2 years (age range 18 to 74 years). Seventy-six (54.3%) patients were males, and 64 patients were females with a male to female ratio of 1.2:1 (Table 1).

Table 1: Demographic features

	Overall (n=140)	Portal (n=107)	Non-portal (n=32)
Age			
Mean	44.66±13.20	44.09±12.29	45.94±15.80
Median	45	45	47.5
Sex			
Male	76 (54.3%)	60 (56%)	16 (50%)

Abdominal distension (100%), weight loss (82.14%), pedal oedema (75.71%), abdominal pain (47.86%) and jaundice (42.86%) were the main clinical features (Table 2).

Table 2: Clinical presentation of the study participants

Clinical Features	Present (N, %)	Absent (N, %)
Abdominal distension	100(100)	0(0)
Jaundice	80(57.1)	60(42.9)
Abdominal pain	73(52.1)	67(47.9)
Fever	94(67.1)	46(32.9)
Chills	105(75.0)	35(25.0)
Weight loss	25(17.9)	115(82.1)
Pedal oedema	34(24.3)	106(75.7)
Hematemesis	126(90.0)	14(10.0)
Crepitations	118(84.3)	22(15.7)
Periorbital oedema	126(90.6)	14(9.4)
Hepatomegaly	108(77.1)	32(22.9)
Clubbing	122(87.1)	18(12.9)
Palmar erythema	110(78.6)	30(11.4)
Splenomegaly	128(91.4)	12(8.6)
Others	108(77.1)	32(22.9)

One hundred and three (73.57%) patients had a diagnosis of chronic liver disease and 18(12.86%) had a diagnosis of malignancy other than HCC as the cause of their ascites. Out of the 103 cases of ascites caused by chronic liver disease, liver cirrhosis accounted for 69 cases while hepatocellular carcinoma was 34. Other causes include heart failure, nephrotic syndrome, chronic kidney disease, abdominal tuberculosis and unknown cause constituted 0.71% (Table 3).

Table 3: Causes of ascites

Causes	Frequency	Percentage
Portal hypertension		
Chronic liver disease	103	73.57
Liver cirrhosis	*69*	*49.28*
Hepatocellular carcinoma	*34*	*24.29*
Heart failure	4	2.86
Non-Portal hypertension		
Abdominal tuberculosis	4	2.86
Chronic kidney disease	6	4.29
Nephrotic syndrome	4	2.86
Malignancy excluding HCC	18	12.86
Unclassified cause		
Unknown cause	1	0.71
Total	140	100.0

Note: Data are presented as frequencies and percentages.

Ascites was then classified as having either PH causes (chronic liver disease, congestive heart failure) and NPH causes (malignancy, nephrotic syndrome, chronic kidney disease, abdominal tuberculosis) (Table 4). After excluding 1 patient for whom the cause of ascites could not be clinically determined, 139 patients with ascites were included in sensitivity and specificity analysis. Of these, 107 patients had ascites clinically determined to be due to causes related to portal hypertension. SAAG rightly classified the causes of ascites into portal and non-portal hypertension at a cut-off value of ≥ 11 gm/L and < 11gm/L ($P < 0.0001$) (Table 4). SAAG at ≥11 gm/L had a sensitivity of 91.59%, specificity of 84.38%, positive predictive value of 95.15%, negative predictive value of 75.0% and diagnostic accuracy of 90.0% (Table 5). Total ascitic fluid protein correctly classified the causes of ascites with portal hypertension and without portal hypertension at a cut-off value of ≥ 25 g/l and <25g/l

(P < 0.0001) but with low diagnostic accuracy (Table 4 and 5).

Table 4: Ascitic fluid total protein (AFTP) and SAAG in patients with portal hypertension and non-portal hypertension causes of ascites.

	Portal hypertension causes	Non-Portal hypertension causes	Total	p-value
SAAG ≥11 g/L	98	5	103	
SAAG < 11 g/L	9	27	36	p < 0.0001
Total	107	32	139	
AFTP 25 ≥g/L	25	24	49	
AFTP < 25 g/L	82	8	90	p <0.0001
Total	107	32	139	

Table 5: Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy (DA) of SAAG and AFTP for separating portal hypertension and non-portal hypertension causes of ascites.

PARAMETER	SAAG	AFTP
Sensitivity	91.59	23.36
Specificity	84.38	25.00
PPV	95.15	51.02
NPV	75.0	8.89
DA	90.0	23.74

Discussion

Ascites can be a clinical feature of conditions with high morbidity and mortality such as abdominal tuberculosis, abdominal lymphoma, malignancy or liver cirrhosis. Ascites constitutes a recurrent indication for hospitalization of patients in internal medicine departments in Ghana, but its causes remain under reported in this country. Successful treatment of ascites depends upon an accurate diagnosis of its cause and a large number of patients with ascites have diseases that may be potentially curable. Classification of types of ascites according to the level of serum-ascites albumin gradient (SAAG) is the best single test for classifying ascites into portal hypertension (SAAG >11 gm/L) and non–portal hypertension (SAAG < 11 g/L) causes.[8] This study was therefore to determine the aetiology of ascites and the usefulness of SAAG in differentiating the causes of ascites in Ghanaian context, so that patients can be managed appropriately and effectively.

Chronic liver disease (liver cirrhosis and hepatocellular carcinoma) was the commonest cause of ascites accounting for 73.57% of cases, followed by malignancies excluding HCC; 12.86%. Collectively, other causes constituted 13.58% of the cases of ascites in this study. This is comparable with other studies conducted in Africa and in the Western world. [1, 2, 5, 11-12] For instance, these findings are similar to a study conducted in Nigeria which showed similar aetiologies of ascites.[11] However, patients in the Nigeria study had a lower prevalence of liver cirrhosis (44%), and high percentages of tuberculous peritonitis (23%) and malignant ascites (22%). This could be due to the fact that, the referral pattern of these patients may vary from country to country or institution to institution. In KBTH there is a separate unit for managing tuberculosis (TB) and those with suspected TB are not seen at the main medical ward and cancer cases are seen mainly by the surgeons. Also due to the availability of potent anti-tuberculous medication, it is possible that the prevalence of TB has fallen in Ghana and Africa as a whole. The similarities of the causes may be due to the common aetiologic factors that the patients are exposed to especially in sub-Saharan Africa.

The etiological spectrum of ascites is vast and practically includes pathology of all the systems. SAAG has been found to be effective in differentiating ascites into portal and non-portal hypertension causes. Narrowing the causes to portal and non-portal hypertension will limit the laboratory and imaging investigations needed to do to come out with the definitive aetiology especially in developing country like Ghana. The diagnostic accuracy of SAAG in the present study to classify ascites into portal hypertension and non-portal hypertension aetiology was 90.0%. These values are comparable to the results obtained by Goyal et al. (97%) and Runyon et al. 96.7%).[8, 13] Gupta R et al.[14] also found that SAAG at a cut-off level of 1.1 g/dL had an accuracy of 92% in distinguishing cirrhotic ascites from tuberculous and malignant ascites, which was similar to this study. The diagnostic accuracy of AFTP in this study was 23.74% which was far lower than SAAG in differentiating portal hypertension and non-portal hypertension as a cause of ascites. This is comparable to studies conducted by Akriviadis et al.,[15] and Gogoi et al, [16] they found out that the diagnostic accuracy of SAAG was high in differentiating the causes of ascites compared to AFTP.

The mean age of the respondents was 44.66±13.20 years. This is disturbing due to the fact that these

patients are in their economically productive years of life, and this has implications on productivity. This is similar to other studies conducted in other African countries [4,10] that looked at the causes of ascites that stated the mean age, but lower than a similar study done in Qatar.[17]

Similarities and differences in the mean age may be due to etiologies of ascites and especially prevalence of chronic viral hepatitis in the population, as well as the age of acquiring the viral infection since cirrhosis has been found to be the most common cause of ascites in all the studies.

Hepatitis C and alcoholic liver disease are more frequent causes of liver cirrhosis in Europe and the Americas, compared with sub-Saharan Africa, being caused mostly by viral hepatitis B acquired in infancy. The male: female ratio for this study was 1.2:1 which is similar to a ratio of 1.3:1 that was reported by Ouattara et al. in Côte d'Ivoire [5]. This may be due to the similarities in the causes of ascites and the fact that both countries are located in sub-Saharan Africa with exposure to similar aetiologic factors.

Limitations

Patients with malignant ascites from surgical ward and abdominal tuberculosis from TB ward could have been sampled to increase the numbers of non-portal hypertension causes of ascites, this could have given more insight into the clinical significance of SAAG. Another limitation is the fact that we could not specifically measure portal pressure and had to rely on clinical diagnosis of which cases were classified as PHT or NPHT based on disease pathophysiology.

Conclusion

In conclusion, the results of the present study show that SAAG is a test with satisfactory diagnostic accuracy in separating ascites related to portal hypertension from the forms of ascitic fluid collection caused by mechanisms unrelated to portal hypertension. This could be used as a first line investigation in the etiological diagnosis of ascites to better inform appropriate investigation requests in a resource limited setting.

Moreover, SAAG is a more readily accessible clinical test compared with other more sophisticated tests in most of the district hospitals in Ghana, therefore its application could be more widely utilized.

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APPENDICEAL BASE LIGATION WITH THE HAND-MADE POLYDIOXANONE (PDS) EXTRACORPOREAL KNOT

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Abstract

Objective: This study describes our experience with a low cost handmade polydioxanone (PDS) extracorporeal knot to reduce the cost of laparoscopic appendectomy in a surgical practice.

Methodology: This retrospective study was conducted from January 2018 to December 2019 in a general surgical unit of the University College Hospital Ibadan. The files of 20 patients with complete data for whom extracorporeal hand-made PDS'0' knots were used for appendiceal stump closure during laparoscopic appendectomy were retrieved.

Results: The mean age was 28.4 ± 13.2 years. There were nine male and eleven female patients. All the operations were performed by the same surgical team. The mesoappendix was coagulated with bipolar cautery and cut with scissors. The appendix base was double ligated with two extracorporeal knots and divided. The mean duration of surgery was 59.2 ± 31.2minutes. The median length of hospital stay was 2days. The mean duration of follow up was 2.80 ± 0.50 months. One patient developed superficial port site infection.

Conclusion: The handmade extracorporeal knot used in this retrospective study for securing appendicular stump was found to be safe and cheaper than pre-tied extracorporeal loop. This will reduce dependency upon preformed endoloops making the procedure cheaper. There was no incidence of failed application of the handmade extracorporeal knot.

Key words: *laparoscopy; appendectomy; extracorporeal*

Introduction

Appendicitis is the most common surgical emergency in general surgery[1] Laparoscopic appendicectomy (LA) has gained global acceptance over open appendicectomy which is an older technique. While studies have demonstrated minimal differences in operative times for both laparoscopic and open appendicectomy with experienced surgeons, LA has fewer wound infection rates, faster recovery, and earlier return to work in comparison with open appendicectomy[2, 3]. Postoperative complication rates are slightly less in LA. [(3)] Despite this evidence, LA has failed to gain unequivocal acceptance by the general surgical community as an alternative to open appendicectomy (OA) especially in developing countries.

Some reasons often mentioned against the universal acceptance of laparoscopic appendicectomy include the elevated cost of laparoscopic surgery[4]. However, the cumulative cost inclusive of admission, treating complications and medications is in favour of LA[5].

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Utilising reusable instruments in laparoscopic surgery reduces the overhead cost of the procedure.

The most critical part of LA is a safe closure of the appendix stump to prevent intra-abdominal complications from faecal leak into the abdominal cavity. The appendix stump may be closed in several ways which are broadly divided into traditional ligatures (such as intracorporeal or extracorporeal ligatures or Roeder loops) and mechanical devices (such as clips, stapling devices or electrothermal devices[6,7].

Many modifications have been made to reduce cost of laparoscopic appendectomy further in developing countries. These include the one- or 2-trocar techniques, instrument-assisted knotting, and closure of the stump by clip applier, staplers or the endoloop suture. However, despite these wide range of stump closure techniques, these appliances are either not readily available or significantly increase the cost of surgery for the patient. Two PDS sutures with an approximate price equivalent of one American dollar (USD) are required for two handmade loops. On the other hand, the endoloop costs an equivalent of 15 USD each in Nigeria making the hand-made loop a much cheaper alternative.

Secondly laparoscopic surgeons with limited experience may not be adept in intracorporeal knotting. We present our experience with the use of hand -made

extracorporeal PDS Roeder's knots for securing the appendix stump.

Materials and Methods

Patients and Method

This retrospective study was carried out in Department of Surgery University College Hospital from January 2018 to December 2019. Within this study period sixty-nine patients with appendicitis were admitted. Twenty-three patients had laparoscopic appendicectomy with the hand-made extracorporeal knots. The files of 20 patients who had the appendix stump closure with hand-made extracorporeal knots PDS'0' at laparoscopic appendectomy were retrieved. The complete records of three patients could not be obtained making a data retrieval rate of 87%. Prior to surgery every patient was informed about the details, risks, and benefits of the technique. Routine consent was obtained all patients. Exclusion criteria for laparoscopic appendicectomy included patients with clinical or radiological features of ruptured or perforated appendicitis, patients with previous abdominal surgery, patients not fit for general anaesthesia, non-consenting patients. Procedures which were converted to an open procedure were not included in this review because no extracorporeal knot was applied. Paediatric patients are not treated by this surgical division.

Procedure

All the operations were under general anaesthesia. One gram of cephalosporin and 500mg of metronidazole was administered as preoperative antibiotics. Pneumoperitoneum was created using the veress needle through an umbilical port. Subsequently a 10mm trocar was inserted through the umbilical port. Consequently, a 10mm trocar and a 5mm trocar were inserted in the left iliac fossa and the suprapubic regions, respectively.

A 10 mm zero-degree telescope was inserted through the umbilical port while a yohan forceps was inserted through the 5 mm supraumbilical port. An 5mm adaptor was attached to the 10mm left iliac port which was used for introduction of the 5mm Maryland dissector, the 5mm scissors or the 5mm bipolar forceps as required.

Sequel to the establishment of the three ports, the caecum was identified, and the appendix was located and retracted towards the anterior abdominal wall with the yohan forceps. This displayed the mesoappendix which was sequentially coagulated close to the appendix base with the bipolar forceps and divided with the scissors until the base of the appendix was adequately exposed. Subsequently a hand tied PDS '0' Roeder's knot was introduced through the 10mm port using a 5mm knot pusher. The appendix was guided into the loop of the knot using the yohan forceps. The knot was manipulated to the base of the appendix and was tightened at the base of the appendix by advancing the knot pusher. Two Roeder's knots were applied to the base of the appendix about 0.2 to 0.4 cm apart. The appendix was then coagulated with the bipolar forceps at the energy of 35 watts about 0.5 cm and 1cm distal to the applied loop to seal the lumen following which the appendix was divided between these coagulated points.

This was to avoid spillage of enteric contents. The appendix was retrieved through the 10mm trocar in the left iliac fossa. The appendix stump was visualised to ensure there was no bleed. The operating ports were removed under direct vision while the trocar in the umbilical port was withdrawn with the telescope partially withdrawn. The fascia closure of the umbilical port was with Nylon '0' while other ports had only skin closure done.

To form the endoloop we used the (1: 3: 1) method. First, a loop was made around the assistant's fore finger with one short limb and one long limb. Next a simple knot was made with one throw resulting in a long limb and a short limb. Then with the shorter limb, three winds were made around both limbs. After that the third wind a half hitch was made. The loop was tightened and checked for sliding (Figure 1). The long limb of the suture was passed through a 5mm reusable knot pusher. The duration for making the two loops was about two minutes.

Each knot was tested by sliding the knot forward slightly to make sure it would secure the appendix base. If the knot did not slide it was reconstructed using the same suture.

Figure 1 The Configuration of Roeder's knot

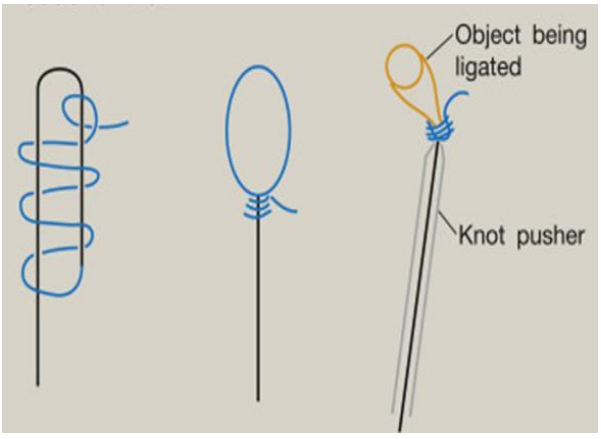


Figure 2 Application of the first knot

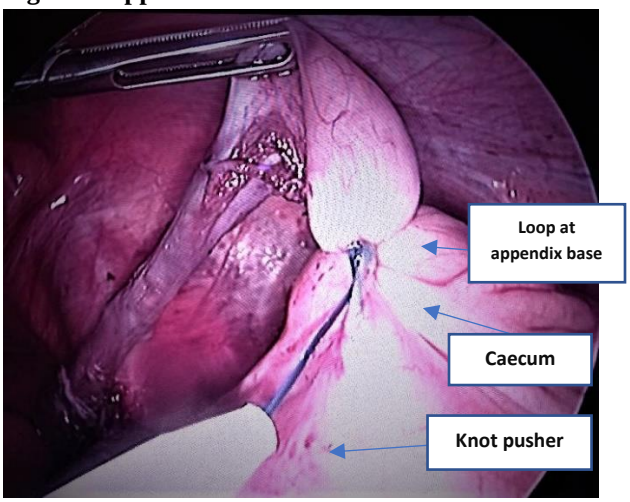
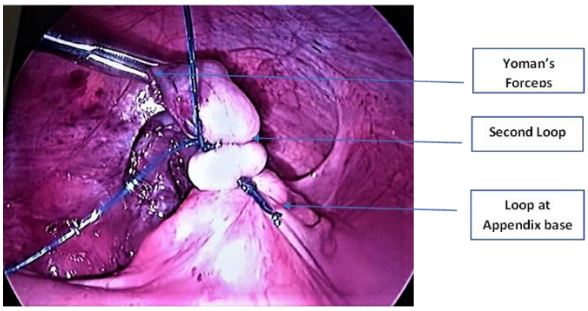


Figure 3 Application of the Second knot



Results

Twenty patient records were reviewed. The mean age was 28.4 ± 13.2 years. Table 1 shows the socio-demographic and clinical characteristics of the study subjects. The mean duration of surgery was 59.2 ± 31.2minutes. The median estimated blood loss (EBL) was 10 ml. In all patients, 2 sutures (one each) were used for the endoloops. The median length of hospital stay was 2days. The mean duration of follow up was 2.80 ± 0.50 months.

Discussion

Although the laparoscopic surgery is well established globally, laparoscopic appendicectomy unlike laparoscopic cholecystectomy has not been accepted as a gold standard in low-income countries, Nigeria inclusive. The relatively high fee of the procedure which is due to the cost of instrumentation is one of the hinderances to its acceptance[4,5]. The crux of laparoscopic appendicectomy is the closure of the appendix stump. Methods of closure of the stump include intracorporeal or extracorporeal knots and mechanical devices such as GIA stapling devices, clips, or electrothermal devices[6,7].

Table 1 Socio-demographic and clinical characteristics of the study subjects

Variable	Frequency (%)
Gender	
Male	9 (45)
Female	11 (55)
Comorbidity	
Present	3 (15)
Absent	17 (85)
Diagnosis	
Acute appendicitis	6 (30)
Subacute appendicitis	14 (70)
ASA-PS grade	
I	17 (85)
II	3 (15)
Appendicectomy type	
Interval	17 (79.4)
Early	3 (20.6)
Appendiceal location	
Retrocecal	16 (88.2)
Pre-ileal	1 (2.9)
Pelvic	2 (6.0)
Paracolic	1 (2.9)
Complication	
Yes	1 (5)
No	19(95)
Duration of admission	
17 (3 days)	
2 (4 days)	
1 (5 days)	

Although mechanical devices are more expensive, it remains unclear whether they truly provide safer closure of the appendix stump than their cheaper ligature counterparts. When the appendix is significantly inflamed, these ultra-modern devices cannot be relied upon in serving their function. However, the degree of local inflammation and the expertise of the operating surgeon play a decisive role in the technique of closure of the stump. The use of non-absorbable polymeric clips is less expensive than the GIA stapler but in the stump closure however these

clips may not be suitable when the diameter of the appendix exceeds 1 cm.[8]. Manual polyglactin suture knots for closing the appendix stumps have been demonstrated to be safe[9]. Similarly polypropylene knots have also been demonstrated to be safe[10]. We present our experience with the use of handmade PDS suture in our facility. PDS is a slowly absorbable monofilament suture composed of the polyester, poly (p-dioxanone).

The median duration of postoperative hospital stay was two days which is like other studies[11]. However, the two patients who were discharged on the fourth post operative day had prolonged ileus. The third patient with prolonged stay of five days had superficial surgical site infection which resolved with oral antibiotics. The mean duration of surgery of 59.2 ± 31.2minutes is not significantly different from 62+/-26.2 minutes in a previous review of laparoscopic appendicectomy using pretied extracorporeal knots[12]. The mean duration of admission prior to discharge of two days was also like a previous study on laparoscopic appendicectomy using the generic pretied extracorporeal knot[12].

Our experience in this descriptive study demonstrates that the use of handmade PDS loops for closure of the appendiceal stump in laparoscopic appendectomy resulted in no stump leakage. We have demonstrated that extracorporeal handmade PDS loop for the closure of the appendiceal stump in laparoscopic appendectomy is reliable. The cost of a pretied extracorporeal knot was 12United States Dollars (USD) while a PDS suture cost approximately 2 USD. Consequently, the cost of laparoscopic appendicectomy may be further reduced. There was no intraabdominal knot failure.

Conclusion

The handmade PDS endoloop is a cheap and easily applicable method which further reduces the cost of laparoscopic appendicectomy in poorer countries without significantly compromising safety. It is a cheaper method of stump closure especially for younger surgeons without laparoscopy suturing skills. The limitations of this study are the small sample size, retrospective study design and the lack of a control arm of the study.

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CLINICAL AUTOPSY AS AN OUTCOME MEASURE AND TOOL FOR QUALITY IMPROVEMENT AT THE CAPE COAST TEACHING HOSPITAL

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Abstract

Objective: We set out to investigate, the relationship between the antemortem clinical diagnosis and the clinical autopsy diagnosis, as a tool to assess the quality of health care in our institution.

Methodology: A retrospective review of clinical records of hospital autopsies done in the Cape Coast Teaching Hospital from 1st January 2011 to 31st December 2014 was conducted. An analysis of the ante mortem diagnosis and the autopsy diagnosis was conducted by the Departments of Internal Medicine and Therapeutics, Community Medicine, and Pathology of the School of Medical Sciences, Cape Coast Teaching Hospital. Discrepancies were identified and classified according to the Goldman criteria as major missed diagnosis and minor missed diagnosis.

Results: Fifty hospital autopsy cases were reviewed. There was no error in 20(40 %) of the cases. Of the 30 cases (60%) had discrepancies and were classified using the Goldman criteria,12 out of the 30 (40%) were major class I type errors, 15(50 %) were major class II type errors and and the remaining 3(10%) were minor class IV type errors. The diseases were categorized into: others (causes of death that could not be categorized under either infections, cancers, cardiovascular disease, pregnancy related and metabolic) 15 (30%), infections 14 (28%) and cancers 10 (20%) were commonly autopsied, and most were from the medical ward.

Conclusion: Significant discrepancies between the ante-mortem clinical diagnosis and the autopsy diagnosis at the Cape-Coast Teaching Hospital were identified. No statistically significant relationship was found between clinical departments and ACD/AD discrepancy or between category of disease and ACD/AD discrepancy.

Key Words: *audit, antemortem, post-mortem, diagnosis, Cape Coast, Ghana*

Introduction

With the current emphasis on evidence-based medicine and quality in health care, autopsy diagnoses can help evaluate the medical treatments or interventions that a patient receives, and whether or not those interventions are appropriate.[1] Clinical autopsies are carried out with permission from relations of patients who die in the care of clinicians. They are done to investigate only natural deaths (solely due to disease). In low resource settings, such as the Cape Coast Teaching Hospital some important diagnostic methods are not readily available, or where available may not be affordable. Audits of autopsies carried on clinical cases are a cheap and reliable way of ensuring quality in clinical care. Clinical autopsy rates have however plummeted worldwide[2,13,14,] and Ghana is no exception[15]. The cause of this decline in Ghana are many and include; religious and traditional beliefs, financial considerations, physicians fear of litigation, lack of interest in autopsies among both pathologists and other clinicians, and the unavailability of trained pathologists to serve the many hospitals.[2] This is despite the demonstration in literature of a high prevalence of errors in antemortem clinical diagnosis discovered at autopsy and multiple studies suggesting no significant decrease in these errors over time.[3]

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Shojania et al of University of California at San Francisco-Stanford in their systematic audit of articles comparing autopsy diagnosis (AD) and antemortem clinical diagnosis (ACD) titled 'The Autopsy as an Outcome and Performance Measure'concluded that at the level of the individual clinician, the chance that an autopsy will reveal important unsuspected diagnosis in a given case remains significant[11]. They also reported that clinicians do not seem to be able to predict the cases in which such findings are likely to occur[11]. Finally, they reported that existing literature thus demonstrate that ACD, whether obtained from death certificates or hospital discharge data, contain major inaccuracies compared with AD and thus the healthcare system as a whole can benefit enormously from autopsy data, by substantially enhancing the accuracy of vital statistics, which play important roles in research, funding, and other policy decisions.[11]

However, in an editorial on Shojania et al's article by Bove K.E, Bove notes that the authors in their analysis of 42 previous studies on autopsy discrepancy report that indeed decreases in errors have occurred during

the 40-year time span within which the studies were carried out. This notwithstanding previous reports based on individual studies to the contrary. This is against the background of the competing effect of clinical selection of more difficult cases for autopsy, as autopsy rates have decreased.[4] This study includes only studies that reported major errors, were deemed most likely to have affected patient outcomes. Bove notes that clinicians participated in these judgments in about two thirds of the studies, he mentions that this is a critically important feature for any effort to place autopsy-based diagnoses in realistic clinical context.[4]
It has been reported in some studies that discrepancy rates vary for various departments with higher discrepancy rates reported for intensive care patients and for surgical patients. These studies also report a decrease in discrepancy rates with an increase in clinical autopsy rates.[4]In a study that focused on patients who die in the intensive care unit, Perkins et al conclude that postmortem examinations remain a useful tool in confirming diagnostic accuracy and should be considered in all patients who die in the intensive care unit. Although they were limited by the number of cases studied (38 cases) they conclude that they did not find an association between the length of ICU stay and the number discrepancies found at autopsy[7].

Benefits derived from the autopsy which can be of immense value in the attainment of health goals in a poor resource setting largely relate to the role of the autopsy in detecting discrepancies in clinical diagnosis and in revealing unsuspected complications of treatment. Other benefits include detection of new patterns in old diseases, revealing disease course and cause of death to next of kin of a deceased patients, aiding the investigation of environmental, occupational, and lifestyle-related diseases and also providing tissue for research.[7] The autopsy can thus serve as a clinical performance measure and also serve as an instrument for quality improvement. This study aims at studying the current discrepancy rates between AD and ACD at the Cape Coast Teaching Hospital.

Methodology

A retrospective review of the clinical records of patients who died and were autopsied in the Cape Coast Teaching Hospital between 1st January 2011and 31st December 2014 was done. A total of 774 autopsies were conducted in this period. Seventy-eight (78) (10%) of the cases were classified as clinical autopsies. Six hundred and ninety-six (696) (90%) cases were medicolegal cases referred to our hospital's autopsy suite from various Coronial districts after dying in the communities. The causes of these 696 deaths were mostly unnatural (accidents, suicides and homicides). These medicolegal autopsies were excluded from the study. The ACD was compared to the AD. Only clinical autopsies were included in the study. Cases autopsied but without available clinical records were excluded from the study. The data was reviewed by 2 pathologists and the discrepancies classified according to the Goldman criteria (**TABLE 1**). Detailed analysis of cases in relation to departments, disease category and their various relationships was done. Tests of significance were calculated. Secondary data from selected patient records and their respective autopsy data were used in the study. All medico-legal cases and cases with missing records were excluded from the study. A descriptive analysis of the data was done according to the Goldman criteria for clinical autopsy discrepancies.

Table 1- Goldman criteria for autopsy discrepancies

CLASS	DESCRIPTION
CLASS I	Missed major diagnosis with a potential adverse impact on survival that would have changed management
CLASS II	Missed major diagnosis with no potential impact on survival that would not have changed therapy
CLASS III	Missed minor diagnosis related to terminal disease but not related to the cause of death
CLASS IV	Other missed minor diagnosis
CLASS V	Absolute autopsy agreement between antemortem and autopsy diagnosis
CLASS VI	Uncertain autopsy diagnosis

Results

A total of 774 autopsies were conducted from January 2011 to December 2014. Seventy-eight (78) (10%) of the cases in this period were classified as clinical autopsies. Out of the 78 clinical cases, 28 were excluded due to unavailable or incomplete clinical records leaving 50 cases, that were used in the study. Out of the 50 cases studied, 20(40%) were males and 30(60%) females (**TABLE 2**). Majority of the cases (18) comprising thirty six percent of the deaths were recorded in the department of medicine. This was followed in decreasing order by the department of surgery 8(16%), Intensive Care Unit 7(ICU) 14%, and Pediatrics 3(6%). The departments of Obstetrics and Gynecology (O&G) and the Accidents and Emergency (A&E) had 8(16%) and 6(12%) respectively, (**TABLE 2**). Regarding discrepancies between AD and ACD, the results showed no discrepancy in 20(40) % of the cases. Of the 30 cases (60%) that had discrepancies, 12(40%) had a postmortem diagnosis, that if recognized would have altered the therapy or survival

(Major class I type errors), 15(50 %) had a postmortem diagnosis, that if recognized would not have altered therapy or survival though major (Major class 2 type errors) and 3(10%) had a postmortem diagnosis, that was not related to the primary disease that caused death but may have altered survival (minor class IV type errors). The diagnoses were categorized into infections, cardiovascular diseases, metabolic disease, cancers, pregnancy related and others (Others are the diseases (cause of death) that cannot be grouped under the other categories based on the aetiology of the disease that is;infections, cancers, cardiovascular disease, pregnancy related and metabolic). Majority of the cases belonged to the category of others 15(30%) followed by infections 14(28%), and then cancers 10(20%). The metabolic diseases category had the least number of autopsies requested on them 1(2%) (**TABLE 2**).

Table 2- Frequency distribution of the cases analyzed

		Frequency	Percent (%)
Gender	Male	20	40.0
	Female	30	60.0
	Total	**50**	**100.0**
Unit	A&E	6	12.0
	Medical	18	36.0
	Surgical	8	16.0
	ICU	7	14.0
	Pedics	3	6.0
	O&G	8	16.0
	Total	**50**	**100.0**
Goldman's Classification	Major class 1	12	24.0
	Major class 2	15	30.0
	Minor 4	3	6.0
	No error	20	40.0
	Total	**50**	**100.0**
Category of diseases	Infection	14	28.0
	Cardiovascular	4	8.0
	Metabolic	1	2.0
	Cancers/ tumor	10	20.0
	Others	15	30.0
	Pregnancy related	6	12.0
	Total	**50**	**100.0**

Table 3: Unit Group * Goldman Classification System Crosstabulation

System			Goldman Classification				Total
			Major class 1	Major class 2	Minor 4	No error	
Infection	Unit Group	A&E	0 (0.0%)	0 (0.0%)		1 (100.0%)	1 (100.0%)
		Medical	2 (25.0%)	3 (37.5%)		3 (37.5%)	8 (100.0%)
		Surgical	0 (0.0%)	0 (0.0%)		2 (100.0%)	2 (100.0%)
		ICU	1 (50.0%)	0 (0.0%)		1 (50.0%)	2 (100.0%)
		Pedics	0 (0.0%)	1 (100.0%)		0 (0.0%)	1 (100.0%)
	Total		3 (21.4%)	4 (28.6%)		7 (50.0%)	14 (100.0%)
Cardiovascular	Unit Group	Medical		2 (100.0%)		0 (0.0%)	2 (100.0%)
		ICU		1 (100.0%)		0 (0.0%)	1 (100.0%)
		O&G		0 (0.0%)		1 (100.0%)	1 (100.0%)
	Total			3 (75.0%)		1 (25.0%)	4 (100.0%)
Metabolic	Unit Group	A&E				1 (100.0%)	1 (100.0%)
	Total					1 (100.0%)	1 (100.0%)
Cancers/ Tumor	Unit Group	A&E	0 (0.0%)	0 (0.0%)	1 (100.0%)	0 (0.0%)	1 (100.0%)
		Medical	2 (50.0%)	1 (25.0%)	1 (25.0%)	0 (0.0%)	4 (100.0%)
		Surgical	1 (50.0%)	1 (50.0%)	0 (0.0%)	0 (0.0%)	2 (100.0%)
		ICU	0 (0.0%)	1 (100.0%)	0 (0.0%)	0 0.0%)	1 (100.0%)
		Pedics	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (100.0%)	1 (100.0%)
		O&G	0 (0.0%)	1 (100.0%)	0 (0.0%)	0 (0.0%)	1 (100.0%)
	Total		3 (30.0%)	4 (40.0%)	2 (20.0%)	1 (10.0%)	10 (100.0%)
Others	Unit Group	A&E	1 (33.3%)	1 (33.3%)	0 (0.0%)	1 (33.3%)	3 (100.0%)
		Medical	1 (25.0%)	1 (25.0%)	1 (25.0%)	1 (25.0%)	4 (100.0%)
		Surgical	1 (25.0%)	1 (25.0%)	0 (0.0%)	2 (50.0%)	4 (100.0%)
		ICU	1 (33.3%)	0 (0.0%)	0 (0.0%)	2 (66.7%)	3 (100.0%)
		Pedics	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (100.0%)	1 (100.0%)
	Total		4 (26.7%)	3 (20.0%)	1 (6.7%)	7 (46.7%)	15 (100.0%)
Pregnancy related	Unit Group	O&G	2 (33.3%)	1 (16.7%)		3 (50.0%)	6 (100.0%)
	Total		2 (33.3%)	1 (16.7%)		3 (50.0%)	6 (100.0%)
Total	Unit Group	A&E	1 (16.7%)	1 (16.7%)	1 (16.7%)	3 (50.0%)	6 (100.0%)
		Medical	5 (27.8%)	7 (38.9%)	2 (11.1%)	4 (22.2%)	18 (100.0%)
		Surgical	2 (25.0%)	2 (25.0%)	0 (0.0%)	4 (50.0%)	8 (100.0%)
		ICU	2 (28.6%)	2 (28.6%)	0 (0.0%)	3 (42.9%)	7 (100.0%)
		Pedics	0 (0.0%)	1 (33.3%)	0 (0.0%)	2 (66.7%)	3 (100.0%)

		O&G	2 (25.0%)	2 (25.0%)	0 (0.0%)	4 (50.0%)	8 (100.0%)
	Total		12 (24.0%)	15 (30.0%)	3 (6.0%)	20 (40.0%)	50 (100.0%)

Further analysis of the contribution of each department to the Goldman's error category showed that the leading department (internal medicine) contributed 41.7% of major class I errors, 46.7% of major class II errors, 66.7% of minor class IV errors and 20% to the no errors. (**TABLE 3**). When the major class I errors were further analyzed, it was found that majority of them belonged to the disease category of others (33.3%), followed by infections and cancers (25% each) and then by pregnancy related diseases (16.7%). When further analyzed, it was realized that, although most of the cases from the department of internal medicine were infections (44.4%), the department contributed only two (2) of these to the major class I error category with the other six (6) split equally (3) between major class II errors and the no error category. No statistically significant relationship was found between departments and category of diseases and Goldman's error categories. (**TABLE 3)**

Discussion

The value of autopsy in clinical audit has been highlighted in studies, and it has been suggested that auditing discrepancies between autopsy findings and clinical diagnosis may be used to improve diagnostic accuracy.[2] By analyzing discrepancy rates between AD and ACD, a reliable database can be developed to support mortality audits. Our study showed that there was complete agreement between the ACD and AD in 40 % of the cases; a clinical autopsy was however requested. This is in line with the use of clinical autopsies to confirm clinical suspicions, study the state of individual organ systems and study the extent of a known diagnosed condition. These kinds of request provide additional scientific material for publications and for medical education.

As stated in a review by Bove KE, an essential use of the clinical autopsy in this era of declining rates is the educational benefit to the clinician, such as the ability to assess the severity or extent of a disease correctly identified or strongly suspected antemortem.[2] In the same review,other benefits observed include, the opportunity to evaluate the efficacy of therapies, unrestricted access to tissue samples for additional diagnostic testing, and finally, the opportunity to extend understanding of pathologic processes by collecting and studying samples from many patients with the same disease at different stages in the diseases' natural history. The above benefits remain important justifications for conducting clinical autopsies.[2] Though our ACD/ AD concordance figure of 40% is lower than the 62% quoted in other studies, the lower concordance between the ACD and AD in our setting may be attributable to the lack of some diagnostic methods in the Cape Coast Teaching Hospital or the inability of some patients to afford these tests when they are even available. It may also be the case that clinicians do not request autopsies for the above stated reasons once they are certain of the ACD. Instead, clinicians may prefer to request autopsies when they are not certain about the ACD. By selecting cases considered more difficult in the clinical setting, the concordance between the ACD and the AD is likely to decrease.

On the other hand, if cases are selected randomly without regard to clinical difficulty, this is likely to improve concordance between ACD and AD. Out of the 30 (60%) cases that had discrepancies, 40% had postmortem diagnosis that if recognized earlier by clinicians, would have altered therapy or survival (Major class 1 type errors). A few examples of theMajor class 1 type errors identified include;an AD of pyogenic meningitis (infection) and ACD of severe pre-eclampsia/eclampsia (pregnancy related) , AD of perforated appendix (others) and ACD of peptic ulcer disease (others), an AD of tuberculous bronchopneumonia (infections) and ACD of community acquired pneumonia (infections). 50 % had postmortem diagnoses, that if recognized would not have altered therapy or survival (Major class II errors).

Selected examples include an AD of hepatocellular carcinoma (cancers) and ACD of alcoholic liver disease (others), an AD of progressive massive fibrosis of the lung (others) and ACD of lung cancer (cancers). Ten percent (10%) had minor postmortem diagnosis that were not related to the primary disease that caused death (minor class IV type errors). This falls within the general median error range of 4.1%-49.8% in Kaveh et al[10] study. In that study, it was concluded that the possibility that a given autopsy will reveal important unsuspected diagnoses has decreased over time, but remains sufficiently high that encouraging ongoing use of the autopsy as an audit tool appears to still be warranted.[10] By analyzing the results of 53 distinct autopsy series over a 40-year period, Kaveh et al showed statistically significant decreases over time for major errors detected at autopsy.[10] In our case, no such previous studies have been carried out and thus are unable to compare and comment on the trends over time, however further studies in this area will be

encouraged using larger populations to add on to literature.. Findings of unchanged discrepancy rates between ACD and AD are most pronounced in studies on critically ill patients who die in intensive care units. In this regard our study is limited by the number of ICU patients studied (7), though further analysis showed that ICU cases accounted for 16.7% of major class I discrepancies, 13.3% of major class II discrepancies and 15.0% of minor class IV discrepancy. When tests for statistical significance was carried out, no statistically significant relationship was found between cases from the ICU and Goldman's discrepancy categories. When this was done for other departments, there was still no statistically significant relationship between departments and the Goldman categories. Neither was there a statistically significant relationship between the category of disease and the Goldman criteria. Postmortem histology has been reported by some studies to further increase discrepancy rates. Some of these studies conclude that; despite the advances in the diagnosis and treatment of critically ill patients, autopsies continue to show major discrepancies between the ACD and AD. [5, 6, 7, 8,] These studies further conclude that considering that there is only moderate agreement between AD and ACD, autopsy remains a valuable procedure, the goal of which is not to uncover mistakes made by clinicians or to judge clinicians but rather to help instruct clinicians by providing them with the information to learn through their own mistakes.[9,10,11]

In a study titled 'Minimizing mistakes in clinical diagnosis' Ermenc B. report that even though it is expected that progress made in medical diagnostic methods will be accompanied by a similar improvement in diagnostic accuracy, in reality the discrepancy rates has remained the same. In his view, autopsy is the best source of information on diagnostic accuracy. He suggests that an increase in the number of clinical autopsies performed and the follow-up of these autopsies could reduce the number of diagnostic mistakes.[5] The stability in error rates has been attributable to increased selection bias towards difficult cases by clinicians.[5] Clinical selection occurs in the Cape Coast Teaching Hospital with clinicians selecting the most confounding cases for autopsy. With progressively fewer autopsies performed in many centers over time including the Cape Coast Teaching Hospital, it is postulated that clinical selection of diagnostically challenging cases for autopsy might offset true gains in diagnostic accuracy reported at autopsy, creating the erroneous impression that there is a high rate of inaccuracies.[4] However, it is also argued that several prospective studies have shown clinicians to have little ability to identify cases that will yield "diagnostic surprises," so clinical selection might exert little effect on rates of autopsy detected diagnostic errors.[5, 12] The extent to which clinical selection contributed to the rates of errors in this study cannot be quantified though it played a role in the selection of cases.

In Ghana, studies of this nature are lacking and there are no baseline studies comparing trends over a set period. Focusing on this high rate of major errors may suggest autopsy data as potential fuel for allegations of medical malpractice. However studies have demonstrated that standard-of-care issues, not diagnostic imprecision, are at the heart of most malpractice lawsuits.[5] Bove in his study cautions that 'it must be recognized that a certain degree of diagnostic imprecision may be unavoidable, given that medical care (including postmortem evaluation of manifestations of disease) is not an exact science, that our tools are not perfect, and the time to apply them prior to death may be short'.[4] Future research into the factors leading to errors in ACD, establishing optimal means of using autopsy data in performance improvement strategies, and exploring different mechanisms for encouraging autopsies should be encouraged in low resource settings such as the Cape Coast Teaching Hospital.[3]

Conclusion

There is a significant discrepancy rate between the ACD and the AD at the Cape Coast Teaching Hospital. There is however no statistically significant relationship between clinical department and ACD/AD discrepancy or between category of disease and ACD/AD discrepancy. Establishing optimal means of using autopsy as an audit tool and autopsy data in performance improvement strategies and exploring different mechanisms for encouraging autopsies must be given needed attention and focus.

Limitations

Our sample size of 50 patients is admittedly small and thus may not be an objective basis to draw conclusions statistically significant relationships. Again, considering that each department has unique patients, this may have affected the rate of discrepancy between the various departments. Again, some departments were more likely to request clinical autopsies than others. This is determined by the expertise and experience of those requesting permission for the autopsy and by cultural beliefs about

the urgency for burying the deceased. Finally, without a systematic randomized way requesting autopsies, there will always be a bias towards selecting cases based on level of difficulty and this may ultimately create the impression of high rates of discrepancy between ACD and AD.

Ethics & Consent

Ethical clearance was obtained from the University of Cape Coast Institutional Review Board through the department of Community Medicine for the project to be carried out in the 2014/15 academic year. In addition, the Cape Coast Teaching Hospital granted institutional accent for the project to be carried out in the facility. Back then, there was no ERC. Consent was not sought from relations of the deceased since the study was not about the causes of death but the ACD and AD concordance. No individuals were identified in this study.

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THE ECONOMIC BURDEN OF HOUSEHOLDS WITH CHILDREN LESS THAN FIVE YEARS PRESENTING WITH PNEUMONIA AT KOMFO ANOKYE TEACHING HOSPITAL, KUMASI, GHANA

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Abstract

Objective: Pneumonia is a leading cause of hospital admission among children less than five years in sub-Saharan Africa. It is also associated with considerable economic cost to the households affected. This study sought to quantitatively measure the economic burden of households with children less than 5 years admitted at the Komfo Anokye Teaching Hospital (KATH) on account of pneumonia.

Methodology: This was a cross-sectional study involving children less than 5 years admitted to the KATH for pneumonia. A consecutive sampling technique was used to select 157 eligible participants from the Paediatric Ward of KATH from June to August 2016. A structured questionnaire and data abstraction form was used to collect primary and secondary data respectively. We applied point (median) and interval estimation (interquartile range) on the various cost components (Pre-admission cost, direct cost and indirect costs). Estimates of the disability adjusted life years (DALY) was done using the prevalence-based approach.

Results: The median preadmission cost was estimated at GH₵ 70 [US$ 18] ranging from GH₵ 5(US$ 1) to GH₵ 600 (US$ 154). Households spends an average of GH₵ 600 (US$ 154) (IQR: GH₵ 387.68 [US$ 99], GH₵ 778 [US$ 199] in treating an episode of childhood pneumonia in Komfo Anokye Teaching Hospital. The median direct non-medical cost was GH₵ 60 (US$ 15). The median indirect cost was GH₵ 165 (US$ 42). The median DALY recorded was 1,253.476 YLL.

Conclusion: Pneumonia poses economic burden on households whose children are affected considering their low socio-economic status.

Key words: *Economic burden, Children less than five years, household, Pneumonia, Ghana*

Introduction

Pneumonia is a leading cause of hospital admission among children less than five years in sub-Saharan Africa [1]. The global prevalence in 2010 was estimated at 120 million episodes (14 million of them progressed to severe episodes) in children younger than 5 years. The global death toll of the disease is estimated at 1·3 million in 2011 of which 81% occurred in the first 2 years of life.[2]

Pneumonia may be associated with considerable economic costs to the health system and to individual households. A study conducted in USA revealed that the mean direct cost in treating a child under 5 years suffering from pneumonia is estimated at $ 2,055 per person per year. In this estimation, greatest portion of this cost (47%) is being paid by the Medicare policy with 4% being paid by the family or household. [3]The study further concludes that pneumonia attributable expenditure is strongly driven by high inpatient.

In Pakistan, the average household cost of treating an episode of pneumonia is estimated as $1.46 and $7.60 for referred cases. [4] Though this estimate is considerably low, it excludes other relevant costs being incurred by households. An estimate that took into account all societal average cost per episode of pneumonia arrived at US$22.62 (for non-severe pneumonia), and US$142.90 for severe pneumonia.[5] The breakdown for household expenditures revealed that medicines has been estimated to constitute the highest proportion (40.54%) of costs incurred during a visit to the health facility, followed by meals (23.68%), hospitalization (13.23%) and transportation (12.19%).[5]

In this era of harnessing scarce resources towards increasingly demand for universal coverage of health care amidst increasing cost of providing cost-effective health care and weak households' ability to

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pay status, the necessity to quantitatively measure the overall economic burden of illness and the relative costs of individual diseases such as pneumonia becomes critical. Although the direct costs for treating pneumonia are known to be high, it is likely that the financial burden is significantly underestimated as most studies overlook indirect costs (That is the forgone earnings due to taking care of a child suffering from pneumonia). Ghana depends enormously on donors. Donor agencies have contributed colossally towards the lessening of morbidities and mortalities connected with pneumonia and support for pneumonia research around the world.[6] In 2011, a total of US$ 1,004.7million was given by key donors such as Gates foundation and Gavi, the vaccine alliance for vaccines and research support to address the global menace of pneumonia.[6] These efforts have been skewed towards medical approaches leaving the socio-economic dimension. This has resulted in inadequate information on the economic burden of the disease. The present study therefore seeks to determine the economic burden of households with children less than 5 years presenting with pneumonia at Komfo Anokye teaching hospital in Kumasi, Ghana.

Significance for public health

Although, surveillance systems exist in health facilities in Ghana and other African countries, the focus has been to estimate the epidemiology of the disease with no attempt to explore its burden on the household, facility and the health system. The established measures of disease burden such as direct and indirect estimate of fiscal cost of managing the disease and Years of Life Lost (YLL) estimates with DALY make it possible to quantify the potential economic burden occasioned by pneumonia. There is dearth information on most of the studies conducted in sub-Saharan Africa (where the burden is high) on these estimates. In view of the high prevalence of pneumonia in children under five in Ghana coupled with scarce resources, it is important to determine the economic burden of households with children presenting with pneumonia in a low resource setting to generate empirical evidence for public health policy initiatives.

Materials and Methods

Study site

The study was conducted in the paediatric wards of the Komfo Anokye Teaching Hospital (KATH), the second largest hospital in Ghana located in its Ashanti Region. KATH serves a population of over 4 million within and outside Ashanti Region. It is the main referral centre from the middle to the northern zone of Ghana.

Study design

A prospective cross-sectional study that involved children less than 5 years admitted to the KATH for pneumonia was done from June to August 2016.

Sample size and sampling technique

A consecutive sampling technique was employed to select 157 eligible subjects from the Paediatric Ward of KATH from June to August 2016. The sample size was estimated based on previous study that reported pneumonia burden of 16.8% and 22.3% in rural and urban settings respectively[7] The sample size was estimated to detect a difference of 8% with a power of 80% which corresponds to 0.84 and 95% confidence interval which corresponds to 1.96 standard values and an alpha of 0.05. A child was included when he/she was aged 5 years or younger and admitted with a clinical diagnosis of pneumonia. The clinical signs to warrant inclusion included cough or difficulty breathing and have either severe pneumonia (lower chest wall indrawing) or very severe pneumonia (cyanosis, difficulty breastfeeding/drinking, vomiting, convulsions, lethargy, unconsciousness, or head nodding).

Data collection tools and techniques

A structured questionnaire was used to collect primary data from caregivers of subjects and data collected from the patient medical record using a structured data extraction form. Primary data included demographic variables, cost of transportation and feeding whilst secondary data extracted from medical records included cost of diagnostics, consumables, cost of ward procedures and cost of drugs.

Data analysis

Data was entered into Microsoft Access 2013 and was exported to STATA 13.0 (Standard Edition) for analysis. Data on occupation was grouped under professions (academically trained personnel such as teachers, nurses, etc. were grouped as professionals. Persons who have learnt trade and are working as such (skilled) and those in apprenticeship (semi-skilled) were grouped as skilled/semi-skilled. Data on the various cost components (Pre-admission cost, direct cost and indirect costs) were analysed by estimating the point estimate (median) and the interval estimates (interquartile range; 25^{th} and 75^{th}

percentile). The costs were further converted from GH₵ to US$ using an exchange rate of 1:3.9 respectively. Estimates of the DALY was done by summing Years Lived with Disease (YLD) and YLL using the prevalence-based approach. For this approach, the duration of pneumonia for each case was multiplied by the disability weight (Assumed to be 50%) to arrive at YLD. YLL were calculated as the number of death attributable to pneumonia through the period under study multiplied by the standard life expectancy. DALYs were therefore estimated as the sum of YLL and YLD and reported as absolute numbers.

Ethics approval and consent to participate

Permission to conduct the study was obtained from the Committee on Human Research Publications and Ethics (CHRPE), of Kwame Nkrumah University of Science and technology and the Research and Development Unit of KATH in Ghana. The Ethical number provided upon approval is: CHRPE/AP/399/16. Written Informed consent were obtained from respondents to affirm their willingness to participate.

Results

Socio-demographic characteristics of respondents

The children had a median age of 7 months ranging from 1 week to 59 months. More than half (n=94, 59.87%) of the children were less than 1 year old and the male to female ratio was 1.2:1. Majority (82.17%, n=129) of the children had been subscribed to the National Health insurance Scheme. More than half (61.78%) of the respondents resided in urban areas with diverse educational backgrounds. Trading was found to be the occupation of most of the caregivers constituting about 43% whilst 21 (13.38%) of the caregivers were unemployed. The median income of the caregivers was 300 Ghana cedis monthly ranging from persons with no monthly income to a monthly income of up to 1500. (Table 1)

Table 1: Socio-demographic characteristics of respondents

Variable	Frequency (N=157)	Percentage (%)
Age		
up to 11 months	94	59.87
12-23 months	19	12.10
24-35 months	20	12.74
36-47 months	10	6.37
48-59 months	14	8.92
median (min, max)	7 months (1 week, 59 months)	
Sex of children Male	86	54.78
Death	20	12.74
Residential status		
Rural	60	38.22
Urban	97	61.78
Maternal education		
None	20	12.74
Primary	28	17.83
JHS	53	33.76
SHS	37	23.57
Tertiary	19	12.10
Occupation		
Professionals	22	14.01
Skilled/semi-skilled	21	13.38
Catering	10	6.37
Traders	68	43.31
Farmers	15	9.55
Unemployed	21	13.38
Income of caregiver		
< 200 GHC	43	27.39
200-400	60	38.22
401-599	7	4.46
600-1000	34	21.66
> 1000 median (Min, Max)	13 300 (0.00, 1,500)	8.28
Female	71	45.22
Health Insurance status		
have health insurance	129	82.17
does not have health insurance	28	17.83
Outcome of hospitalisation		
Survived	137	87.26

Pre-admission cost

Prior to hospitalization, majority (75.00%) had sought healthcare elsewhere. Most (72.88%) of them indicated as having sought treatment from a lower level Public hospital with the remaining seeking care from a private health facility. A median cost of GH₵ 70 (US$ 18) was incurred ranging from GH₵ 5 (US$ 1) to GH₵ 600 (US$ 154) (see Table 2).

Table 2: Pre-admission cost

Variable	Frequency	Percentage (%)
Did patient seek healthcare prior to hospitalisation? (N=157)		
Yes	118	75.16
No	39	24.84
where treatment was sought pre-hospitalisation (N=118)		
Lower level Public hospital	86	72.88
Private Hospital	32	27.12
cost of care for previous treatment (GH₵) (N= 118)		
up to 50	51	43.22
51-100	28	23.73
101-200	21	17.80
201-and above	18	14.25
median cost GH₵ (US$)	*70.00 (18)*	
minimum cost incurred GH₵ (US$)	*5.00 (1)*	
maximum cost incurred GH₵ (US$)	*600.00 (154)*	

Source: Author's field data, 2016

Direct medical cost incurred

Estimates of the cost that are directly associated with children admitted with pneumonia was done. The items that were costed includes diagnostics, sanitation, accommodation, drugs and consumables. The median cost incurred for laboratory services was GH₵ 120. Households with children under 5 years suffering from pneumonia spends an average of GH₵ 84 (IQR: 25th percentile= GH₵ 46.25, 75th percentile= GH₵ 182) on drugs. Ward procedures and consultations cost an average of 89 Ghana cedis with more than 75 percent spending up to 100 Ghana cedis. In total, households spend an average of GH₵ 600 (25th percentile=387.68, 75th percentile= GH₵778) in treating an episode of childhood pneumonia in KATH. Assessment of the mode of payment indicated a median cost of GH₵ 125 is being paid for by the NHIS. An average of GH₵ 340 Ghana cedis is being paid out of pocket by households per pneumonia episode. (Table 3)

Table 3: Direct medical cost estimates incurred by under five years hospitalised for pneumonia in KATH.

VARIABLE	Median cost GH₵ (US$)	25th percentile GH₵ (US$)	75th percentile GH₵ (US$)
Hospital resource items being costed			
Laboratories/Diagnostics	120 (31)	70 (8)	144 (37)
Sanitation	10(3)	10 (3)	10 (3)
Accommodation	54(14)	36 (9)	76 (19)
Consumables	76 (19)	55 (14)	100 (26)
ICU	4 (1)	4 (1)	4 (1)
Documentations	16(4)	16 94)	16 (4)
Feeding	80 (21)	54 (14)	128 (33)
Ward procedures and consultation	89 (23)	67 (17)	120 (31)
Cost of drugs	84 (22)	46.25 (12)	182 (47)
Total Direct medical cost incurred as KATH inpatient	600 (154)	387.68 (99)	778 (199)
Payment Mechanism			
Average payment by Insurance	125 (32)	0.00 (0)	230 (59)
Average out of pocket payment	340 (87)	230(59)	499(128)

Direct non-medical cost

The study found that more than half (58.60%) of the respondents visited the healthcare facility with a public transport. Private cars were used by 12 representing 7.64%. The direct non-medical cost incurred by households during the hospitalisation was assessed. The elements that were captured in this cost analysis was the cost of transporting the sick child to the hospital, the cost of feeding the sick child, the

cost of feeding child and caregiver whiles on admission and transport cost incurred by other household members. (Table 4).

Table 4: Summary of cost elements in the direct non-medical cost

Cost elements	Median cost GH₵ (US$)	25th percentile GH₵ (US$)	75th percentile GH₵ (US$)
Cost of transporting sick child to the hospital	20 (5)	10 (3)	30 (8)
Cost of feeding child	12 (3)	7 (2)	15 (4)
Cost of transport incurred by household members at visits to the hospital	12 (3)	8 (2)	20 (5)
Cost of feeding for the caregiver whiles in the hospital	15 (4)	10 (3)	20 (5)
Average direct non-medical cost (combined)	**60 (15)**	**40 (10)**	**79 (20)**

Indirect cost incurred

The forgone earnings by households were captured in the cost analysis as the indirect cost incurred for seeking medical treatment with an episode of pneumonia. Almost all (91.72%) of the respondents were of the opinion that time of hospitalisation could have been invested in an economic activity. However, loss of income due to the hospital days revealed that a median income lost for non-economic activity is GH₵ 165 (25th percentile= GH₵ 80, 75th percentile= GH₵ 420). Majority (82.17%) paid for the hospital bills with their savings whereas about 15% borrowed money to pay the bills. In the opinion of most respondents (n=130, 82.80%), the cost of managing an episode of pneumonia is high. (Table 5).

Table 5: Summary of indirect cost of managing an episode of pneumonia by a household

Variable	Frequency	Percentage (%)
Could time of hospitalisation been invested in an economic activity (n=157)		
Yes	144	91.72
No	13	8.28
Average income lost for not working throughout hospital days (GH₵) n=141		
Up to 180	80	56.74
181 to 299	17	12.06
300 cedis and above	44	31.21
-median	*GH₵ 165(US$ 42)*	
-25th percentile	*GH₵ 80 (US$ 21)*	
-75th percentile	*GH₵ 420 (US$ (108)*	
Sources of payment		
Savings	129	82.17
Borrowing from bank, family or friend	24	15.29
Donations from friends and relatives	4	2.55
Rating cost of healthcare		
High cost	130	82.80
Moderate	25	15.92
Low	2	1.27

A descriptive summary of the median cost incurred by a household relative to the cost category was done. The study revealed that direct medical costs accounts for the highest (67.0%) burden of household costs per treatment of an episode of pneumonia. (Figure 2)

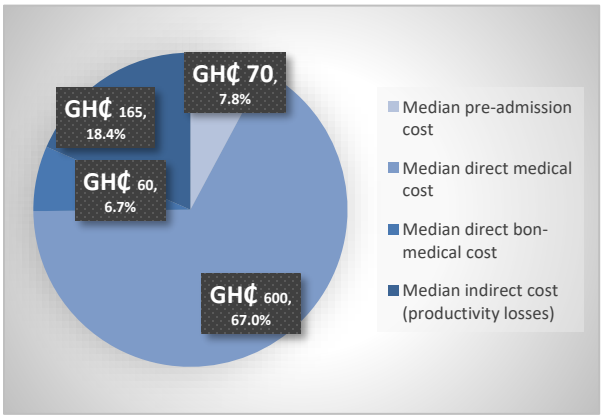

***Figure 2**: Relative per case median cost (%) per cost categories incurred by households in treating an episode of pneumonia at KATH.*

Disability adjusted life years due to pneumonia

The study showed that the DALY burden for children aged 1month to 23 months is highest

compared to other age groups with over 8000 DALY's. Comparing the DALY's by residential status and gender, it was observed that DALY's were on the rise among cases from urban areas with female gender accounting for the highest. (Figure 3)

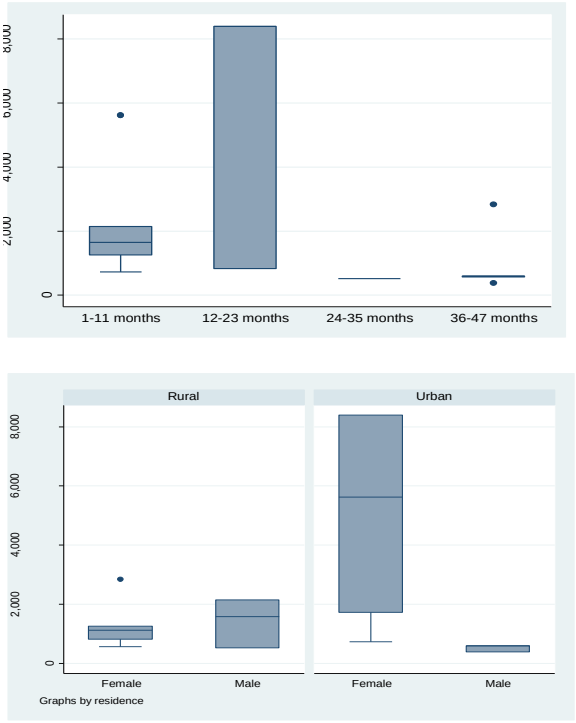

Figure 3: DALY's caused by pneumonia by age group, sex and residential status

Discussion

Health insurance schemes have been shown in several studies in Africa and Asia to improve health care utilization and to protect households from catastrophic out-of-pocket health expenditures.[8] In Ghana, the main health insurance policy since 2005 is the National Health Insurance Scheme (NHIS) which in 2015 had coverage of 38%[9]. The national percentage coverage is far less than was realised in the study and this may be attributable to the tertiary level at which the study was conducted which would be biased towards the critically ill. Other studies however have shown that the NHIS has a significant exclusion of the poor in the country.[9,10]

The educational levels of caregivers were even across the educational categories. Various occupational categories were identified in the study with trading found to be the dominant occupation. This to a large extent is due to the fact that the study was conducted at a setting where the main occupation is known to be trading. More than 50% earned less than 400 Ghana cedis (US$ 102.6) monthly, thus about 13 Ghana cedis (US$ 3.3) a day by the average household, which alludes weak economic standing.

Majority of the respondents sought healthcare elsewhere prior to hospitalization, reflecting the tertiary nature of the study site and its characteristic of being one of the main referral hospital in the northern part of the country. Policy encourages that persons seeking care must utilize lower level health facilities which are mostly closer enhancing accessibility and minimizing the costs. The study showed a significantly lower cost incurred from these facilities. Although most of the studies reviewed were silent on pre-admission costs [11–14], it is important to account for these as they all contribute to the economic burdens to these households. The observation that majority of the respondents sought healthcare in lower level health facilities and private health facilities is consistent with a study conducted in Vietnam. [15] In their study conducted, it was found that more than half of caregivers indicated that they had sought care from other sources, including lower-level hospitals, private and public clinics, and pharmacies and incurred some costs before admission. Pneumonia pre-admission median cost incurred in their study was almost USD 5 higher than was found in our study. Kitchin et al (2011) underestimated pre-admission costs[16] though it could affect the cost analysis of the true burden of the disease on the finances of these households affected.

The inpatient cost analysis of this study employed the societal perspective considering four main categories; the direct hospitalization cost, the consumption cost for patients and other household members that are not directly related to the hospitalization cost (direct non-medical cost) and the indirect cost or production losses. The inclusion of these elements in the costing analysis is consistent to some of the studies reviewed.[4,11,14,15,17–19] Study findings of the direct medical costs compares with studies conducted in Columbia where inpatient cost estimate of pneumonia in children under 5 was estimated at a median cost of US$ 263 (IQR 27–546)[13] though it is lower. A closer similarity of this results was found in India where the median provider cost for treating an episode of childhood pneumonia at a tertiary health centre was estimated at US$ 146.59. [14] In the Indian study, the cost of treating an episode of pneumonia was lower among cases seen at the secondary health facilities.

The difference in price was about twice as much as the cost incurred in secondary health facilities (that is US$ 83.89 vrs US$ 146.59). In this present study, a similar observation was made as healthcare costs at the lower level facilities was about eight times lower

than the cost incurred at KATH, the tertiary health facility. In Pakistan, a slight similarity was observed in the cost of treating an episode of pneumonia, as the study arrived at an estimate of US$ 71 and US$ 235 for pneumonia and severe pneumonia respectively. [20] The similarities in direct medical cost (healthcare provider cost) in the studies from Columbia, India and Pakistan could be due to the similarity in our economic status. These countries like Ghana are classified as low resource settings.

The direct non-medical cost of the disease was estimated by considering cost of transporting child to the hospital, transport costs by household members by visitation, cost of feeding child and caregiver. These items are in the costing sheet compares with numerous cost estimates. [4,15] The median direct non-medical cost of seeking pneumonia care was substantially lower compared to the findings reported in earlier study conducted in Hanoi, Vietnam. [15]

This study found a direct non-medical cost per managing an episode of pneumonia as US$ 50.00. This high difference in the Direct Non-Medical Costs (DNMC) could be due to the inclusion of miscellaneous (cost of lodging by caregivers, soap bought, diapers, etc). In our study, none of the caregivers indicated paying for lodging fee instead, slept at the ward with sick children.

The present study estimated the indirect cost incurred cautiously keeping in mind that arguments still continue on whether or not the indirect cost should be incorporated in healthcare cost estimation. [17] The indirect cost was calculated by considering the estimated forgone earnings due to time spent in facilities by caregivers' taking care of the sick children. This study has shown that, almost all the respondents agree that time of hospitalization could have been invested in an economic activity for financial gains and therefore they lost income due to the child's sickness. This important revelation further heightens the relevance of the indirect cost component in healthcare cost estimation of diseases. The estimated indirect costs in our study is considerably higher than in a study conducted in Pakistan which estimated a household indirect cost of treatment of pneumonia at US$ 24.07.[4] The Pakistan study was conducted in a rural setting (district Haripur, Khyber Pakhtunkhwa province)[4] whereas the present study was conducted in an urban setting (Kumasi, the capital city of Ashanti region) with high differences in socio-economic status.

As argued by Young et al (2000), these costs incurred by caregivers influence the scarcity of resources and therefore the wealth of households and the society at large.[17] Ghana with a minimum wage of GH₵ 6.00 cedis (GH₵ 180.00 a month) is comparable to the median indirect cost found in this study, GH₵ 165 (IQR; GH₵ 80, GH₵ 420). This suggest that a significant portion if not all of monthly income available for a household is lost through pneumonia hospitalisation. This also indicate to a large extent the fall in productivity which has far reaching implications for community and national development.

The DALY estimate in this study sought to capture the premature death associated with pneumonia in children less than five years. The present study findings with a median DALY of 1,253 per 10,000 years of life lost (YLL) indicates the extent of burden caused by pneumonia in this age group. The increased DALY rates observed among the age groups of 1 month to 23 months further reflect the increased pneumonia mortality found in this study. Similarly, a report by Kaplan on the global burden of diseases found an increased DALY rates in children less than 24 months when compared with other age groups across the European regions.[6]

A recent publication in the Lancet on the global burden of pneumonia recorded the highest DALY rates among children less than 2 years. [21] The DALY estimate also compares with a high DALY rates observed in a study conducted in Latin America and the Caribbean on the economic burden of Pneumococcal Disease and Cost-Effectiveness of a Pneumococcal Vaccine which recorded annual DALY estimate of 617,261 pre-vaccination in 1990. In 2006 when the post vaccination assessment was done, annual DALY of 295,385 was recorded.

This intervention averted DALY of 52%.[22]Although this study found an impressive proportion of children immunised with pneumococcal conjugate vaccine, consistent achievement could significantly reduce the DALYs due to pneumonia. The high DALYs observed in children up to 23 months in this study implies that childhood survival interventions targeted at reducing the burden of pneumonia would yield the highest health benefits and DALYs averted in children less than 2 years of age, especially in Ghana.

Overall, this study provides a comprehensive estimate of the economic burden of households with children less than 5 years admitted on account of pneumonia at KATH. As a result, the estimated total direct and indirect cost is not applicable to cases seen at out-patient. Also, the assumption of 50% (0.5)

disability weight used in the DALY calculation could potentially underestimate or overestimate the correct YLL due to pneumonia. Nevertheless, the DALY and other economic indices used are useful tools to measure and compare the burden of a given condition or disease including pneumonia and can be used as a basis for policy interventions.

Conclusion

The direct cost of managing a case of pneumonia was relatively high when juxtaposed to the average household income. As a result, most caretakers indicated that cost of care was high and faced difficulties in payment of medical bills with various means of payment through out-of-pocket despite the high subscription to the NHIS. The median preadmission cost, direct non-medical and indirect cost was GH₵ 70.00 (US$ 18), GH₵ 60 (US$ 15) and 165 (US$ 42) respectively. The DALYs observed was high with the highest shown in children up to 23 months. These findings indicate the need to re-evaluate the effectiveness of the national health insurance policy to reduce out of pocket payments.

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Authors' contribution

Osei Francis Adjei, Ansong Daniel and Mensah Kofi Akohene conceptualized and designed the study supervised and coordinated data collection. They also drafted the initial manuscript, reviewed and revised the manuscript, and approved the final manuscript as submitted. Agyei-Baffour Peter, Joseph Bonney and Kwarteng Owusu Sandra conceptualized and designed the tools used for data collection and trained research assistants. They also revised the manuscript and made inputs into the methodology. Amuzu Evans Xorse, Mensah Nicholas Karikari, Ofori Kobina Timothy, Sarpong Phans Oduro and Osei-Peprah Ida conducted data collection, made contacts to the study respondents, followed up on subjects throughout hospitalization, and carried out the data cleaning and made inputs into the study design. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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BARRIERS TO EARLY INFANT DIAGNOSIS AND SERVICE DELIVERY IN TWO HIGH HIV DISTRICTS IN GHANA

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Abstract

Objective: Ghana has made significant progress in its efforts to control Human Immunodeficiency virus (HIV) infections, however 31% of HIV exposed infants received early infant diagnosis (EID) services. This paper examines the factors influencing EID service delivery in two high HIV burden districts in Ghana.

Methodology: This study was conducted in two districts in the Eastern region of Ghana, Lower Manya Krobo (LMK) District (high HIV burden with low EID coverage) and New Juabeng Municipality, NJM (high HIV burden with relatively higher coverage for EID). This analysis describes the first phase (exploratory study) of a three-phased implementation research spanning over 24 months. A total of 420 women with children < 2 years in each study area were involved. Key informant interviews and focus group discussions were conducted among mothers and health workers. Data (quantitative and qualitative) were analysed with appropriate statistical measures.

Results: Relatively more women from LMKD knew about the risks for mother-to-child transmission of HIV (83.6% vs. 79.8%) and more women in LMKD had children <2 years tested for HIV. In contrast to findings from the survey, knowledge on EID during Focus Group Discussions was better in NJM than LMKD. Major demand and supply -side barriers and challenges to EID were identified.

Conclusion: Health system (supply side) and community based (demand side) barriers mitigated against the EID coverage in the two districts. More community sensitisation, improved innovative means of transporting samples and effective tracking of mothers with HIV exposed infants and linking them up to care is recommended.

Key Words: *Early Infant Diagnosis, Mother-to-Child Transmission, HIV, Ghana, Sub-Saharan Africa.*

Introduction

Ghana has made significant progress in its efforts to control Human Immunodeficiency virus (HIV) infections. Over the years, the country through the National AIDS/STI Control Programme (NACP) and with assistance from the Global Fund and other development partners has developed and implemented strategic plans, such as the National HIV and AIDS Strategic Framework I 2001-2005, National HIV and AIDS Strategic Framework II 2006-2010 and the National HIV and AIDS Strategic Plan (NSP) 2011-2015 [1]. The implementation of all these strategic plans have contributed immensely to reduction of HIV infections in Ghana. For example, results from the 2016 HIV Sentinel Survey (HSS) [2], show a reduction of national HIV prevalence among pregnant women from 3.6% in 2003 to 2.4%. The 2016 prevalence however, was an increase from the 2015 prevalence of 1.8% and 2014 prevalence of 1.6% [2].

The prevalence of HIV in the general population in Ghana is 1.6% [2]. An estimated 290,000 people are living with HIV in Ghana, among whom 32,000 are children. In addition, 20,000 new HIV infections are known to occur annually, of which 13,000 occur in adults and 7,000 among children. An estimated 15000 deaths attributed to HIV and AIDS occur annually, with over 2500 children dying as a result of HIV and AIDS annually in Ghana [2]. One of the key strategic interventions for HIV control in Ghana is Prevention of

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Mother to Child Transmission (PMTCT) of HIV. Mother to Child Transmission of HIV (MTCT), also known as vertical transmission, is the transmission of HIV virus from an infected pregnant woman to her child during pregnancy, childbirth or through breast feeding[3,4]. In the absence of interventions, it is estimated that vertical transmission of HIV will occur between 15 to 45% of pregnant women who are infected with HIV virus and their babies[3,4].

However, MTCT of HIV can be reduced below 5% with a series of interventions delivered to both mother and newborn throughout the period when transmission could occur. Ghana has thus adopted Prevention of Mother to Child Transmission (PMTCT) as one of the high impact interventions to control HIV infections in the country. The PMTCT program also offers an excellent opportunity to diagnose all HIV infected children early enough through Early Infant Diagnosis (EID) using a virology test such as the Polymerase Chain Reaction (PCR)[1].

This provides an opportunity to initiate Antiretroviral Therapy (ART) in order to significantly enhance the survival of children who acquire HIV through vertical transmission[1,5]. To increase the coverage and diagnoses of HIV infected infants early enough for clinical management, the application of e-health interventions has become increasingly important. This facilitates the ease and speed of transmission of information from health facility to the sample testing site and the relaying of information back to the client.

Prevention of Mother to Child Transmission of HIV (PMTCT) is considered a high impact intervention to control HIV infections and has been prioritized in all the strategic plans of the country. The national programme target for 2017 is to test and counsel 579,132 pregnant women representing 95% of expected pregnancies[2].

Results from the Ghana Demographic and Health Survey (GDHS) 2014[6] show that 97% of pregnant women attended antenatal care with 87% of these attending at least 4 antenatal visits and an estimated 74% of delivery were attended by skilled birth attendant.

Similarly, 77% of children between the ages of 12-23 months were fully immunized. Despite these relatively high coverages, only 31% of HIV exposed infants received EID[2].

The end term evaluation report of the National HIV and AIDS Strategic Plan (NSP) 2011-2015[7], shows that despite the reduction of HIV prevalence in Ghana, the overall transmission rate of HIV from mother to child including breastfeeding mothers is estimated at 16% in 2014 as against 31% in 2009[7]. This is far above the target of the Ghana AIDS Commission (GAC) and the National Aids Control Program (NACP) which is to reduce vertical transmission below 5% by 2020[8].

Mortality rate among infected infants is far higher than adults, without access to treatment and care about 30% of HIV infected infants will die before their first birthday while 75% before their fifth birthday [9,10] (WHO, 2010b; Stringer et al, 2008). This paper examines the context of PMTCT service delivery and factors influencing the uptake of EID services among clients in two high HIV burden districts in the Eastern region of Ghana.

Materials and Method

Study design

An Implementation Research Design composed of three phases: Exploratory Study (in both districts); Implementation phase (in experimental district) and Monitoring and Evaluation (in experimental district).

This analysis is on the exploratory phase, which adopted a mixed methods approach to explore barriers to uptake of PMTCT/EID using qualitative methods, and then determining the extent of the problem in the district population using quantitative methods. In general, a desk review; a survey (quantitative approach); and Key Informants Interviews (KI), and Focus group discussions (FGD) were employed.

Study Population

Study participants included:

1. Health workers directly involved in the provision of PMTCT/ EID services- doctors, midwives, CHOs/CHNs (KI, FGD).
2. Laboratory Personnel at the testing site i.e., Regional PHRL directly involved in EID/DBS (KI).
3. Health Facilities Managers and District Directors of Health Services (KI).
4. Clients/caregivers, i.e., women 18 years and above (regardless of HIV status) with children less than two years (FGD, Survey)

Study area/site

The study was conducted in 2016, in two districts in the Eastern region of Ghana, Lower Manya Krobo District- Agomanya (high HIV burden with low EID coverage) and New Juabeng Municipality-Koforidua (high HIV burden with relatively higher coverage for EID). The two districts have relatively high coverage for immunization, (over 90% coverage for Pentavalent-1 vaccine) and this service is provided through the

same platform as EID at 6-weeks[6]. The Eastern region is one of the four priority regions of Ghana, based on HIV prevalence from programme data and the HIV sentinel survey[2]. The two study areas have relatively high median HIV prevalence, 6.2% in Lower Manya Krobo District (the highest in the country) and 2.6% in New Juabeng Municipality according to the 2015 HIV sentinel survey[2].

The Lower Manya Krobo district is more rural with predominantly Krobo Ethnic group and has an estimated total population of 81941 and 37853 as population of women in fertile age (WIFA) in 2016. It has a total of 23 health facilities, one district hospital, one ART centre and 14 PMTCT sites.

The New Juabeng Municipality is an urban and more cosmopolitan area and has an estimated total population of 212398 and 119982 as population of women in fertile age (WIFA) in 2016. It has a total of 74 health facilities, one regional hospital, two ART Centres and 15 PMTCT sites.

Sample size determination

The 2014 Ghana Demographic and Health Survey (GDHS) shows 43% of females and 20% of males (aged 15-49 years) had ever been tested for HIV[6]. The estimated prevalence of the willingness of mothers to have their children also tested for HIV through EID is 43%[11]. The sample size was therefore based on this estimate. In all, 420 women with children < 2 years in each district were selected for the survey.

The survey employed the modified World Health Organization (WHO) cluster sampling method to select eligible subjects (Yawson et al, 2014). In each of the two districts, at most 420 women were selected. Each district was segmented into four clusters by natural/geographical boundaries (i.e., sub-district clusters).

A cluster was chosen by a simple random sampling technique and all eligible subjects within households who consent to be part were included. Houses in the two study sites have standard house numbering systems (National health insurance or census designations). The households were coded using the house number and a three-digit code (e.g., MK 12/001 for a household within a house with house number MK 12).

Field workers were clearly educated on how to assign the codes to the households in selected communities in the two districts. In each household, the head of the household was contacted (in his/her absence an adult member of the household 18 years and above was contacted) and permission sought to interview women with children less than two years in the household. This was done until the sample size was obtained.

Purposive sampling methods were used to select service providers, laboratory personnel and health facility managers directly involved in PMTCT/EID services for the Focus group discussions and the key informant interviews.

Data collection methods and analysis

A structured questionnaire was used to collect demographic characteristics, socioeconomic and sociocultural factors including beliefs on causes and prevention of HIV, willingness for HIV testing and willingness to have children tested for HIV, and health seeking behaviours. In addition, information on barriers to EID services (delays in getting samples taken, and delays in notification and receipt of results from health facilities etc) was obtained. The questionnaire was pre-tested at Upper Manya Krobo District, a neighbouring district with similar characteristics as the experimental district.

Key Informant interviews were conducted for personnel at the regional Laboratory and health service providers (midwives, general nurses, community health officers and community health nurses) in selected health facilities in each District (6 key informants from each district).

Two FGDs were conducted in each district/ municipality for midwives and Community Health Officers / Community Health Nurses (10 in number for each FGD session) from all ART and PMTCT sites in the two study sites. Interviews Guides were employed for data collection in both the Focus group discussion and Key Informant Interviews.

Data Management and Statistical Analysis

All data were treated with a high level of confidentiality. Unique identifiers and codes were employed to de-identify the participants and were used for computer-based data entry in the exploratory phase. In all cases, questionnaires, documentations and computerized records of the survey were kept in locked cabinets and computer files respectively. These documents were accessible to the lead and co-investigator only.

Manual Thematic content analysis was used for analysis of qualitative data. Quantitative data from survey were analysed with SPSS version 20 to determine simple descriptive statistics such as proportions, frequencies and ratios for categorical data; while mean± standard deviation was used continuous measures.

Ethical considerations

Ethical clearance for this study was obtained from the Ethics Review Committee of the Ghana Health Service with proposal approval identification number GHS-ERC: 05/09/16.

The study was in conformity to the guidelines of the 1975 Helsinki Declaration. All participants provided written informed consent. Permission was obtained from Heads of institutions, District Health Authorities as well as Traditional Authorities in the study areas.

Results

Basic demographic and socioeconomic characteristics of Participants in the two districts

The median age for the 840 participants in the survey was 28± 6.3 years. The median age of participants in the two districts were Lower Manya Krobo Districts (LMKD) 28± 6.3 years and New Juabeng Municipality (NJM) 28± 6.2 years.

Table 1 demonstrates that participants from NJM had relatively higher proportions with secondary education or higher compared to LMKD. There were relatively higher proportions of widowed, single mothers and cohabiting women in LMKD compared to NJM. In addition, there was a higher proportion of Muslims in NJM relative to LMKD.

Participants from LMKD had relatively higher proportions of those currently employed compared to NJM [247(58.8%) vs. 203 (48.3%)]. Significantly, more women have stayed longer in the current place of residence in LMKD compared to NJM. About 97% of participants in both districts had NHIS card for accessing health services (Table 1).

Knowledge on HIV and risk of mother-to-child transmission of participants in the two districts

Table 2 demonstrates knowledge on HIV and risk of transmission from mother to child. Almost all the participants in both districts had heard of HIV and AIDS mainly from health workers. There was a higher proportion with knowledge on HIV prevention among participants in NJM than in LMKD (93.8% and 90.2% respectively). Interestingly, 12.1% of participants from LMKD indicated that the avoidance of spiritual curses could prevent one from getting HIV.

It is important to note that 75.5% of participants in NJM knew that an HIV positive pregnant woman could infect an unborn child, however 87.9%of all the participants knew about mother to child transmission through breastmilk.

Table 1: Basic demographic and socioeconomic characteristics of Participants in the two districts

Characteristics	District		Total	Chi Square/ Fishers Test (p-value)
	Lower Manya Krobo (high HIV burden with low EID)	**New Juabeng** (high HIV burden with relatively higher coverage for EID)		
	n=420	**n=420**	**N=840**	
Educational Level				
Primary	93(22.1)	57(13.6)	150(17.9)	
Middle/JHS	212(50.5)	218(51.9)	430(51.2)	28.69**(0.001)**
Secondary/High School	55(13.1)	79(18.8)	134(16.0)	
University/College	15(3.6)	21(5.0)	36(4.3)	
Vocational/Commercial/ Technical	3(0.7)	17(4.0)	20(2.4)	
None	42(10.0)	28(6.7)	70(8.3)	
Marital Status				
Married	192(45.7)	280(66.7)	472(56.2)	
Divorced	2(0.5)	2(0.5)	4(0.5)	
Widowed	8(1.9)	1(0.2)	9(1.1)	48.31**(0.001)**
Separated	12(2.9)	0(0.0)	12(1.4)	
Cohabiting	133(31.7)	94(22.4)	227(27.0)	
Single	73(17.4)	43(10.2)	116(13.8)	
Duration of stay in current place of residence				
Less than 6 Months	53(12.6)	30(7.1)	83(9.9)	
Between 6mths- 1 year	36(8.6)	39(9.3)	75(8.9)	
Between 1 and 2 years	51(12.1)	62(14.8)	113(13.5)	14.62**(0.023)**
Between 2 and 5 years	82(19.6)	99(23.6)	181(21.5)	
Between 5 and 10 years	57(13.6)	74(17.6)	131(15.6)	
More than 10 years	141(33.6)	116(27.6)	257(30.6)	
Currently employed				
Yes	247(58.8)	203(48.3)	450(53.6)	
No	173(41.2)	217(51.7)	390(46.4)	9.27**(0.002)**
Possession of Valid NHIS Card				

Yes	407(96.9)	408(97.1)	815(97.0)	0.04(0.839)
No	13(3.1)	12(2.9)	25(3.0)	
Member of a Social Club in Area of Residence				
Yes	58(13.8)	41(9.8)	99(11.8)	3.31(0.069)
No	362(86.2)	379(90.2)	741(88.2)	

Characteristics	**District**		**Total**
	Lower Manya Krobo (high HIV burden with low EID)	**New Juabeng (high HIV burden with relatively higher coverage for EID)**	
Heard of AIDS			
Yes	410(97.6)	416(99.0)	826(98.3)
No	10(2.4)	4(1.0)	14(1.7)
Total	420	420	840
Heard of HIV			
Yes	411(97.9)	417(99.3)	828(98.6)
No	9(2.1)	3(0.7)	12(1.4)
Total	420 (100)	420	840
Know How HIV is transmitted			
Yes	379(90.2)	394(93.8)	773(92.0)
No	41(9.8)	25(6.0)	66(7.9)
Total	420 (50.0)	420	840
Main source of information			
Health Worker	267(65.1)	222(53.1)	489(59.1)
Family Member	2(0.5)	5(1.2)	7(0.8)
Friend	18(4.4)	12(2.9)	30(3.6)
Media	84(20.5)	136(32.5)	220(26.6)
Church/Mosque	3(0.7)	3(0.7)	6(0.7)
Social Club	1(0.2)	3(0.7)	4(0.5)
Others	35(8.5)	37(8.9)	72(8.7)
Total	410	418	828
Knowledge of risk factors for HIV transmission			
Sexual intercourse	347(82.6)	366(87.1)	713(84.9)
Sharing sharps	302(65.7)	276(65.7)	578(68.8)
Blood transfusion	106(25.2)	49(11.7)	155(18.5)
Sharing needles	106(25.2)	25(6.0)	131(15.6)
Spiritual causes	51(12.1)	5(1.2)	56(6.7)
Family curse	40(9.5)	3(0.7)	43(5.1)
Others	54(12.9)	47(11.2)	101(12.0)
Know prevention of HIV			
Yes	354(84.3)	390(92.9)	744(88.6)
No	66(15.7)	30(7.1)	96(11.4)
Total	420	420	840
Can a healthy-looking person have HIV			
Yes	351(83.6)	335(79.8)	686(81.7)
No	69(16.4)	85(20.2)	154(18.3)
Total	420	420	840
Can HIV positive pregnant woman infect unborn child			
Yes	366(87.1)	317(75.5)	683(81.3)
No	54(12.9)	103(24.5)	157(18.7)
Total	420	420	840
Can HIV positive mother infect child through breastmilk			
Yes	380(90.5)	369(87.9)	749(89.2)
No	40(9.5)	50(11.9)	90(10.7)
Total	420	420	840

Pregnancy and HIV testing history of mother and child

The HIV testing histories of participants indicated that approximately over 9 out of 10 participants had had an HIV test NJM (92.6%) and LMKD (95.5%) done mainly during their last pregnancy. Only 20.5% of children from LMKD and 16.9% of children from NJM had been tested for HIV due to reasons illustrated in Table 3 which were corroborated by mothers in the focus group discussion.

Mother 1 indicated *'I think the baby is too small to be at risk for HIV. I may not do the test because it the child is too young to have the disease'.*
Mother 2 puts her view quite succinctly *'The test for the baby is not necessary because the disease does not have a cure, hence there is no point in testing to know and to worry my little baby with needle pricks'.*

Table 3 shows a higher proportion of LMKD participants considered HIV testing for children useful, were aware of the test results of their children and had made follow up visits to the health facility where the child was tested. In contrast, the focus group discussion among participants indicated limited knowledge and awareness on the need for EID and noted that health

workers do not explicitly explain to mothers why the child need to be tested.

Mother 3 said '*I do not know much about this test. The nurses normally say they want to test the child to know if he or she has HIV disease just like it is done when you are pregnant. They do not offer any prior advice or counselling. When health workers come to us for outreach services, they must mention it*'.

Table 3: Pregnancy and HIV testing history of mother and child in the two districts

Characteristics	District		Total
	Lower Manya Krobo (high HIV burden , low EID)	New Juabeng (high HIV burden higher coverage for EID)	
Number of children			
1-4	382(91.0)	396(94.3)	778(92.6)
5 or more	38(9.0)	24(5.7)	62(7.4)
Total	420	420	840
Ever tested for HIV			
Yes	389(92.6)	401(95.5)	790(94.0)
No	31(7.4)	19(4.5)	50(6.0)
Total	420	420	840
Were you tested in last pregnancy			
Yes	387(92.1)	399(95.0)	786(93.6)
No	33(7.9)	21(5.0)	54(6.4)
Total	420	420	840
Has child less than 2 years ever been tested for HIV			
Yes	86(20.5)	71(16.9)	157(18.7)
No	334(79.5)	349(83.1)	683(81.3)
Total	420	420	840
Reasons for child not ever been tested			
Never had opportunity	87(20.7)	115(27.4)	202(24.0)
Child not at risk	59(14.0)	59(14.0)	118(14.0)
Not necessary	53(12.6)	59(14.0)	112(13.3)
Have tested negative previously	27(6.4)	46(11.0)	73(8.7)
Test is for adults	19(4.5)	8(1.9)	27(3.2)
Child not sick	15(3.6)	12(2.9)	27(3.2)
Health worker not Confidential	12(2.9)	5(1.2)	17(2.0)
Don't have time	11(2.6)	2(0.5)	13(1.5)
Afraid of outcome	2(0.5)	3(0.7)	5(0.6)
Is HIV testing of child useful			
Yes	392(93.3)	382(91.0)	774(92.1)
No	28(6.7)	38(9.0)	66(7.9)
Total	420	420	840
Willing to get child tested			
Yes	400(95.2)	405(96.4)	805(95.8)
No	20(4.8)	15(3.6)	35(4.2)
Total	420	420	840
Ever sent child for immunization			
Yes	415(98.8)	412(98.1)	827(98.5)
No	5(1.2)	8(1.9)	13(1.5)
Total	420	420	840
How many times gone for immunization			
None	2(0.5)	8(1.9	10(1.2)
1	21(5.1)	15(3.6)	36(4.3)
2 or more	391(94.4)	397(94.5)	788(94.5)
Total	414	420	834

Findings from the focus group discussion

Participants generally indicated that challenges with scheduling of visits by health workers and not keeping the scheduled appointments were major barriers to EID. In addition, lack of privacy and confidentiality in discussing issues with the health workers and the fear of disclosure to spouse or family were noted to be major barriers.

Mother 4 intimated strongly *'The nurses who do the test should "shut their mouth". They talk too much and spread the news about the status of patients to other people'.*

Mother 5 indicated her challenge in accessing care for the baby as '*Some of us don't get the time to always bring our babies to the hospital. I work under someone as a trader, and you do not always get permission when you request for it'.*

Despite these barriers, most of the test for the children were conducted before the age of 12months, mainly in the hospital setting as demonstrated in Table 3. Almost all the children of the 840 participants had received immunization as well. The mothers however, expressed their concerns in accessing health care at the health facilities:

Mother 6 stated that *'The nurses should be patient when we come to their service delivery points. They should take time and explain things to us. Yes, the way*

the health workers talk to us sometimes discourages us from coming back'.

Mother 7 was of the view that *'If this test can be done at home for our babies, I will prefer that very much. Cost of transportation and the long waiting times discourages some of us from using the service'*

Health workers in health facilities of the two districts provided reasons for the barriers to EID services as challenges with transporting samples to the laboratory due to unavailability of transport or paying for the transfer of samples to the laboratory, delays in getting feedback on results of sample analysis from the Regional Laboratory. In addition, delays in relaying results of test to clients because mothers do not come back to the health facilities again with their babies and that key personnel in charge of some health facilities where HIV testing are done are not trained to conduct EID.

Health worker 1, '*Our main challenge is with transporting the samples to the Laboratory. Sometimes we use personal funds to transport the samples. We usually cannot rely on the hospital'.*

Health worker 2, '*The results delay for too long in the regional laboratory and when we finally get them, clients referred to us from other districts do not come for the results. We can't reach them on phone either'***.**

Regional Laboratory Personnel 1 indicated '*samples may be taken in the health facility but it takes too long in getting to the laboratory, example, this sample* (personnel shows a sample) *was taken 20th October, 2015 at the facility but got here in January, 2016'.*

Regional Laboratory Personnel 2 stated 'Sometimes *the health facilities are notified but coming here for the results is always the challenge. Currently, they prompt us when their drivers or other officers are coming here for other assignments so that it can be collected on their behalf. In fact, getting the results to them timely is difficult'.*

Discussion

The study demonstrates that participants from the more urban and cosmopolitan New Juabeng Municipality (NJM) had relatively higher proportions with secondary education or higher compared to the more rural and indigenous Lower Manya Krobo District (LMKD). Interestingly, relatively more women in LMKD have higher knowledge on the HIV and the risk of transmission of HIV from mother to child. These findings are not surprising due to the urban nature of NJM compared to the relatively more rural and more indigenous LMKD. Many more women usually stay for much longer periods in these settings (as demonstrated in this study Table 1). The relatively higher knowledge of women in the more rural district, could potentially be due to increased routine health education on HIV by health workers. In addition, it may be because repeated health education messages are provided by health workers in such a high HIV burden district[2], and that the relatively longer duration of stay of mothers in the LMKD foster long-lasting relationships with the health workers in the rural health facilities.

Regardless of the relative differences in knowledge, almost all the mothers in both districts had heard about HIV and AIDS which agrees with findings from the Ghana Demographic and Health Survey, 2014 which found an almost universal knowledge on HIV by women 15-45 years (i.e., 0ver 97%)[6]. The national efforts towards control of the HIV epidemic have provided several focused HIV activities in these high burden districts[1].

It was observed that, most of the women received information of HIV and prevention of mother-to-child transmission of HIV (PMTCT) from health workers. This emphasises the need to reduce missed opportunities in the health facilities concerning testing for HIV by pregnant women and mothers. The Child welfare clinics (CWC) offer opportunities for early infant diagnosis (EID) as most mothers are likely to send their children for immunization. The first CWC attendance/ immunization service is at six weeks, which also provides an opportunity for EID. This study observed a high rate of immunization among the children of these mothers, however with a concomitant lower coverage for EID. This demonstrates missed opportunities for EID at the service provision points.

HIV testing services is the primary gateway to all systems of AIDS-related care[13,14,15]. One critical means of curbing new infections and AIDS-related deaths especially among children is by encouraging early diagnosis through testing within the first two months of delivery. In Ghana, significant investments have been made to increase access for HIV testing [1,16]. However, several bottlenecks exist to the delivery of EID services to infants.

This study through a qualitative assessment has demonstrated that key health system challenges (supply side) and community-based factors (demand side) inhibit the coverage and uptake of EID services. Key

demand side factors identified were mothers who know their status from previous testing unwilling to get their children tested and hence view the testing of the child as unnecessary; mother thinking the baby is too small to be at risk of HIV, persistence of HIV and AIDS related stigma and mothers getting lost to follow up, especially after delivery. These belief systems and social and community factors limit access to care for the children. These mothers may have tested some time ago in early pregnancy, however, there still exist the risk of acquiring HIV in pregnancy and hence the need to get re-tested at 34 weeks in pregnancy. The rate of testing at 34 weeks in pregnancy is generally low in Ghana[1].

Key health system (supply side) challenges included poor EID sample management (unavailability of transport; delays in retrieving results of tests from Regional Laboratory (even after notifications have been sent electronically), and delays in relaying test results to clients. Poor healthcare worker capacity was another challenge observed as in some health facilities where HIV testing is done, the key personnel had not been trained to provide EID services. Early infant diagnosis improves survival of the child when treatment is initiated early. Delays in relaying the results to mothers create difficulties for attending clinicians and discourages mothers from continuing with care. The availability of ART has transformed what was once a deadly disease into a manageable chronic condition[17]. However, due to these barriers related to HIV treatment, not all persons in need of ART in resource-limited settings utilize the service. This has dire consequence for the survival of these children[18-21].

Limitation

The assessment was based purely on responses from mothers and health care workers there was no objective measure to ascertain the veracity of their answers. The sample size was, however, large enough to mitigate this challenge.

Conclusion

Both health system (supply side) and community based (demand side) barriers mitigated against the EID coverage in the two districts. More community sensitisation on the need and benefit of EID is imperative, as well as the training of key health providers who offer PMTCT to provide EID services and training/ refresher on PMTC/EID for those previously trained. Reduction of missed opportunities and optimising testing of infants during immunisation/ child welfare clinic, whenever the mothers/ caregivers visit the health facility will be key to improve coverage.

In addition, effective local arrangement at the district level and the Regional Laboratory is necessary to overcome difficulties in sample transfer and all locally available opportunities should be explored.

Declarations

Ethics approval and consent to participate

Ethical clearance for this study was obtained from the Ethics Review Committee of the Ghana Health Service with proposal approval identification number GHS-ERC: 05/09/16. The study was in conformity to the guidelines of the 1975 Helsinki Declaration. All participants provided written informed consent. Permission was obtained from Heads of institutions, District Health Authorities as well as Traditional Authorities in the study areas.

Consent to publish

All participants were informed about the study and consent obtained. Participants provided written informed consent, duly administered and witnessed before data collection. Participants were informed that the findings would be shared with Ghana Health Service and the wider scientific community.

Availability of data and materials

All data obtained from participants have been fully represented and provided in the three tables contained in the results section of the manuscript.

Competing interests

The authors declare that they have no competing interest. The views expressed in this paper are those of the authors. No official endorsement by the Ministry of Health or Ghana Health Service is intended or should be inferred.

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Authors' contributions

AEY, EA, NAHS and PB developed the concept, AEY, NAHS and DA assisted with data collection. AEY and NAHS analysed the survey data. AEY and NAHS wrote the first draft manuscript, all authors contributed to the writing and reviewing of the various sections of the manuscript. All the authors reviewed the final version of the manuscript before submission. All authors read and approved the final manuscript.

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Abbreviation

ANC	Antenatal Clinic
ART	Antiretroviral Therapy
ARVs	Antiretroviral
CHN	Community Health Nurse
CHO	Community Health Officer
CHPS	Community-Based Health Planning and Services
CWC	Child Welfare clinic
DBS	Dried Blood Spot
DHIMS	District Health Information Management System
EID	Early Infant Diagnosis of HIV
eMTCT	Elimination of Mother to Child Transmission of HIV
GAC	Ghana AIDS Commission
GDHS	Ghana Demographic and Health Survey
GHS	Ghana Health Service
HIV	Human Immunodeficiency virus
HSS	HIV Sentinel Survey
LMK	Lower Manya Krobo
MTCT	Mother to Child Transmission of HIV
NACP	National AIDS/STI Control Programme
NJM	New Juabeng Municipality
NSP	National HIV and AIDS Strategic Plan
PMTCT	Prevention of Mother to Child Transmission of HIV
UNICEF	United Nations Children Fund
WHO	World Health Organization

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COVID-19 ASSOCIATED HIGH MORTALITY AMONG PATIENTS WITH ACUTE STROKE IN A UNIVERSITY HOSPITAL IN KUMASI, GHANA – A RETROSPECTIVE STUDY

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Abstract

Objectives: The World Stroke Organization (WSO) has raised concerns about the global impact of COVID-19 on occurrence of stroke and its implications for stroke care, especially in low-middle-income countries. We sought to describe the profile and outcomes of acute stroke admissions in relation to COVID-19 status.

Methodology: This is a retrospective study involving all stroke patients admitted to the University Hospital, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana from 1st March, 2020 to 30th November, 2020. Stroke was diagnosed clinically and confirmed with a head Computerized Tomography scan. After the diagnosis of stroke, all patients with presentations that fitted the case definition of COVID-19 were tested using real time polymerase chain reaction (RT-PCR). Bivariate analysis was performed to identify factors associated with in-patient mortality. Statistical significance level was set at $p < 0.05$.

Results: A total of 93 patients with confirmed acute stroke were hospitalized within a 9-month period with 3 (3.2%) having confirmed COVID-19 infection. All COVID-19 cases had ischemic stroke and all of them died. Bivariate analyses identified COVID-19 status (p=0.016), mean pulse rate (p=0.036) and patients who did not receive angiotensin receptor blocker (ARB) (p=0.029) or calcium channel blockers (CCB) (p=0.016) were associated with in-patient mortality.

Conclusion: COVID-19 occurring with acute stroke is a predictor of mortality in this sample of Ghanaians. In this era of COVID-19 pandemic, patients with acute stroke should also be screened for the infection and managed appropriately to minimize death.

Key Words: *COVID-19, Hospital, Mortality, Stroke, Ghana*

Introduction

The 2019 Coronavirus disease (COVID-19) is a pandemic associated with a multi-systemic involvement including causation of cerebrovascular diseases.[1,2] Stroke in patients with COVID-19 may arise from the exaggerated inflammatory response, vascular endothelial dysfunction, hypercoagulability and increased risk of thromboembolism associated with the disease.[1] The average duration for onset of cardiovascular events from severe acute respiratory syndrome 1 and 2 (SARS-CoV-1 and SARS-CoV-2) infections has been reported as 10 to 28 days.[2] The spike protein surface unit on SARS-CoV-2 adheres tightly to the angiotensin converting enzyme 2 (ACE2), impairs its end-organ protective properties, potentially causing endothelial damage and neurological injury.[1]The incidence of stroke and non-specific neurological manifestations among patients with COVID-19 admitted to hospitals in China has been reported as 5% and 36.4% respectively.[2,1] Several cases of COVID-19-related stroke have also been recorded in Italy,[3] United Kingdom[4] and the United States of America,[5] the epicentres of the pandemic. The World stroke Organisation (WSO) has raised concerns about the global impact of COVID-19 on occurrence of stroke, disease severity and their implications for stroke care, especially in low-middle-income countries (LMICs).[6] Since 12th March, 2020 when Ghana recorded her first two imported cases of COVID-19[7] a recent study has revealed a 7.5% increase in stroke admissions at a tertiary institution with an attendant rise in stroke case fatality.[8] In the present study, we sought to assess the impact of COVID-19 co-infection on stroke presentation and its outcomes in a Ghanaian medical center.

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Conflict of Interest: None Declared

Methods and Materials

Study Design and Setting

The University Hospital, Kwame Nkrumah University of Science and Technology (KNUST), Kumasi is one of the centres in Ghana designated for

testing of suspected cases and treatment of confirmed COVID-19 patients.[9] It is a 125-bed quasi-government facility equipped to provide specialist and general medical services. This was a retrospective study which included data of all 93 cases of acute stroke admitted between 1st March and 30th November, 2020. The data was obtained from medical records which were documented during their period of hospitalization.

Study Context

As of 1st January, 2021, the cumulative number of confirmed COVID-19 cases in Ghana was 75,836 with 533 deaths. Preventive and relief measures have been instituted by the Government, Health Ministry and their agencies. However, the population and health facilities continue to reel under the burden of COVID-19.

Clinical and laboratory assessments

Patients with suspected stroke on admission had a computerized tomography (CT) scan of the head to confirm the diagnosis. Cardiovascular co-morbidities such as hypertension and diabetes were assessed through self-reports. Basic laboratory investigations performed included a full blood count, blood urea and creatinine measurements, chest x-rays and chest CT scan when indicated. Stroke patients with symptoms suggestive of COVID-19 and who satisfied the Ghana Health Service/Ministry of Health case definition of COVID-19[10] had nasopharyngeal samples taken. The samples were taken to the Kumasi Centre for Collaborative Research into Tropical Medicine (KCCR) and tested for severe acute respiratory syndrome coronavirus-2 (SARS-COV-2) using real time polymerase chain reaction (RT-PCR).[11] Patient disposition on discharge were classified into alive or dead.

Statistical analysis

Comparisons of demographic, vascular risk factors, laboratory results, treatment instituted and vital status were performed using Fishers' exact tests for categorical variables and Student's t-test for continuous variables. A multivariate logistic regression model was constructed to assess factors associated with in-patient mortality. Bivariable analyses were first conducted, and variables associated with stroke mortality at a p-value of <0.10 were included in the final adjusted model. In all analysis, p-value of <0.05 was considered statistically significant. Statistical analysis was performed using GraphPad Prism version 7 and SPSS Stata version 16 (StataCorp LLC, College Station, TX, USA).

Results

Demographic and Clinical Characteristics of Patients

Over the period of observation, 93 stroke patients were admitted. The mean age of the patients was 62.2 (SD ±15.0) years with 50 (53.8%) of them being female. [Table 1] Of the 93 patients with acute stroke, 61 (65.6%) were ischaemic, 14 (15.1%) were haemorrhagic, seven were untyped, two were ischemic with hemorrhagic transformation, and nine had normal CT findings despite being symptomatic of stroke. Three (3.2%) stroke patients tested positive for COVID-19. Approximately 87% (n = 81) had hypertension with a mean systolic blood pressure of 181.1 (SD ± 33.5) and mean diastolic blood pressure of 118.0 (SD ± 107.2). Calcium channel blockers (CCBs) were the most prescribed antihypertensives (n = 71; 76.3%) followed by angiotensin-converting enzyme inhibitors (n = 51; 54.8%). Majority (n = 75; 80.7%) received antiplatelets and 61 (65.6%) were also on statins [Table 1].

Table 1. Demographic and Clinical Characteristics of patients

Characteristic	Frequency (n=93)	Percentage, %
Age, mean ± SD	62.2 (SD ±15.0)	
Gender		
Male	43	46.2
Female	50	53.8
Marital status		
Single	7	7.5
Married	67	72.0
Widowed	12	12.9
Divorced	3	3.2
Not Known	4	4.2
Stroke Type (CT Scan)		
Ischemic	61	65.6
Haemorrhagic	14	15.1
Ischemic with hemorrhagic transformation	2	2.2
Normal	9	9.7
Not known	7	7.5
Covid-19 status		
Positive	3	3.2
Negative	90	96.8
Co-morbidities		
Hypertension		
Yes	81	87.1
No	12	12.9
Diabetes Mellitus		
Yes	31	33.3
No	62	66.7
Old Stroke		
Yes	16	17.2
No	77	82.8
Chronic Kidney Disease		
Yes	4	4.3

No	89	95.7
Sickle Cell Disease		
Yes	1	1.1
No	92	98.9
Methyldopa		
Yes	13	14.0
No	80	86.0
Hydralazine		
Yes	23	24.7
No	70	75.3
Diuretic		
Yes	43	46.2
No	50	53.8
ARB		
Yes	24	25.8
No	69	74.2
ACE		
Yes	51	54.8
No	42	45.2
BB		
Yes	37	39.8
No	56	60.2
CCB		
Yes	71	76.3
No	22	23.7
Statins		
Yes	61	65.6
No	32	34.4
Antiplatelet		
Yes	75	80.7
No	18	19.3
Anti-diabetic		
Yes	33	35.5
No	60	64.5
VTE prophylaxis		
Yes	36	38.7
No	57	61.3
WBC, mean ± SD	8.7 (SD ±4.3)	-
Neutrophils mean± SD	6.9 (SD ±8.7)	-
lymphocytes, mean ± SD	2.8 (SD ±7.3)	-
Platelets, mean ± SD	227.2 (SD ±84.3)	-
Haemoglobin, mean ± SD	13.0 (SD ±2.5)	-
eGFR, mean ± SD	65.7 (SD ±36.8)	-
Systolic BP, mean ± SD	181.1 (SD ±33.5)	-
Diastolic BP, mean ± SD	118.0 (SD ±107.2)	-
Pulse, mean ± SD	97.2 (SD ±21.3su)	-
Total cholesterol, mean ± SD	5.2 (SD ±1.5)	-
LDL-cholesterol, mean ± SD	3.2 (SD ±1.4)	-
HDL-cholesterol, mean ± SD	1.3 (SD ±0.5)	-
Triglyceride, mean ± SD	1.3 (SD ±0.5)	-
Duration of hospital stay, mean ± SD	5.8 (SD ±5.9)	-

Clinical and radiological characterization of COVID-19 cases with acute stroke

Three (3) of the hospitalized patients with acute stroke had confirmed COVID-19. One of them was an 81-year-old man who presented with altered level of consciousness but no obvious lateralizing sign. Computed tomography (CT) scan of the head showed subacute left temporal and occipital infarcts and left basal ganglia lacunar infarcts with microvascular disease (Figure 1). The second case was a 69-year-old woman who presented with sudden right sided weakness. Head CT scan showed a subacute left basal ganglia lacunar infarct with background microvascular disease and cerebral atrophy (Figure 2). The third patient was a 62-year-old man with right hemiparesis and right facial nerve palsy and expressive aphasia. A head CT scan taken on the day of presentation showed an effacement of sulci and gyri on the left in the middle cerebral artery territory (Figure 3).

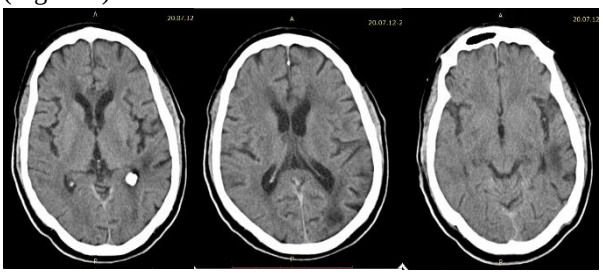

Figure 1. 81-year-old Ghanaian with COVID-19 with an ischemic stroke. Hypodense lesions in the left occipital and left temporal lobes are noted with periventricular and deep white matter hypodensities.

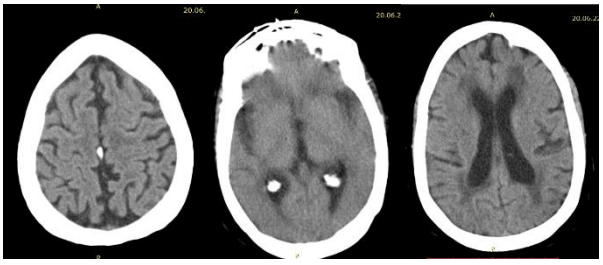

Figure 2. 69-year-old woman with COVID-19 who presented with sudden right-sided weakness *CT Scan image showed a sub-acute left basal ganglia infarct with periventricular and deep white matter hypodensities and prominence of the sulci and gyri with dilated ventricles.*

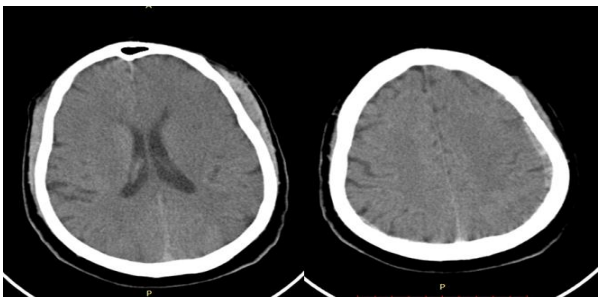

Figure 3. *62-year-old man with COVID-19 presented with right hemiparesis and right facial nerve palsy and expressive aphasia. Head CT shows effacement*

of sulci and gyri in the left middle cerebral artery territory indicative of an infarction.

Factors associated with mortality among stroke patients

Table 2 compares demographic and clinical characteristics of stroke cases that were discharged alive or dead. The mean age of patients with stroke that died was 64.5 years (SD ±13.7) and 61.4 years (SD ±15.5) in those discharged alive. There was statistically significant association between mortality and patient's COVID-19 status (p = 0.016), mean pulse rate whilst on admission (p = 0.036) and patient's medications such as angiotensin receptor blockers (ARB) (p = 0.029) and Calcium Channel Blockers (CCB) (p = 0.016) [Table 2].

Unadjusted analysis for factors associated with mortality were not being prescribed ARB nor CCB, higher white blood cell counts and pulse pressure. Upon adjustment for covariates, none of the factors were independently associated with mortality. [Table 3]

Table 2. Characteristics of stroke patients that Died and those Discharged alive (N=93)

Characteristic	Died (n=24)	Discharged Alive (n=69)	P-value
Age, mean ± SD	64.5 (SD ±13.7)	61.4 (SD ±15.5)	0.383
Gender, n (%)			0.646
Male	10 (41.7)	33 (47.8)	
Female	14 (58.3)	36 (52.2)	
Stroke Type (CT Scan) [a]			0.316
Ischaemic	13 (54.2)	48 (69.6)	
Haemorrhagic	4 (16.7)	10 (14.5)	
Both	1 (4.2)	1 (1.4)	
Normal	4 (16.7)	5 (7.2)	
Not known	2 (8.3)	5 (7.2)	
Covid-19 status[a]			0.016
Positive	3 (12.5)	0 (0.0)	
Negative	21 (87.5)	69 (100.0)	
Co-morbidities			
Hypertension			1.000
Yes	21 (87.5)	60 (87.0)	
No	3 (12.5)	9 (13.0)	
Diabetes Mellitus			0.615
Yes	7 (29.2)	24 (34.8)	
No	17 (70.8)	45 (65.2)	
Old Stroke			1.000
Yes	4 (16.7)	12 (17.4)	
No	20 (83.3)	57 (82.6)	
Chronic Kidney Disease			1.000
Yes	1 (4.2)	3 (4.4)	
No	23 (95.8)	66 (95.6)	
Sickle Cell Disease			1.000
Yes	0 (0.0)	1 (1.5)	
No	24 (100.0)	68 (98.5)	
None			1.000
Yes	1 (4.2)	4 (5.8)	
No	23 (95.8)	65 (94.2)	
Type of Medications			
Methylodpa[a]			0.503
Yes	2 (8.3)	11 (15.9)	
No	22 (91.7)	58 (84.1)	
Hydrallazine[a]			0.412
Yes	4 (16.7)	19 (27.5)	
No	20 (83.3)	50 (72.5)	
Diuretic			0.963
Yes	11 (45.8)	32 (46.4)	
No	13 (54.2)	37 (53.6)	
ARB[a]			0.029
Yes	2 (8.3)	22 (31.9)	
No	22 (91.7)	47 (68.1)	
ACE			0.580
Yes	12 (50.0)	39 (56.5)	
No	12 (50.0)	30 (43.5)	
BB			0.827
Yes	10 (41.7)	27 (39.1)	
No	14 (58.3)	42 (60.9)	
CCB			0.016
Yes	14 (58.3)	57 (82.6)	
No	10 (41.7)	12 (17.4)	
Statins			0.385
Yes	14 (58.3)	47 (68.1)	
No	10 (41.7)	22 (31.9)	
Antiplatelet			0.416
Yes	18 (75.0)	57 (82.6)	
No	6 (25.0)	12 (17.4)	
Anti-diabetic			0.082
Yes	5 (20.8)	28 (40.6)	
No	19 (79.2)	41 (59.4)	
VTE prophylaxis			0.187
Yes	12 (50.0)	24 (34.8)	
No	12 (50.0)	45 (65.2)	
WBC,mean ± SD[b]	10.2 (SD ±4.6)	8.2 (SD ±4.1)	0.050
Neutrophils mean± SD[b]	7.2 (SD ±4.8)	6.8 (SD ±9.7)	0.858
lymphocytes, mean ± SD[b]	2.0 (SD ±1.5)	3.1 (SD ±8.5)	0.511
Platelets, mean ± SD[b]	218.9 (SD ±78.0)	230.2 (SD ±86.7)	0.575
Haemoglobin, mean ± SD[b]	12.9 (SD ±2.8)	13.0 (SD ±2.4)	0.862
eGFR, mean ± SD[b]	60.1 (SD ±35.0)	67.4 (SD ±37.5)	0.455
Systolic BP, mean ± SD[b]	185.5 (SD ±33.3)	179.6 (SD ±33.7)	0.464
Diastolic BP, mean ± SD[b]	110.3 (SD ±20.9)	120.6 (SD ±123.4)	0.691
Pulse, mean ± SD[b]	105.2 (SD ±30.9)	94.5 (SD ±16.5)	0.036
Total cholesterol, mean ± SD[b]	5.5 (SD ±2.1)	5.1 (SD ±1.5)	0.652
LDL-cholesterol, mean ± SD[b]	3.2 (SD ±1.9)	3.2 (SD ±1.4)	0.970
HDL-cholesterol, mean ± SD[b]	1.6 (SD ±0.4)	1.2 (SD ±0.5)	0.130
Triglyceride, mean ± SD[b]	1.3 (SD ±0.4)	1.3 (SD ±0.5)	0.957
Duration of hospital stay, mean ± SD[b]	5.2 (SD ±6.9)	6.1 (SD ±5.5)	0.514

Table 3. Multivariate logistic regression model of associated factors of mortality among admitted stroke patients

Predictors	Unadjusted OR (95%CI)	P-value	Adjusted OR (95% CI)	P-value
Type of medications				
ARB				
Yes	1.00		1.00	
No	5.15 (1.11 – 23.86)	0.036	3.56 (0.73 – 17.46)	0.118
CCB				
Yes	1.00		1.00	
No	3.39 (1.22 – 9.44)	0.019	2.91 (0.93 – 9.18)	0.068
WBC				
Increasing WBC	1.11 (1.00 – 1.23)	0.056	1.07 (0.95 – 1.20)	0.277
Pulse				
Increasing Pulse	1.02 (1.00 – 1.05)	0.064	1.03 (1.00 – 1.05)	0.053

Discussion

In our study, majority of patients (64.9%) presented with acute ischaemic stroke with 87% having a history of hypertension. In West Africa, as in the rest of the world, hypertension is the most dominant risk factor for stroke.[12] In a large epidemiological study in Ghana and Nigeria, we found that the dominant ischemic stroke subtype is small vessel occlusive disease followed by large vessel atherosclerotic disease and cardio-embolic strokes. [12,13,14] In our study, three (3.2%) of the stroke patients tested positive for COVID-19 and all three had ischemic strokes based on non-contrast enhanced CT scans. In Spain, 19% of stroke patients admitted to a hospital were COVID-19 positive.[15] Our relatively low incidence of COVID-19 in stroke patients may be due to the fact that we performed SARS-COV-2 PCR testing for only stroke patients with suggestive symptoms. However, our findings support two studies from the United States of America and China which reported ischaemic stroke as the dominant stroke type in COVID-19 patients.[16,17]

In this study, two of the ischemic strokes among COVID-19 positive patients were attributed non-lacunar strokes in the middle cerebral artery territory and one was a lacunar or small vessel occlusive disease. Pathophysiologically, the severe acute respiratory syndrome coronavirus 2 (SARS-COV-2), though a respiratory virus, is able to evoke thrombosis in the arterial vasculature via inflammation, endothelial dysfunction, thrombin generation and platelet activation.[4,16] There have been reports linking COVID-19 with large-vessel acute ischemic strokes.[18,19] A rare case of small vessel cryptogenic stroke has been reported elsewhere.[20] Due to limited resources, severity of illness of patients and restrictions with movement of COVID-19 patients, we could not carry out detailed investigations such as cerebral angiography, carotid doppler ultrasonography or echocardiography.

In this cohort of patients with acute stroke, all three patients with COVID-19 died and therefore COVID-19 status could not be included in our multivariable analysis. COVID-19 associated strokes have been suggested to be more severe with high mortality rate due to a direct viral endotheliopathy or creation of a prothrombotic state engendered by infection-induced cardiac arrhythmias, immune-mediated platelet activation and perhaps dehydration.[16,21] Multivariate logistic regression showed that non-usage of calcium channel blockers (CCBs) and angiotensin receptor antagonists (ARBs) were marginally but not significantly associated with increased risk of mortality. CCBs are effective in mitigating the so-called ischaemic cascade, have an excellent anti-atherosclerotic properties and hence have the potential to prevent, as well as ameliorate, the severity of the atherothrombotic type of stroke at the large pre-cerebral artery level.[22] Some CCBs, especially the dihydropyridines, are also effective in the management of small vessel disease of the brain.[23]

The pathophysiology of COVID-19 and hypertension share a common pathway of the renin–angiotensin system (RAS).[24] A study during the early phase of the COVID-19 pandemic suggested a worsening outcome for infected patients with hypertension who were prescribed ARBs,[25] however, another study reported beneficial effects.[26] Angiotensin receptor blockers (ARBs) confer reno-protective advantage to patients and hence as renal function improves there is enhanced stroke survival.[27] ARBs have been recommended for BP control in people with stroke ahead of angiotensin converting enzyme inhibitors (ACE)[28]. This may explain why among our patients with stroke, those who were not on CCBs or ARBs were at increased risk of mortality.

In previous studies, high pulse rate was found as a predictor of mortality in acute stroke.[29,30] Bivariate analysis in our study showed mean pulse rate to be associated with stroke outcomes but this was lost in multivariate analysis. Tachycardia may be as a result of severe stroke (NIHSS > 15), large vessel stroke or atrial fibrillation.[31] The pulse rate of patients with stroke should be monitored and measures taken to control it to prevent mortality.

A limitation of our study is the small sample size. However, this was the total number of acute stroke cases admitted to the hospital over a period of 9 months. This is a reflection of the impact of COVID-19 on overall patient attendance at the University Hospital.[9] Additionally, COVID-19 testing was conducted only on patients with stroke who had additional symptoms suggestive of respiratory tract infections. Magnetic resonance imaging would have been ideal as a neuroimaging modality to characterize ischemic lesions but this was not available at the study site. We also did not assess stroke severity with validated stroke severity assessment instruments. In spite of these, our study, which to our knowledge is the first in sub-Saharan Africa, characterizes stroke presentations in this era of COVID-19 pandemic and provides useful data on predictors of mortality. A bigger multi-centre study which involves testing all stroke patients for COVID-19 will increase the statistical power of causality and generalizability.

Conclusion

Approximately 3% of patients with acute stroke had COVID-19 and all of them died. Due to atypical presentations of COVID-19 and its high risk of stroke, we recommend that patients with acute stroke admitted to hospitals should be actively screened for possible SARS-CoV-2 infection.

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SPECIAL ARTICLE

THE ROLE OF THE DIABETES SPECIALIST TEAM IN THE MODERN MANAGEMENT OF DIABETES MELLITUS: A CALL FOR ITS IMPLEMENTATION IN GHANA

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Summary

Many chronic illnesses require patient-centred care where behavioural change aimed at dealing and coping with the socio-psychological as well as the physical impact of the disease is emphasized.

Diabetes presents such a challenge especially in the developing world where both human and material resources are limited in dealing with this complex disease. Most centres in Ghana and Africa in general, rely on overburdened practitioners who have responsibilities to other acute and chronic illnesses in addition to diabetes care.

The Diabetes Specialist Team (DST) has become a tool in overcoming these complexities to improve care and outcomes. They work in a team with specialised and sometimes overlapping skills. Core members include Consultant physician diabetologists, specialist diabetes nurses, podiatrists, dieticians and clinical psychologists.

The positive impact of DST is noticed in the aspects of diabetes preventive services, early diagnosis, patient education, medication use, risk factor and complication identification and management, together with in-patient care and management of special groups.

Recognising that the needs of persons living with diabetes are under served, coupled with the fact that developing countries are expected to experience the greatest burden in terms of numbers and complications of diabetes, more resources are needed to reverse these expected grim statistics. Efforts should be made to develop and deploy DST as much as possible to provide specialised and dedicated services in the routine management of diabetes at least at the district or municipal health level. Resources are needed to maintain and snowball the impact of this approach.

Key Words: *Diabetes mellitus, diabetes specialist team, multi-disciplinary, outcomes*

Introduction

‘*’The greatest improvement in the productive powers of labour, and the greatest part of skill, dexterity, and judgment with which it is anywhere directed, or applied, seem to have been the effects of the division of labour’’. (Adam Smith, 1776)”.*

Medical practice traditionally, especially in Africa, has been set up in a way to deal mainly with acute problems and does not adequately cater for the demands and needs of persons with chronic illnesses. In the care of individuals with chronic illnesses, behavioural change aimed at dealing and coping with the socio-psychological as well as the physical impact of the disease is key [1]. In recent years, multidisciplinary approach to deliver chronic care has been emphasized where the individual care components are integrated into a structured care model to achieve the desired impact [1]. Diabetes is a multi-faceted illness and therefore requires a multi-disciplinary care approach to achieve the desired results [1,2].

The core components of diabetes care identified by Diabetes UK ‘Task and Finish’ Group include diabetes preventive services, early diagnosis, patient education, medication use, risk factor and complication identification and management, together with in-patient care and management of special groups [2]. They assert that these can best be delivered by specialised team of diabetes care givers [2].

The situation is even more paramount for us in Africa because of the fact that not only is diabetes care rudimentary and underdeveloped, but the number of

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persons also living with diabetes is going to experience the largest increases in the next decade with its attendant morbidity and mortality [3]. The underdeveloped nature of diabetes care in Ghana and sub-Saharan Africa was demonstrated by Amoah et al in 1999, when they assessed and surveyed five regional hospitals in southern Ghana for facilities and resources for diabetes care [4]. They found out that only Korle Bu Teaching Hospital had a running diabetes clinic which also had serving diabetologists. Interestingly, none of the five facilities had a trained diabetes educator or chiropodist and only two facilities had an eye specialist or trained dietician. Laboratory facilities and basic care equipment were woefully inadequate, and at that time none of the facilities had on-going chronic haemodialysis service [4]. This assessment brought to the fore the unsatisfactory nature of both human and material resources in chronic diabetes care. It emphasized the urgent need for training healthcare personnel and provision of the needed equipment and support services to provide a comprehensive diabetes care model.

Following from the results of the above survey and assessment, a national diabetes care and education programme was developed through international collaboration of medical schools, industry financiers and government health care institutions [5]. They adopted a 'top-down' approach where diabetes teams were trained consisting of physicians, dieticians and nurse educators at two teaching hospitals. They in turn trained teams consisting of physicians, dieticians or diet therapy nurses, nurse educators and pharmacists at regional and sub-regional levels to offer care and education to patients and the community. After three years of the programme, trained diabetes health care teams, diabetes services and diabetes registers were available in all regional and about 63% of sub-regional health facilities [5] and had greatly reduced travelling distances for patients seeking diabetes care. Unfortunately, such interventions were not sustained and many of the teams have been disbanded.

Components and benefits of DST care approach

The need for a DST in the management of diabetes is highly encouraged so as to overcome some of the shortcomings of conventional management which include poor adherence to diabetes management guidelines, inadequate time for consultation, complexity of care, inadequate education of the patient, lack of confidence on the part of care givers, and inadequate follow up of patients [6].

It noteworthy that the results of the Diabetes and Complications Clinical Trial (DCCT), United Kingdom Prospective Diabetes Study (UKPDS) and the Steno-2 and their -follow up studies, have all demonstrated the benefit of intensive treatment compared with conventional therapy on the overall glycaemic control [7-11]. These studies also demonstrated that early aggressive therapy produces lasting effects in terms microvascular and macrovascular complications rendering such interventions cost effective. Significantly, the intensive treatment was achieved through the use of multidisciplinary diabetes care employing the DST to achieve targets [7-11].

Key members of the Diabetes Specialist Team (DST) include Consultant physician/ diabetologists, specialist diabetes nurses, podiatrists, dieticians and clinical psychologists [2]. Furthermore, there may be the involvement of ophthalmology, nephrology, specialist pregnancy diabetes teams, and maturity onset diabetes of the young (MODY) services[2].

Patient Education & Integration of Care

Diabetes related micro and macrovascular complications confer an increased morbidity and risk of premature death but this can be reduced with lifestyle intervention which is the cornerstone in diabetes care [12]. Though, patients find it difficult to comply with and sustain these interventions [13], both lifestyle interventions and other aspects of diabetes management can be greatly improved by attending a structured diabetes education program, and this is highly recommended [14-16].

The diabetes education and self-management program for on-going and newly diagnosed intervention for people with type 2 diabetes (DESMOND) and Dose Adjustment for Normal Eating (DAFNE) for type 1 patients are examples of structured education programmes available to diabetes patients in the United Kingdom (UK) [17,18] which are delivered by accredited educators and have been found to improve outcomes. Unfortunately, such structured education programmes are unavailable in most parts of Africa including Ghana. Glasgow RE [19] suggests that patient education may improve self-management and compliance to therapy and also motivate patients to implement lifestyle changes with regards to diet, smoking habits and physical exercise. This is important to achieve better diabetes control and to delay or prevent the development of complications. Aside structured education, a process of systematic and regular review of patients together has been shown to improve the management of diabetes [20]. This can be

achieved by a central computerized tracking system or by nurses who regularly contact patients[20].

Whilst diabetes can be managed mainly at the primary care level, very often both secondary and tertiary care are needed especially when treatment become more complex and complications develop [14,20]. It is therefore important that guidelines on diabetes management, teaching and training should be integrated and such inter linkages be made clear and simple at all levels of care [14,16, 20]. It the hope of the author that DSTs be at least established in each district or municipal hospital.

Diabetes Physician/Consultant or Diabetologist

These are normally Consultant physicians with specialist training and accreditation in diabetes and they have the responsibility of providing specialist consultations and are generally seen as the leader of the DST. Among other things, they provide consultancy advise to other colleagues in other specialty units and clinics, training of other members and support staff of the DST, leadership and strategic planning, research and coordination as well as support of all staff in the provision of the highest service standards possible, provision of support to self-help groups and ensuring the proper inter linkages, referrals and continuity of care [2,21]. Due to the commitments of most diabetologists to the practice of endocrinology and other general medical duties and the differing strengths of the other members of the DST and support staff as well as work load differences, the frequency of visits and contact time of the diabetes consultants vary from centre to centre and locality [21]. In Africa, unfortunately the number of diabetologists and endocrinologists are few and may further compound this situation [3]. Non-consultant medical staff, depending on their availability and workload can and should be trained to assist the diabetes consultants in service provision, training, research and supervision [21]. At the district level and centres without consultants, the team could be led by the non-consultant medical staff.

Diabetes Specialist Nurse

These are key personnel in the DST who anchor the whole diabetes management programme and must have undergone a specialist training course [21]. Diabetes nurses serve as educators and counsellors, monitoring and motivating patients to be compliant with their medications and lifestyle modifications. They serve to provide initial and ongoing education and advice to both patients and carers and by so doing help patients to get adapted to their disease and develop efficient skills in self-care [21]. Both in the clinic and community setting, diabetes nurses associate with dieticians to deliver a range of interventions and help in the attainment of clinically significant improvement in blood glucose control, blood pressure and lipid profile, aimed at decreasing morbidity and mortality. In certain centres diabetes nurses with other support staff provide home visits as part of a comprehensive health care package [21]. Through a systematic review process of patient data and records, diabetes nurses may take steps to reduce the number of patients who default and get lost to follow up, an approach that helps to reduce diabetes related complications [21,22].

Diabetes specialised nurses can offer motivational interview to patients who lack treatment compliance. A pilot study reported that screening for psychological problems and mental derangement by diabetes nurses, with a subsequent psycho-educational and motivational intervention, resulted in a positive outcome [23].

Specialist Dietician

Dieticians who provide specialist services must be certified after some training in diabetes, and it is recommended that all newly diagnosed diabetics and their carers should be encouraged to see them within four weeks of diagnosis [21]. Dieticians have a constructive effect on the health of patients with diabetes, encouraging an appropriate diet-related behaviour. Such behaviour is accompanied with an improvement of blood glucose control, having an impact in reducing the risk of diabetes complications [24]. The importance of healthy eating, sufficient physical activity and attainment of a positive self-esteem has been supported by dieticians, as the three main steps to attaining a healthy weight [25]. Dieticians help patients attain a healthy body weight by modifying their nutrient intake and by so doing help prevent the development of chronic complications of diabetes[26]. They are responsible for informing diabetes patients about the nutritional composition of food. They also recommend the daily caloric intake but at the same time, help patients in maintaining blood glucose, lipid, and lipoprotein profiles within normal values [24, 26]. They employ a flexible approach in food selection, adhering to patients' preferences and traditions, with the aim to provide an optimal quality of life[27].

Foot care services / Podiatrist service

The podiatrist is concerned with the maintenance of foot health to prevent complications, by providing patient education and expert care. Every newly diagnosed patient with diabetes should have a

screening foot examination by a specialist podiatrist, and this should be repeated, at least once annually [21, 28]. All patients with category 2 and 3 risk classification based after a comprehensive foot examination should be seen by the podiatrist every 1-3 months to avoid or delay the complications of diabetes [28].

The multidisciplinary team approach to foot care improves screening and considerably decreases amputation rate [28,29]. The role of the podiatrist involve preventing and treating diabetic foot ulcers, which are associated with a high risk of mortality [30]. They improve the awareness and ensure the delivery of an appropriate management in diabetic peripheral neuropathy, limiting any unnecessary morbidity [31]. As part of a larger foot care service, joint multidisciplinary foot care services are encouraged to reduce duplication of visits [21]. Notwithstanding, in many parts of Africa including Ghana, there are very few podiatrists, if any. In their absence, nurses and other medical staff may be trained to provide basic foot care education and examination. In the larger scheme of things, general surgeons with interest in foot care, vascular surgeons and interventionists may be consulted for both diagnostic and restorative care.

Clinical Psychologist

Access to psychology services should be made available to the patients and carers around the time of diagnosis and anytime during the course of their treatment, and ideally, they should be part of the core DST team [21]. Psychological services are particularly useful when patients are newly diagnosed, those who are in transition from adolescent to adult care, those experiencing psychological barriers like fear of needles, issues of non-compliance especially in adolescents, factitious hypoglycaemia as well as anxiety or depression related issues [21]. The work of the psychologist may include serving as a liaison between diabetes and mental health services, education, training as well as research [21].

Monitoring and discussing psychological wellbeing are extremely important. Distress in diabetes could occur secondary to patient's concerns about disease evolution, lack of support, emotional burden and access to care which if not managed could undermine the attainment of positive outcomes in diabetes management [21, 23, 32, 33]. It is associated with a higher risk of diabetic complications, poor control of Hb1Ac, functional impairment and increased risk of mortality [21,23,32,33]. All patients with distress secondary to diabetes should be ideally referred to a psychologist for management [21,32]. Social stigma deters a high proportion of patients to engage with psychological services[21, 23,32].

Screening for depression is critical and valid tools for screening have been developed and are best done in a clinical setting. Some of these screening tools include the Beck Depression Inventory (BDI) [34] and the Patient Health Questionaire-9 (PHQ-9) [35]. Once identified, treatment with psychotherapy, self-management or pharmacotherapy improves depressive symptoms and distress [36]. In the absence of a qualified psychologists, diabetes educators could be trained to offer such motivational and support services. They must however be empowered to recognise their limitations and to know when to refer patients to see a qualified psychologist.

Other Specialist Services

Specialist Diabetic Pregnancy Service

Multidisciplinary team approach is key in achieving good pregnancy outcomes [37]. It involves the specialist diabetes midwife and an obstetrician ensuring timely delivery, according to the underlying maternal and foetal condition [21, 22, 37]. In addition, they provide pre-pregnancy counselling and help to optimize blood glucose before conception, check on medications and advice on smoking and alcohol cessation [21, 22, 37]. They assist in maintaining normoglycaemia throughout pregnancy and labour [21]. The paediatrician handles complications arising as a result of diabetic pregnancy [37]. The diabetes educator advises on blood glucose monitoring, diet, different types of insulin injections and exercise. A dietician helps to plan a diet, tailored to the patient needs and calorie requirement [21, 22, 37]. The service of an eye specialist is essential in monitoring for any diabetes retinopathy, which may worsen in pregnancy [21,22,37]. Due to the diversity of the members needed to set up such a team, this team approach to pregnancy may only be possible at the secondary and tertiary levels.

Nephrology Service

Patients with diabetes are essentially managed in primary care. A screening programme for early detection of nephropathy and eventual end- stage renal failure (ESRF) is vital [38]. The American Diabetes Association [39] recommends that yearly urine micro albumin estimation should done five after diagnosis in type 1 diabetes and immediately after diagnosis in type 2 diabetes. All T1DM and T2DM patients with progressive renal insufficiency or serum creatinine >150ùmol/l should be referred to a nephrologist for assessment and continued shared management (update

reference) [40]. Also, the Canadian Diabetes Association recommends the referral to nephrologists when estimated glomerular filtration rate (eGFR) <30 ml/min/1.73mm^2 or earlier if albumin creatinine ratio (ACR) is persistently >60mg/mol, or if the individual is unable to achieve blood pressure targets or remain on reno-protective therapies due to adverse effects [41]. Methods to prevent and reduce the progression of nephropathy include tight glucose control (glycated haemoglobin < 7%), blood pressure control <140/80 mmhg, the use of angiotensin conversion enzyme inhibitors and angiotensin receptor blockers receptors as well as the avoidance of nephrotoxic drugs [39].

Patient education and counselling is essential [39,41]. The screening and monitoring could be provided by all grades of medical doctors including general practitioners but must recognise when to refer to nephrologist as discussed above.

Ophthalmic services

It is essential that both human and material resources are mobilised to provide comprehensive and a well-structured eye service for diabetes patients [21,39]. Local protocols should be developed for screening and management of diabetic eye provided [21]. The ADA recommends yearly eye screening in diabetes but in type 1 this should be done within five years [39]. The screening could be done by ophthalmic nurses. Once retinopathy is identified, this screening should be done by an optometrist or ophthalmologist, but the frequency should be increased when retinopathy is progressive or life threatening. Support for the visually handicapped should also be provided [39]. Tight glucose and to some extent blood pressure control slows the progression of retinopathy [39].

In-patient Diabetes Services

The basic structure of the inpatient diabetes team comprises of a consultant specialist in diabetes and at least one diabetes inpatient specialist nurse. They must have access to the other members of the DST when needed. The multidisciplinary in-patient team helps to set standards, plan pathways, train and support the delivery of personalized care both on medical and non-medical wards.

Hospitals should provide specialist diabetes in-patient teams to deliver high-quality cost-effective care, so as to reduce hospital stay and to provide effective patient centred care and outcomes [2,21]. At the primary level, general practitioners could lead this service.

Others

Other specialised services may include genetic testing for maturity onset diabetes of the young (MODY) which is an autosomal dominant condition and can occur at any age [42]. Consider genetic testing for MODY in the absence of obesity, in all non-ketotic diabetes patients independent of age; If obese and non-ketotic, then consider it in young and middle-aged patients[42]. Others services include specialised and adolescent diabetes care and also care of the elderly with diabetes [2,21].

Conclusion and Policy Redirection

Diabetes mellitus is a chronic multifaceted disease with high morbidity and mortality. It requires a multi-targeted approach to achieve targets to prevent and reduce macrovascular and microvascular complications and also sustain such benefits in the long term [7-11].

The complexities of diabetes care require that such intensive approaches could be achieved by a good organised care delivery system using the DST which ensures specialisation of the individual component care givers with a lot of inter linkages [(1, 2)]. Indeed, in all of this, patient empowerment is central [2,21]. Unfortunately, in Africa, both the specialist personnel and organisation hardly exist.

The ministry of health and the Ghana Health Service (GHS) must vigorously encourage the setting up the of DST across the whole country to provide focused care to a complex disease. At the minimum, the team could comprise of a general practitioner with some further training in diabetes, a diabetes nurse, a diabetes educator, a registered dietician and an ophthalmic nurse. They must work towards laid down protocols with linkages to specialist services at secondary and tertiary centres. Effort and resources must be committed to maintain its impact in the long term, whilst ensuring that members of the DST have the highest level of human care and empathy.

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CASE REPORT

A RARE CASE OF CONJUNCTIVAL RHINOSPORIDIOSIS MIMICKING A NEOPLASM IN GHANA.

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Abstract

Introduction: Rhinosporidiosis has not been reported in the literature, in Ghana. It is however endemic in India, mostly presenting as tumorous growths within the nasal cavity and conjunctiva. Rhinosporidiosis is a chronic granulomatous infection caused by *Rhinosporidium seeberi* an organism initially thought to be a fungus, but now newly classified as belonging to a group of fish parasite DRIP clade (Mesomycetozoa) located in the middle (-meso) of the animal(-zoea) and fungal(-myceto) divergence. It has been proposed to be acquired by direct inoculation of traumatized mucosal membranes through contact with contaminated water bodies with aquatic animals as natural hosts. It usually presents as a red granular polypoid mass which may mimick a neoplasm.

Case Presentation: An 8-year-old boy was seen at the Eye clinic with a four-week history of a painless right palpebral conjunctival growth which progressively increased in size over the period. It was excised because it was suspicious for a neoplasm (Papilloma). Histopathological examination confirmed conjunctival Rhinosporidiosis. We report the clinical and histopathological findings of this entity and review the existing literature.

Conclusion: Conjunctival Rhinosporidiosis although rare occurs in our setting. *Rhinosporidium seeberi* is found in river bodies within our communities and Health care givers should be aware of this infection, which may mimick a neoplastic lesion. It should be included in their differential diagnoses of individuals who present with polypoid conjunctival and nasal masses, who hail from areas with stagnant freshwater bodies in which they routinely bathe or swim.

Key words: *Conjunctival Rhinosporidiosis, Papilloma, Rhinosporidium seeberi, Mesomycetozoa, Ghana*

Introduction

Rhinosporidiosis is a chronic granulomatous disease affecting the mucous membranes with common sites being the nose and nasopharynx (81.1%), and the eye (14.2%). Rare sites of infection include the penis, lips, skin, and uvula[1-6]. Rhinosporidiosis involving the eye is known as Oculosporidiosis[3] and the commonest sites reported in the ocular and adnexal region are the conjunctival surface (90%)[7,8] followed by the lacrimal sac (5-24%)[7-10]. The condition mostly affects males between the second and fourth decades of life[7].

The disease occurs in the Americas, Europe, Africa, and Asia but is most common in the tropics with the highest prevalence in Sri Lanka[9]. A survey of school children from Pallam, India found 11 cases in 781 children (prevalence of 1.4%)[11]. In Africa, cases of oculosporidiosis have been reported in South Africa, Malawi, Zambia, Kenya, Tanzania, Congo, Ivory Coast, and Cameroon with no report in the literature from Ghana[1]. Studies have linked infections to swimming or bathing in freshwater ponds, lakes, or rivers[11,12].

The causative agent of the disease, *Rhinosporidium Seeberi*, is believed to be an eukaryotic parasite that continues to elude growth in culture[13,14,15]. *R. Seeberi* was considered a fungus although it was originally thought to be a protozoan parasite[12] but is now classified under the class Mesomycetozoa, using ribosomal DNA analysis[7]. This class is in the middle (meso-) of the fungal (-myceto) and animal (-zoa) divergence with its morphological characteristics resembling those of *Coccidioides immitis*[1,9]. Both organisms have mature stages that consist of large, thick-walled spherical structures containing smaller daughter cells (endospores)[9]. *R. seeberi* is visualized

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Conflict of Interest: None Declared

with fungal stains such as methanamine silver and periodic acid-Schiff as well as mucicarmine. [9].

R. seeberi begins its life cycle as a parasite measuring 8µ and grows by nuclear division until it reaches a size of about 200 to 300µ containing at this stage, over 4,000 nuclei, which form up to 16,000 spores[16]. The mature parasite, now called Sporangium, has a double-contoured chitinous envelope with a germinal spore through which the spores are discharged[16]. Each spore subsequently develops into a separate Sporangium[16]. This organism occurring in the eye may give rise to oculosporidiosis, as its manifestations in the eye and its adnexa are more profound than those in the nose (rhinosporidiosis)[16].

Transmission of the disease occurs through traumatized epithelium (transepithelial infection), coming into contact with contaminated water and/or soil[17,18]. Patients subsequently develop a mass with polypoid morphology, associated with bleeding, pruritus, and sneezing for nasal involvement[19,20]. Clinically, Rhinosporidiosis is a slow-growing, tumor-like mass (polyp), usually of the nasal mucosa or ocular conjunctivae. It is friable and causes a foreign body sensation, with irritation and watering from the eye with no effect on visual acuity according to some isolated case reports[7]. Diagnosis is established through histopathology with the demonstration of granulomatous chronic inflammation with stromal fibrosis around several thick-walled sporangia at different stages of maturation and containing numerous endospores[1,9]. The differential diagnoses include papilloma and pyogenic granuloma.

Case Report

An 8-year-old boy, who hails from a coastal town and is a usual swimmer in the community stagnant freshwater pond presented to the Eye clinic with a four-week history of a painless right palpebral (upper eyelid) mass which progressively increased in size over the period with an associated sensation of a foreign body in the eye resulting in tearing and mild discharge. It started as an itch with no associated loss of vision. Routine laboratory investigations revealed only microcytic anaemia and his medical history was otherwise unremarkable. A diagnosis of conjunctival papilloma was made, with surgical excision of the mass for histopathological analysis. We received a tan polypoid mass in formalin measuring 13x10mm at the histopathology lab. All the specimen was processed for examination. Haematoxylin and eosin-stained sections showed a partly ulcerated lesion covered by residual stratified squamous epithelium in areas. The underlying stroma was laden by heavy mixed inflammatory cells predominantly lymphoplasmacytic in nature and surrounding numerous thick-walled sporangia containing nucleated basophilic endospores. In a focus, few of the sporangia had ruptured with spilling of endospores into stroma inciting a neutrophilic abscess reaction. These are captured in ***figure 1a*** to ***figure 1h*** below. A Periodic Acid Schiff stain (PAS) was done to outline the cuticle layer of the sporangia and confirm the histologic diagnosis of Rhinosporidiosis as shown in ***figure 2.***

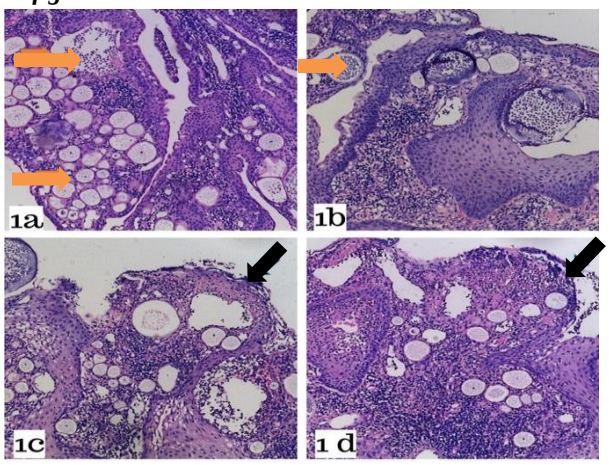

Figure 1a and Fig 1b *- (H&E x 100) - Numerous thick-walled spherical sporangia (orange arrows) containing endospores with surrounding dense lymphoplasmacytic infiltrate.*

Figure 1c *and* ***Figure 1d*** *– (H&E x 100) –Partly ulcerated surface epithelium with focal granulation tissue (black arrows).*

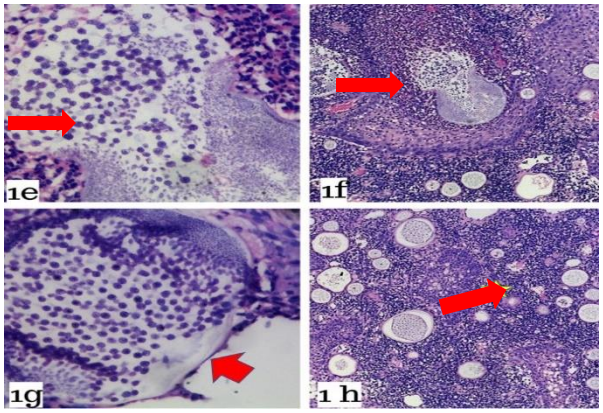

Figure 1e *and* ***Figure 1f****- (H&E x 100&400) - Ruptured sporangia (long arrow) with spilling of endospores into stroma inciting neutrophilic abscess (red arrow).*

Figure 1g *– ((H&E x400) – Sporangium containing numerous endospores located within the surface epithelium.*

Figure 1h *- (H&E x 100) - section shows lymphoplasmacytic infiltrate around sporangia. (Red arrow)*

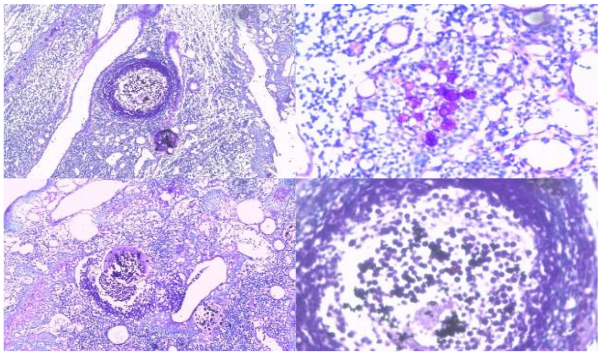

Figure 2: *PAS-stained slides showing various stages of Rhinosporidiosis*

Discussion

Rhinosporidium Seeberi is the identified etiologic agent of Rhinosporidiosis, a mucosal chronic granulomatous inflammatory disease transmitted by bathing in stagnant ponds in which infected animals also bathe. Our patient frequently swims in a stagnant water body in the community. There was however no prior significant history of trauma to the right eye.

The life cycle of *R. Seeberi* has 2 phases, invitro and in human host. It develops spherical cysts with endospores (stage 1). In vitro the released endospores (stage 2) give rise to uniflagellated infectious zoospores (stage 3). When the zoospores (infecting units) infect the host, they encyst (stage 4) and increase in size (stage 4, 5) and undergo cleavage into endospores (stage 1). The endospores can also be directly released within the host's tissues when the sporangia rupture and the cycle is repeated inside the host (stages 1, 4, 5, 1). A pictorial representation of the life cycle of *Rhinosporidium Seeberi* is illustrated in (***figure 3)***. This results in the expanding tumorous lesion with the associated chronic inflammatory changes. This was initially diagnosed in our patient as a conjunctival papilloma.

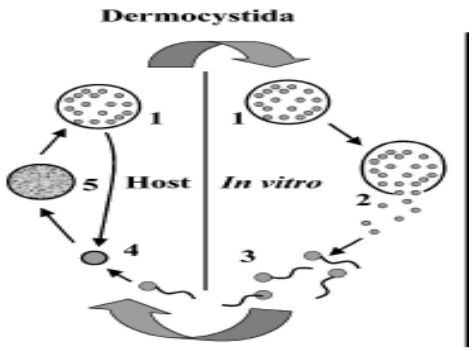

Figure 3*- Depiction of the putative life cycle of members of the orders Dermocystida, from***: *https://doi.org/10.1146/annurev.micro.56.012302.160950*

Clinical features depend on the site of involvement. The lesions are usually seen in the nasal cavity and nasopharynx in majority of patients. These are reddish polypoidal, bulky, friable mucosal masses. Conjunctiva, mouth, larynx, genitalia and skin are the other rare sites of involvement.[1-8,24] For our case we were unable to get a gross photo of the eye lesion before excision. The lesion was initially diagnosed as a papilloma a rather common benign tumor seen in the eye clinic. Our patient presented with a four-week history of foreign body sensation, a swelling of the eye with associated tearing and mild discharge. Clinical presentation however depends on the presence of a tumorous mass at the locations stated early on.

Microscopy showed characteristic morphology, spherical sporangia of various sizes with heavy lymphoplasmacytic infiltrate located in the stroma of the polyp. The overlying mucosa may show focal ulceration or metaplastic changes depending on the site. The largest of the sporangia are usually immediate subepithelial in location which may or may not show evidence of rupture. For our case, there was focal epithelial ulceration as well as several subepithelial and intraepithelial sporangia containing numerous endospores within a stroma laden with heavy lymphoplasmacytic infiltrate. In areas, the sporangia were ruptured releasing endospores into adjacent stroma with surrounding abscess formation **(*figure 1e)***. Periodic Acid Schiff special stain highlights the thick cuticle cyst wall of sporangia and the round nucleated basophilic endospores (***Figure 2***).

The treatment of choice is usually excision of the lesion. However, excision with local cautery is considered the most effective treatment[22,24]. Our patient had excision of the lesion and was given DEXATROL (dexamethasone neomycin polymyxin b) eye drops to be reviewed in a month. Cautery is used to reduce the risk of recurrence which is caused by endospores being released into nearby mucosa. Medical treatment with dapsone and amphotericin B remains controversial, as determining drug sensitivity has been impossible without the ability to grow R. seeberi in vitro. However, dapsone has had some success in treating Rhinosporidioisis; it is believed to act by arresting sporangia maturation and promote fibrosis[7]. Recurrence rates have been noted to vary by infection site with conjunctival and lacrimal sac recurrences being relatively low compared to nasopharyngeal recurrence rates which have been reported in up to 10% of patients[9,21]. An important ocular complication is the formation of staphyloma, which occurs due to scleral

thinning and herniation of the intraocular content[7]. This can lead to rupture and loss of the intraocular content.

Conclusion

Conjunctival Rhinosporidiosis although rare occurs in our setting. It is found in river bodies within our communities and Health care givers should be aware of this infection, which may mimick a neoplastic lesion. There should be a high index of suspicion in individuals who present with polypoid conjunctival and nasal masses, who hail from areas with stagnant freshwater bodies in which they routinely bathe or swim. Routine histopathological examination of all conjunctival lesions in these areas could confirm the endemicity of this condition.

Ethical Considerations

Ethical review is not required for reporting cases in our institution. Informed consent was however sought from the patient's guardians and institutional assent was obtained from the Cape Coast Teaching Hospital.

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ACKNOWLEGEMENT OF REVIEWERS

The Editorial Office of the Ghana College of Physicians and Surgeons would like to acknowledge with reverence and deep gratitude, all reviewers whose effort have been valuable to the preservation of the high quality of articles published in the Postgraduate Medical Journal of Ghana. For this edition we extend especial thanks to the reviewers hereby listed.

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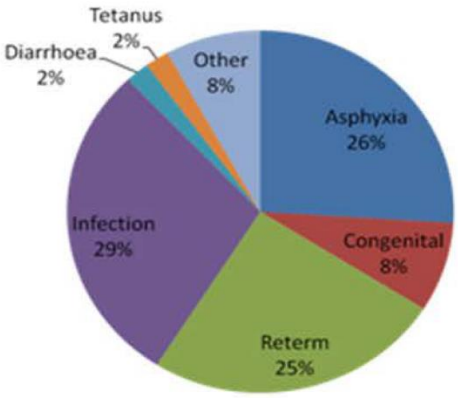
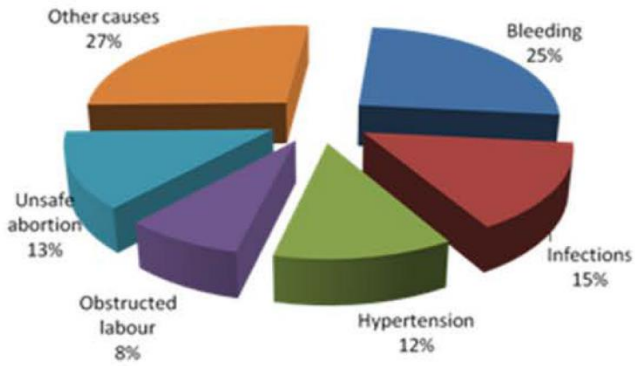
FROM THE PAST

INFANT/ MATERNAL MORTALITY

Estimated causes of Neonatal Deaths in 2000



Causes of maternal mortality in Ghana



Because of African exclusion from the medical services, problems of maternal and child health in Africans were ignored by the Medical Department until 1915 when Dr. F. V. Nanka-Bruce gave prominence to the need for the proper training of African midwives and the construction of a properly equipped maternity hospital to reduce the high loss of lives among mothers and babies.

Governor Clifford appointed a committee to enquire into the causes of maternal and infant mortality but was unable to do much about the committees recommendations because of the First World War.

Governor Guggisberg appointed another committee in 1920 to consider the construction of a maternity hospital and training centre for midwives. In keeping with the committees recommendations the construction of a maternity block in Korle Bu was commenced in 1924, and the foundation stone of a children's hospital laid by Princess Marie Louis in 1925.

During the period 1998 to 2003 infant mortality rate rose from 57 per 1000 live births to 64 per 1000 live births. It has dropped to 50 (2008).

Maternal mortality ratio in Ghana is estimated at between 256 and 540 per 100,000 live births with a lifetime risk of 1 in 35.

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