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CONTENTS

EDITORIAL COMMENTS

Hepatocellular Carcinoma - A Synopsis Of Current Developments

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Abstract

This review highlights the burden associated with hepatocellular carcinoma and the progress made so far in the diagnosis, management, and treatment of the disease. It is based on a search of Medline, the Cochrane database of Systemic Reviews, and citation lists of relevant and current publications. Subject headings and key words used included "hepatocellular carcinoma", "pathogenesis", "liver transplantation", "local ablative therapy", and "novel drug therapies". Additional information was obtained by a manual search of the references from the key articles, current advances in treatment. Only articles in English were included.

Currently, surgical resection and liver transplantation are the treatment strategies offering the best long-term outcomes in patients with hepatocellular carcinoma. Non-transplant treatment as a bridge to transplantation also helps in lessening the risk of tumour progression or death during the waiting period. Targeted multi-cellular therapy with Sorafenib, is the first systemic agent to have yielded survival benefits in patients with advanced disease. Other agents: Brivanib, Erlotinib, monoclonal antibodies, Bevacizumab and Cetuximab, are currently being studied to determine their use in hepatocellular carcinoma. Radionuclide Yttrium-90 microspheres, or combined subcutaneous interferon alpha and intra-arterial infusion chemotherapy, seem to be more promising strategies than Sorafenib treatment to downstage advanced hepatocellular carcinoma, including cases with macroscopic portal venous invasion.

Although numerous modalities of diagnosis and treatment of hepatocellular carcinoma have been studied, there is still need for further evaluation of newer adjuvant treatment to provide more effective and tolerable methods for the patients with hepatocellular carcinoma.

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Introduction

Hepatocellular carcinoma (HCC) is known to be a momentous disease worldwide. HCC is an aggressive tumour that often occurs in the setting of chronic liver disease and cirrhosis. Despite rapid advances in medical expertise over the past decades which have greatly increased the ease and accuracy of diagnosing hepatic tumours, and the widely available diagnostic and treatment options, there has not been a significant reduction in mortality from HCC. This has added to the frustration of both the patients and the care givers.[1] The burden from this disease is worse in sub-Saharan Africa and south-east Asia due to poverty and lack of surveillance strategies for early detection, lack of proper diagnostic procedures or poor access to proper medical care and drugs. Although surgery and liver transplantation remain the most effective approach to intervene in HCC, a majority of HCC patients is still ineligible for surgical intervention.[2] Even in developed countries where more expertise exist for the detection and treatment of the disease, cure is still an illusion. This article gives an overview of current developments in the patho-physiology and management of HCC.

Epidemiology and Genetics

Hepatocellular carcinoma is one of the most prevalent malignant tumours in the world, and is a leading cause of cancer related deaths worldwide.[3] HCC is about the sixth most common cancer in the world in terms of incidence, accounting for between 630-750,000 new cases per year.[4] Chronic hepatitis B and C viral infections (HBV and HCV), mostly in the cirrhotic stage, are responsible for the great majority of cases of HCC worldwide. It is typically diagnosed late in its course, and the median survival following diagnosis is approximately 6 to 20 months.[4] Geographic areas at the highest risk are South- Asia and sub-Saharan Africa, where HBV infection is highly endemic, and is the main cause of HCC.[5] HCC is the commonest cancer of males in Nigeria, being rivaled now by prostatic cancer. In the University College Hospital (UCH), Ibadan HCC accounted for 491 out of 100,000 hospital admissions. It was the commonest

malignancy on the medical wards of UCH, and the commonest cause of death from cancer in middle-aged as well as elderly Nigerians.[6] In Zaria and Maiduguri, HCC was responsible for 19.1% and 17.0% of all cancers respectively. Similarly, HCC is responsible for 38.8% of all cancers of the digestive system.[7]

Virtually all cases of HCC in children are due to chronic HBV infection.[4] In endemic areas in Asia and Africa, where HBV infection is transmitted from mother to newborn, up to 90% of infected persons have a chronic course, with frequent integration of HBV into host DNA. Although HBV can cause HCC in the absence of cirrhosis, the majority (70 to 80%) of patients with HBV-related HCC have cirrhosis.[2] The risk of HCC among persons with chronic HBV infection (those who are positive for the hepatitis B surface antigen [HBsAg]) is further increased if they are male or elderly, have been infected for a long time, have a family history of HCC, have been exposed to the mycotoxin aflatoxin, have used heavy quantities of alcohol or tobacco, are co-infected with HCV or hepatitis delta virus (HDV), or have high levels of HBV hepatocellular replication.[1]

Less common causes include hereditary haemochromatosis, alpha1-antitrypsin deficiency, autoimmune hepatitis, some porphyrias, Wilson's disease[1] and type II diabetes mellitus(due to obesity), and hepatic steatosis often associated with chronic non-alcoholic fatty liver disease, are emerging independent risk factors for the development of HCC.[8]

Hepatogenetic Mechanisms of Hepatocellular Carcinoma

The genetic basis of hepato-carcinogenesis is complex; however it is thought to be a process associated with the accumulation of genetic and epigenetic defects that alter the transcriptional program.[9] Hepato-carcinogenesis is considered a multi-step process involving genetic mutations that facilitate proliferation and/or apoptosis in the hepatocytes leading to continuous inflammatory and regenerative stimuli, starting from the initial phases of chronic hepatitis and then of liver cirrhosis.[10]

Currently, hepatic fibrosis is considered a model of the wound-healing response to chronic liver injury. The excessive extracellular matrix (ECM) deposition that distorts the hepatic architecture by forming fibrotic scars, and the subsequent development of nodules of regenerating hepatocytes defines liver cirrhosis.[11] The clinical importance of liver cirrhosis is related to the associated hepatocellular dysfunction and increased intra-hepatic resistance to blood flow, which result in hepatic insufficiency and portal hypertension, respectively, and to the occurrence of HCC.[11]

HBV and HCV can be implicated in the development of HCC in an indirect way, through induction of chronic inflammation, or directly by means of viral proteins or, in the case of HBV, by creation of mutations (codon 249 mutation in the *p*53 tumour suppressor gene and integration into the genome of the hepatocyte.[12] In HBV-associated HCC, codon 249 mutation in the *p* 53 gene seems more related to exposure to aflatoxin B1 than to hepato-carcinogenesis itself.[12] HCC that occurs in children in high HBV endemic regions could be associated with germ-line mutations, but little information is available; not much is known about chemical hepato-carcinogens in the environment other than aflatoxins. The X gene of HBV seems to play an important role in HBV-associated hepato-carcinogenesis.[13] During the 'pre-neoplastic' phase (chronic hepatitis and cirrhosis), genetic alterations are almost entirely 'quantitative', occurring by epigenetic mechanisms without changes in the structure of genes. In this phase, hepatocytes undergo an intense mitogenic stimulation due to exposure to elevated levels of growth factors, such as insulin-like growth factor (insulin-like growth factor-2, IGF-2), transforming growth factor-α (TGF-α), interleukin 6 as well as inflammatory cytokines, which may lead to activation of the major signalling pathways involved in cell proliferation and angiogenesis. The enhanced expression of growth factors and cytokines is driven by inflammation, the action of viral proteins and regenerative response to cell loss. The mechanism whereby these factors affect gene expression include DNA mutations with consequent activation or inactivation of gene promoters is still being studied.[14]

Pathophysiologic mechanisms

Oxidative stress has emerged as a key player in the development and the progression of liver cirrhosis which is known to be a precursor of HCC.[15] Research has shown that oxidative stress usually result to all forms of chronic liver injury and plays a crucial role in hepatic fibrogenesis and cancer development.[16] Reactive oxygen species (ROS) derived by molecular oxygen include free oxygen radicals [e.g superoxide (O_2-), hydroxyl radical (OH^-)] as well as non-radical ROS [e.g hydrogen peroxide (H_2O_2), organic hydro-peroxides, and hypochloride] released by damaged parenchymal cells directly contribute to the cell degeneration process which activate redox-sensitive intracellular pathways inducing their activation and increasing collagen synthesis.[12] This stressful condition is known to play a major role in cancer development mainly by enhancing DNA damage, and by modifying some key cellular processes. DNA damage caused primarily by hydroxyl radicals, superoxide radicals, and hydrogen peroxide playing an important role in cancer development.[16] Furthermore, heat shock challenges(HSCs) are also an important source of ROS in liver fibrosis.[12,17] Cytochrome P450 2E1 is the main

source of ROS in hepatocytes, while phagocytic and non-phagocytic nicotinamide adenine dinucleotide phosphate (NADPH) oxidase is the key source, respectively, in Kupffer cells and HSCs.[18] The phagocytic form of NADPH oxidase expressed in Kupffer cells has several important functions: besides its defensive effect against bacterial products reaching the liver through the portal system, NADPH oxidase in Kupffer cells is also activated by several stimuli (i.e. alcohol metabolites and tumour necrosis factor-α) to produce ROS. Kupffer cells derived ROS consequently drive pro-inflammatory effects and sensitize hepatocytes to undergo apoptosis, being involved in fibrogenesis and carcinogenesis. Conversely, recent data indicate that HSCs express the non-phagocytic form of NADPH oxidase and demonstrate that ROS participate in the activation and fibrogenic actions of HSCs *in vitro*.[16]

Inflammation, Cytokines and Hepatocellular carcinoma

Studies spanning many decades, have begun to elucidate the important role of cytokines in HCC**.** Growing evidence indicates the involvement of cytokines in hepato-carcinogenesis.[19] As a result of this trend, attempts have been made to clarify changes in cytokine expression levels in patients with HCC. The mRNA and protein expression of cytokines in HCC and liver-related diseases has been demonstrated by immune-histochemistry (IHC), quantitative real-time PCR (qRTPCR), and ELISA.[19] As occurs in most tissues, transforming growth factor-b1 (TGF-β1) is the major fibrogenic cytokine in the liver and it has been clearly demonstrated to play an active role in the process of myofibroblast activation.[16] Connective tissue growth factor (CTGF) promotes tumour growth, angiogenesis, migration and invasion.[16] The expression levels of pro- and anti-inflammatory cytokines have been quantified in HCC tumours and comparative normal samples. Th2-like cytokine profile, including in IL-4, IL-8, IL-10, and IL-5 and Th1-like cytokines including IL-1α, IL-1β, IL-2, IL-12p35, αIL-12p40, IL-15, TNF-α, and IFN have been demonstrated to play a significant role in HCC.[20]

Despite a glut of studies relating to cytokines and HCC, many of which have yielded results that are therapeutically promising, the full extent of the cytokine network and how it contributes to HCC is still not fully understood.[20]

Therapautic options for Hepatocellular carcinoma

Over the years, there have been research into the hepato-carcinogenic pathways leading to the development of HCC. This has lead to the identification of potential targets for intervention and the targeted therapy for the treatment of HCC. The approaches to the treatment of HCC are many. However, surgical resection or liver transplantation are the first-line treatment for patients affected by HCC.[12,15] Surgery is the most important therapeutic approach for patients with HCC.[21]

Treatment guidelines for HCC in Europe were published in 2001 as the European Association for the Study of the Liver (EASL) Consensus[22] and in the USA in 2004 as the American Association for the Study of Liver Diseases (AASLD) Clinical Practice Guidelines.[23] Both guidelines adopted the Barcelona Clinic Liver Cancer (BCLC) staging system, but the latter included a new entity of 'Stage 0 HCC' (carcinoma in situ).[24]

Barcelona Clinic Liver Cancer is a valuable assessment tool that incorporates data on the patient's performance status, number and size of nodules, cancer symptoms, and liver function as determined by the Child–Pugh classification system. HCC may be difficult to diagnose, as it may present with a single, asymptomatic lesion measuring less than 2 cm in diameter, with no vascular or distant metastases.[24]

Surgical Resection

Surgical resection is currently the standard option and treatment of first choice for HCC, given appropriate patient selection. This is currently the only strategy for achieving a potentially satisfactory long-term outcome in patients with HCC and should, therefore, be the treatment of first choice as long as the tumour is adjudged to be resectable.[21] Surgical resection in these cases is associated with an overall survival rate of 90%. Safety of surgical resection has been established over the last few decades, and the mortality rate after hepatic resection in experienced centres is less than 5%. Options for surgical resection are in part determined by the severity of underlying liver disease, which is reflected by the Child-Pugh classification[25] or the Model for End-stage Liver Disease (MELD) score, which is a prospectively developed and validated chronic liver disease severity scoring system to predict survival.[26]

The criteria for selection of patients eligible for surgical resection based on the liver function and tumour status have been proposed.[27] The method adopted for pre-operative evaluation of liver function, which would determine the extent of resection of the liver, may vary among districts and institutions. In most Western countries, the presence/absence of portal hypertension is emphasized as an important criterion, which is estimated along with the Child-Pugh class, and is diagnosed based on the findings in hepatic venous pressure gradient, radiological images of splenomegaly and abdominal collaterals, thrombocytopenia (platelets <100,000/mm^3), and presence of oesophago-gastric varices. One of the classical staging systems under the BCLC criteria

included the criteria for the selection of appropriate treatments and recommended hepatic resection only for patients with a solitary HCC without portal hypertension. Furthermore, this criterion is also included in the guideline for the treatment of HCC established by the AASLD and EASL.[24]

The indications for surgical resection have expanded even to advanced HCCs, as complicated hepatic resection can be safely performed owing to advances in the surgical techniques. At the same time, the minimally invasive approach, namely, laparoscopic hepatectomy, has also come to be increasingly advocated over the last decade. The safety and feasibility of laparoscopic hepatectomy after the learning curve period has been established in high-volume institutions, and the indications have been expanded from partial resection of benign tumours to major resection of malignant tumours, including HCCs.[27]

A major problem is the high recurrence rate even after curative resection, especially in the remnant liver. Although repeat hepatectomy may prolong survival, the suitability may be limited due to multiple tumour recurrence or background liver cirrhosis. Multimodality approaches combining other local ablation or systemic therapy may help improve the prognosis. On the other hand, minimally invasive or laparoscopic hepatectomy has become popular over the last decade. Although the short-term safety and feasibility has been established, the long-term outcomes have not yet been adequately evaluated.[25] Advanced HCCs, such as huge tumours measuring more than 10cm in diameter and tumours associated with macro-vascular invasion or tumour with extra hepatic metastasis, surgical resection is indicated because local ablation, systemic chemotherapy or liver transplantation is not effective.[25]

Laparoscopic Hepatectomy

Laparoscopic liver resection was first reported in the early 1990s for partial resection of segment 6 for a 6cm focal nodular hyperplasia and wedge resection of segment 5 for colorectal liver metastases.[27]

Several surgeons advocate laparoscopic resection for HCC, especially that in a cirrhotic liver, due to its less-invasive characteristic, because less liver mobilization is required and the amount of intravenous fluid needed is reduced due to the minimized insensible fluid loss occurring during this operation as compared with that during open liver resection.[28] As for the survival outcomes, only a few reports based on studies of a small number of cases each have been published, which have shown a comparable short-term prognosis in patients undergoing laparoscopic hepatectomy as compared to that in patients undergoing open hepatectomy.[29] The indications for laparoscopic resection should be appropriately decided according to the types and conditions of the tumours and the technical skills of the surgeons. More importantly, the safety and oncological curative potential must be accorded priority; therefore, conversion to an open procedure should be expedited if bleeding cannot be controlled laparoscopically, or an adequate resection margin cannot be obtained, or adhesions preclude the laparoscopic procedure.[28,29]

Local Ablation

Local ablation of HCC has gained clinical positioning in treating small HCCs. Local ablative therapies such as Radio-frequency ablation(RFA), percutaneous ethanol injection(PEI), and microwave coagulation therapy(MCT) have now emerged as treatment options.[30] Several recent randomized trials of adequate quality have shown RFA to be more effective than the once-conventional method of PEI in treating patients with small hepato-cellular tumours (2 to 3 cm in diameter), with lower rates of local recurrence and higher rates of overall and disease-free survival.[27] Short-term outcomes are excellent, with overall survival rates of 100% and 98% at 1 and 2 years, respectively, but long-term outcomes are consistent with the non-curative nature of RFA, with 5-year recurrence rates as high as 70%. The studies carried out in Europe comparing RFA and surgical resection showed no significant differences in overall or recurrence-free survival; as expected, RFA was associated with lower rates of complications and hospitalization.[27]

Transarterial Chemoembolization (TACE)

Transarterial chemoembolization (TACE) takes therapeutic advantage of the liver's dual blood supply. Hepatocellular cancer cells are preferentially supplied by branches of the hepatic artery, whereas hepatocytes are preferentially supplied by branches of the portal vein.[31] By infusing chemotherapeutic agents directly into vessels supplying the tumour, and subsequently obstructing these vessels with an embolization material, the HCC receives prolonged exposure to the chemotherapeutic agent, and is deprived of it's blood supply. TACE has been shown to improve survival among patients with preserved liver function, particularly those with Child–Pugh class A cirrhosis who do not have extra-hepatic metastases, vascular invasion, or prominent cancer-related symptoms.[32]

Embolic agents used include gelatin sponges, polyvinyl alcohol (PVA) particles and microspheres. The use of steel coils, autologous blood clots and degradable starch microspheres as embolic agents has also been reported.[33]

A novel system combining PVA beads and doxorubicin as drug-eluting beads (DEB) is supposed to release doxorubicin in a slow and controlled manner. A recent study of TACE using DEB has shown that DEB could further improve the pharmacokinetics of the injected doxorubicin and reduce drug-related side effects maintaining the same therapeutic efficacy as TACE.[34]

Lipiodol has been used to treat HCC since it was first reported in 1974. When injected, causes embolization of small vessels of the liver. Lipiodol functions as a micro-vessel embolic agent, as a carrier of chemotherapeutic agents and as an augmenter of anti-tumour effects of TACE by efflux into the portal veins. Though the use of Lipiodol in TACE has been challenged, there is substantial evidence that confirms the efficacy of the use of Lipiodol. Lipiodol is still widely adopted in TACE protocols.[35]

Some chemotherapeutic agents are usually suspended in iodized oil and are delivered as close to a tumour as possible followed by the embolization process. Several chemotherapeutic agents have been used with doxorubicin, and cisplatin being the most common. The usual dose for doxorubicin and cisplatin per session is 10-70 mg, and 10-120 mg respectively.[35] A few RCTs have failed to show significant differences in survival between the use of doxorubicin and other drugs such as cisplatin or epirubicin, and to date, there is no evidence of the superiority of any single chemotherapeutic agent over other drugs or for mono-drug chemotherapy versus combination chemotherapy.[36]

Radio-embolization

Radio-embolization (RE) with yttrium-90 microspheres has recently been used as palliative treatment for patients with Child–Pugh class A cirrhosis and intermediate-stage HCCs.[35] RE has been demonstrated to allow loco-regional therapy of patients with HCC not eligible for TACE or other local therapies.[37] However, there have been no controlled trials comparing yttrium-90 radio-embolization with TACE or with other types of treatment. RE with Y-90 glass microspheres for patients with advanced HCC is a safe and effective treatment which can be utilized even in patients with compromised liver function.[37]

Liver Transplantation

At present, liver transplantation is considered the only curative treatment option for HCC. The current 1-year and 5-year survival rates for HCC patients undergoing orthotopic liver transplantation are 77.0% and 61.1% respectively. The 5-year survival rate has steadily improved from 25.3% in 1987 to 61.1% during the most recent period studied (1996 to 2001).[37]

Among patients with unresectable disease, the most viable surgical option is often liver transplantation, frequently in conjunction with less invasive adjuvant therapy such as TACE or percutaneous ablation.[38] However, liver transplantation is not appropriate for all individuals, and thorough evaluation is necessary to prudently allocate the scarce resources available. The Milan criteria, published in 1996, have served as appropriate selection criteria for patients with HCC who are potential candidates for liver transplantation.[39] In an attempt to identify the most appropriate transplant patients, the Milan criteria, which consider both the number and size of tumour nodules, has emerged as the international standard by which potential transplant candidates are evaluated.[22,39] The Milan criteria which state that patients are eligible for transplantation if they have a solitary tumour less than 5 cm or up to 3 tumours, each no more than 3 cm have been validated in several studies.[39] When surgeons adhere to these criteria, 5-year survival rates after transplantation range from 70% to 80%, and tumour recurrence rates are approximately 10%.[39]

The University of California San Francisco (UCSF) criteria (solitary lesion $\leq$6.5 cm or $\leq$3 lesions each $\leq$4.5 cm, with the total combined tumour diameter $\leq$8 cm) have been evaluated in several recent studies. Since the initial report by Yao and colleagues that demonstrated acceptable survival rates using the UCSF criteria (90% 1-year survival rates and 75% 5-year survival rates), subsequent studies of expanded criteria have continued to demonstrate outcomes similar to those achieved with the Milan criteria.[40]

Chemotherapeutic agents

Sorafenib

A multi-targeted agent, Sorafenib is the first systemic therapy to demonstrate a survival benefit in a randomized trial for unresectable HCC, and has received FDA approval for this indication.[41] A molecular-targeted agent that inhibits tumour cell proliferation and angiogenesis by inhibiting RAF serine-threonine kinase and VEGF, PDGF, Flt-3, c-Kit receptor tyrosine kinase.[42] According to the consensus statements of the Japan Society of Hepatology in 2010, Sorafenib is recommended for advanced HCC with extra-hepatic spread or major vascular invasion such as invasion of the first branch of the portal vein or the main portal branch of the portal vein in patients with Child-Pugh A liver function. Sorafenib is the first, and so far the only drug that has shown overall survival benefits in patients with HCC in a multi-centre, double-blind, placebo-controlled randomised phase III trial (SHARP trial). Median overall survival increased from 7.9

months in the placebo group to 10.7 months in the Sorafenib group.[43]

Emerging Therapuetic Agents

Sunitinib, Brivanib and Erlotinib, and monoclonal antibodies, such as Bevacizumab and Cetuximab, are currently in different phases of clinical trials to determine their efficacy in the treatment of advanced HCC.[44]

Computed tomography-guided brachytherapy

Computed tomography(CT)-guided brachytherapy has been used to treat primary and metastatic liver cancers, including very large tumours >10cm. Prospective trials of CT-guided brachytherapy have been performed with promising survival rates for liver metastases and HCC respectively.[45]

Adjuvant Iodine-125 brachytherapy

This is a procedure carried out after complete hepatectomy. ^{125}I implant into the cut surface of the remnant liver is an effective adjuvant modality for HCC patients after radical hepatectomy. A RCT has demonstrated that ^{125}I brachytherapy is safe and could delay post-operative tumour recurrence. However, more multi-centre RCTs of larger scale are needed to confirm these findings.[46]

Conclusion

Since HCC is largely a very difficult disease to treat and some of the causes and risk factors are well established, surveillance, early diagnosis and definitive treatment remain the key to reducing the morbidity and mortality associated with the disease. Inspite of recent advances in the management of HCC, liver transplantation is still the best curative treatment option.

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Clinical Presentation Of Patients And Distribution Of Colonic Diverticula During Colonoscopy At A Tertiary Hospital In South-West Nigeria

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Abstract

Colonic diverticula disease is an acquired disease which affects adults and is frequently referred to as a western world disease. In Nigeria, studies on colonic diverticulosis are sparse and few of them are case reports. The aim was to describe the clinical presentation and distribution of colonic diverticulosis in patients who presented for colonoscopy.

This study was carried out at the endoscopy unit of the University College Hospital, Ibadan. All consecutive patients who were referred for colonoscopy and who were found to have colonic diverticula during the procedure were recruited into the study. The presence of one or more saccular outpouchings of the colon was described as colonic diverticulosis. The location and distribution of the diverticula within the colon were also described.

The results of 63 patients were analysed, comprising 40 (63.5%) males and 23 (36.5%) females, giving a male to female ratio of 1.7:1. The mean age of the patients was 63.5±11.4 years with a range of 31-91 years. Haematochezia was the most common symptom, followed by abdominal pain. The most frequent locations were the ascending and sigmoid colon in 35 (55.6%) and 33 (52.4%) patients respectively.

In conclusion, the most common symptom of colonic diverticulosis was haematochezia and the most common site was the ascending colon in our practice.

Keywords: Colonic Diverticula, Rectal diverticula, Haematochezia, Nigeria

Introduction

Colonic diverticula disease is an acquired disease which affects adults and is frequently referred to as a western world disease.[1] Diverticula are out-pouches that form within the colon as a result of herniation of the mucosa and submucosa at the entry points of the small arteries that supply the colon. These entry points are described as the weak sites of the muscle layer.[2,3]

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The prevalence of colonic diverticulosis is believed to increase with age and affects about 70% of those who are 80 years and older.[4,5] A rising incidence of the disease has been observed in the United States, Canada and Europe.[6,7,8] Although, colonic diverticulosis has been said to be rare in Africa and Asia, rising incidence has been observed in recent times. In Southeast Asia, the prevalence ranges between 8-22%.[9,10] A prevalence of 0.5-1.7% has been reported in China and South Korea.[11]

In Nigeria, studies on colonic diverticulosis are sparse and few of them are case reports.[12,13] However, in a study done about 30 decades earlier in Ibadan, 603 cases were reported on barium enema.[14] In another study carried out at Ile-Ife, Nigeria using a combination of barium enema, abdominal CT scan and/or colonoscopy, 40 cases were described.[15]

This study was carried out to describe the clinical presentation and distribution of colonic diverticulosis in patients who presented for colonoscopy.

Patients and Method

This was a descriptive cross-sectional study which was carried out at the endoscopy unit of the University College Hospital, Ibadan. All consecutive patients who were referred for colonoscopy and who were found to have colonic diverticula during the procedure were recruited into the study. The procedures followed in this study were in accordance with the revised Helsinki Declaration (2013).

Information obtained from each patient included the age, sex, indication for the procedure, history of other symptoms such as, abdominal pain, diarrhoea, constipation, haematochezia, bloating, fever, weight loss among others. The presence of one or more saccular outpouchings of the colon was described as colonic diverticulosis. The location and distribution of the diverticula within the colon were also described. Pancolonic distribution was defined as involvement of all the parts of the colon from the rectum to the caecum. Diverticulitis was said to be present when there was erythema or hyperaemia surrounding one or more diverticula with or without systemic symptoms such as fever and/or abdominal pain.

The data were analysed using SPSS version 17.0 with level of significance at $p < 0.05$.

Results

The results of 63 patients were analysed, comprising 40

(63.5%) males and 23 (36.5%) females, giving a male to female ratio of 1.7:1. The mean age of the patients was 63.5±11.4 years with a range of 31-91 years. The age category showed that, 21 (33.3%) of the patients were 70 years and older, while only 1 (1.6%) patient was in the age category of 30-39 years. (Figure 1).

The frequency of symptoms showed that haematochezia was the most common, followed by abdominal pain. (Table 1)

With respect to the number of sites of diverticula in the colon, it was observed that 22 (34.9%) patients had diverticula located in just one site in the colon, while in 2 (3.2%) patients, it was pancolonic. (Table 2.)

The results showed that the most frequent location was the ascending colon, which was observed in 35 (55.6%) patients, followed by the sigmoid colon in 33 (52.4%) patients. (Table 3.)

When the colon was divided into right (caecum, ascending, hepatic flexure) and left (splenic flexure, descending, sigmoid, rectum) colon, diverticula were more frequently observed in the right colon (83) compared to the left colon (81). (Table 4).
Univariate analysis of the gender and location of the diverticula in the colon showed male predominance for all the sites. However, the gender difference was not statistically significant. (Table 5).

The results also showed that only 5 (7.9%) patients had evidence of diverticulitis at colonoscopy. In three of these patients, haematochezia was the main symptom, while abdominal pain was the main symptom in one. The remaining patient presented with fever, abdominal pain, diarrhoea and haematochezia.

Discussion

The true prevalence of colonic diverticulosis has been difficult to determine because, most patients with this disease remain asymptomatic. Colonic diverticulosis has been observed to have geographic distribution, being most common in the western populations and said to be rare in rural Africa and Asia.[1,16,17] This present study shows that colonic diverticulosis is not as rare in Africa as was previously thought. This perceived rise in the prevalence of the disease was also observed by some previous studies carried out in Africa.[14,18,19,20] This increase in the prevalence of colonic diverticulosis has been attributed to a change in the African high fibre diet to a western low fibre diet.[14,21]

Also, Africans have been reported to have higher stool weights and reduced stool transit times compared to Caucasians, and these factors are observed to reduce the incidence of colonic diverticulosis.[22,23] However, in a study by Peery *et al*,[24] there was no association observed between low fibre diet and the presence of colonic diverticulosis. But, Gear et al[25] observed that colonic diverticulosis was less prevalent in vegetarians who consumed more fibre.

Apart from diet, other factors especially genetic predisposition may be of importance in the aetiology of diverticular disease among Africans.Some reported case series of colonic diverticulosis among

Table 1: Frequency of symptoms in the patients

Symptom	n (%)
Haematochezia	35 (55.6)
Abdominal pain	25 (39.7)
Weight loss	22 (34.9)
Constipation	13 (20.6)
Excessive flatulence	10 (15.9)
Bloating	9 (14.3)
Diarrhoea	8 (12.7)
Fever	6 (9.5)
Nausea	4 (6.3)
Vomiting	4 (6.3)
Alternating diarrhoea & constipation	4 (6.3)

Table 2: Number of colonic sites of diverticula with the number of patients

Number of colonic sites of diverticula	n (%)
1	22 (34.9)
2	13 (20.6)
3	7 (11.2)
4	6 (9.5)
5	2 (3.2)
6	5 (7.9)
7	6 (9.5)
Pancolonic	2 (3.2)
Total	63 (100)

Table 3: Univariate analysis of gender and colonic sites of diverticula

Site of diverticula	Male, n (%)	Female, n (%)	p-value
Caecum	21 (52.5)	10 (43.5)	0.5
Ascending colon	21 (52.5)	14 (60.9)	0.5
Hepatic flexure	14 (35)	3 (13)	0.06
Transverse colon	21 (52.5)	7 (30.4)	0.09
Splenic flexure	8 (20)	2 (8.7)	0.2
Descending colon	21 (52.5)	8 (34.8)	0.2
Sigmoid colon	22 (55)	11 (47.8)	0.6

siblings of the same family may support this notion.[26,12] Colonic diverticulosis is seen more frequently in the older age group,[27,28,29] and this was our finding in this present study where, 88.9% of our patients were 50 years and older. This is also similar to the findings of Alatise *et al*[15] at Ile-Ife, which is in the same geographical zone where this present study was carried out. Our finding is also similar to the findings in other parts of the world.[20,30,31]

In this study, male predominance was observed and this is similar to the findings of other studies conducted in Nigeria[15] and other parts of the world.[28,30] However, Eide and Stalsburg observed a female predilection in an autopsy study of Norwegians.[29] Madiba and Mokoena also reported female predominance among South Africans.[18] But, some other studies did not find any sex predilection.[20,31] The apparent inability to determine the true sex predilection of the colonic diverticulosis may be connected with the asymptomatic nature of the disease in most instances.

The male predominance observed in our study might be connected with the predominant symptom presented by the patients, which was haematochezia. McConnell *et al*[32] observed that men with colonic diverticulosis tend to present more with haematochezia whereas, women tend to present more with strictures and obstructions.

Colonic diverticulosis is believed to be an asymptomatic disease in most patients.[33] However, the various symptoms that a patient can present with include, abdominal pain, excessive flatulence, constipation, bloating, anorexia, diarrhoea, nausea.[34] These symptoms were observed with various frequencies in our patients but, haematochezia was the most common presentation.

Although, rectal bleeding is said to point to a complicated disease,[35] it was the major symptom presented by patients in several other studies.[15,19,20,36] The reason why most of our patients presented with rectal bleeding might be connected with the predominance of right sided diverticula observed in most of our patients. It has been reported that patients with right sided diverticula tend to present with rectal bleeding as their major symptom.[37]

The distribution of the diverticula in our patients showed the most frequent location to be the ascending colon. This is in contrast to the findings of Alatise *et al*,[15] in which pancolonic disease was observed, and that of Kiguli and Kasozi, in which sigmoid colon was the commonest site.[20]

Western population is said to have predominantly sigmoid diverticulosis compared to the Asians who have predominantly right sided disease.[28,38,39] Right sided diverticula are believed to be congenital in origin, whereas sigmoid diverticula are believed to arise due to raised intracolonic pressure as a result of low fibre intake.[23,25] This observation would support the finding of predominantly right sided disease in our study, but might not explain the findings of Alatise *et al* (pancolonic disease) and that of Kiguli and Kasozi (sigmoid colon disease). It may therefore, imply that factors other than dietary fibre affect the distribution of diverticula within the colon.

In this present study, diverticulitis was seen less frequently (7.9%). Diverticulitis is believed to be the most frequent complication of colonic diverticulosis, seen in 10-25% of patients.[34] Although, the most presenting symptoms are abdominal pain, fever and leucocytosis, the most common symptom in our patients with diverticulitis was haematochezia. The explanation for this is not readily available.

One important finding in this present study was the high prevalence (14.3%) of rectal diverticula among our patients. Rectal diverticula are said to be extremely rare. Prevalence rates of 2-2.4% have been reported among patients with colonic diverticulosis.[40,41] Fagundes *et al*[42] reported a prevalence of 0.15% of all colonoscopies performed over a ten-year period, and a prevalence of 0.74% among patients with colonic diverticulosis. Two major reasons have been proposed

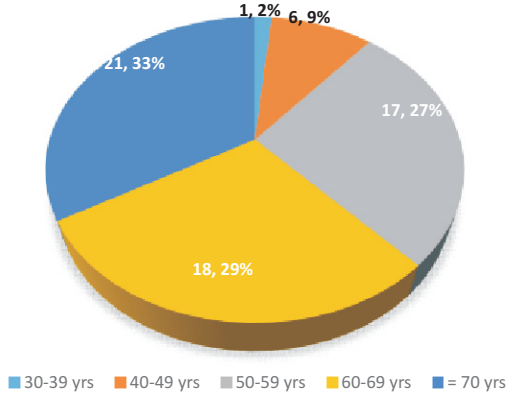

Figure 1: Age category of the patients

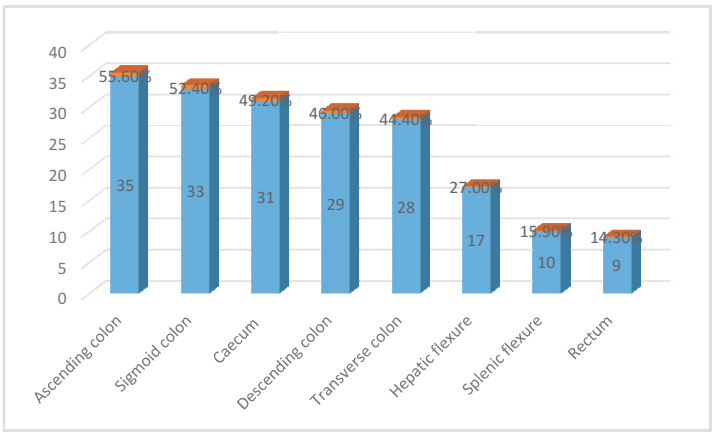

Figure 2: : Colonic sites of diverticula in the patients

for the low occurrence of rectal diverticula. First, the muscle fibres of taenia coli are said to surround the rectum and thereby reinforce it against intraluminal pressures.[43] Secondly, the rectum is thought to be exposed to much less internal pressure from accumulated faeces, as well as a much reduced peristaltic activity compared to the sigmoid colon.[44]

Although, the actual cause of rectal diverticula is not known, some of the acquired causes include recurrent faecal impaction, constipation, rectal trauma, relaxed recto-vaginal septum.[45,46,47] In our patients with rectal diverticula, the actual cause could not be identified, although two (22%) of them had constipation.

In conclusion, the most common symptom of colonic diverticulosis was haematochezia and the most common site was the ascending colon in our practice.

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Five Year Review of Oropharyngeal Cancer Patients At University of Ilorin Teaching Hospital, North Central Nigeria

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Abstract

Oropharyngeal tumours constitutes 10 to 12% of all head and neck malignancies, and Squamous cell carcinoma (SCC) is the most common histological variant seen in 90% of cases. Studies have confirmed the high prevalence of the disease among males, and the roles of alcohol intake and cigarette smoking as risk factors are well documented. This is a retrospective review of socio-demographic and risk factors of oropharyngeal cancers in our practice. All cases of orophyryngeal cancer seen at Ear, Nose and Throat Department of University of Ilorin Teaching Hospital (U.I.T.H) between July 2008 and June 2013 were reviewed. UITH has over 600 beds and is a tertiary institution for the University Medical School.

There were 27 cases, 15 (54.6%) were within 40-60 years, 7 (27.3%) were below 40 years, and 5 (18.2%) above 60 years. Seventeen (63.6%) were females and 10 (36.4%) males with male to female ratio of 1:1.7. Twenty (72.7%) were non-smokers while 7 (27.3%) were smokers. Ten cases (36.4%) had history of alcohol intake while 17 (63.4%) did not take alcohol. Lateral wall and tonsil tumours constituted 55.6% (15) of the total, closely followed by base of the tongue tumours 7 (27.3%), then soft palatal tumours 5 (18.2%). There was none in the posterior pharyngeal wall. Seven patients (26.0%) had surgery followed by chemoradiation, 3 (11.1%) had chemoradiation only, while 17 (63.4%) either declined surgery or defaulted clinic follow-up. Two of the patients (7.4%) had associated HIV infection.

This study showed relative high incidence of oropharyngeal tumours in young and middle aged females; who are non-alcohol drinking and non-smokers. Incidental finding of HIV infection in some of the patients is a pointer to the possible role of sexually transmitted viral infections in the epidemiology of oropharyngeal cancers and a focus for preventive measures.

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Key words: Oropharyngeal cancer, risk factor, sexually transmitted viral infection.

Introduction

Head and Neck Cancers are relatively rare type of tumours in comparison with other malignant tumours[1]. The oropharynyx is the posterior relation of the oral cavity and it is anatomically divided into base of tongue, palatine tonsil, soft palate and posterior pharyngeal wall. Mitotic lesions in any of these sub-sites may initially be silent and become advanced by the time of presentation.Oral and pharyngeal cancers are the sixth most common cancers in the world.[2,3] And pharyngeal cancers localized to the oropharynx constitute about 10-20% of all malignancy of the upper aerodigestive tract and approximately 130,000 new cases are recorded per year in the United State and Europe[4]. Infection-attributable cancer constituted 17.8% of the global cancer burden and human immunodeficiency virus (HIV) and human papilloma virus were known principal agents[5]. In Africa, oral and pharyngeal cancers are the commonest Head and Neck cancers with overall high mortality rate of up to 20% in some series[6]. Generally, late presentation is largely responsible for high mortality in Nigeria with poverty as the root cause.

The male gender is affected 3-5 times more than the female,[4,7,8] and the most significant etiological factor is related to tobacco either in isolation or in synergy with alcohol use[9]. Aside from tobacco smoking, other life style risk factors are tobacco chewing, chewing of betel quid and areca nut, diets low in fruits and vegetables and certain strains of virus, such as the sexually transmitted human papilloma virus.[9,10] Occupational and environmental pollutants and endogenous risks have also been identified.[4,11] Exclusive tobacco consumption is more likely to contribute to epithelial dysplasia than exclusive alcohol use suggesting that tobacco has an independent role in the aetiology of mucosa epithelial dysplasia, which is the hallmark for cancer development.[12]A meta-analysis showed three-fold increase risk of oral cavity cancer and seven fold risk of pharyngeal cancer in current smokers compared with people who have never smoked[13]. However, recent trend have shown that pattern of oropharyngeal tumour are changing with more cases seen among non-smoker, non-alcohol drinker.[14] Andrew et al., demonstrated that 25% of oropharyngeal SCC are unlinked to typical

risks.[15]Available evidence, now considered HPV infection as a validated risk factor for oropharyngeal SCC in both men and women, even in the absence of smoking and alcohol consumption.[14-17] Given this emerging evidence, it has been suggested that use of prophylactic HPV vaccines directed against HPV-16 and HPV-18 infection may reduce Oropharyngeal SCC incidence.[18]

Oropharyngeal cancer has a poor prognosis in the low resource countries due to late presentation.[19]Hence, the need for health education towards preventive measures, early detection and treatment in our environment. This study is a review of socio-demographic variables in the epidemiology of oropharyngeal tumour in a tertiary health institution in Nigeria.

Patient and Methods

This is a descriptive retrospective study of all clinical records of patients who presented to the Ear, Nose, and Throat Department of The University of Ilorin Teaching Hospital with a diagnosis of oropharyngeal cancer from July 2009 to June 2013. Data extracted included Age, sex, occupation, duration of symptoms, predisposing factors, smoking habit and other social history. The site of tumour and clinical features of disease were noted in addition to management modalities of these patients. Data was complemented with information from pathology unit where necessary. Data was analysed using a 2011 IBM SPSS (Statistical Package for social sciences) for windows, version 2.0; Armonk, NY. Results were presented in simple charts and tables utilising descriptive statistics of frequency and percentages and Microsoft excel™ software for graphical presentations. Incomplete documentation and loss to follow up were limitations in this study.

Results

There were a total of 27 cases of oropharyngeal tumours, 17 (63.6%) were females and 10 (36.4%) males with male to female ratio 1:1.7. (Fig. 1). Peak age group was 40-60 years with 15 (54.6%) patients in this category, 7 (27.3%) were below 40 years and 5 (18.2%) above 60 years. (Table 1). Twenty (72.7%) were non-smokers while 7 (27.3%) were smokers. Ten (36.4%) had history of alcohol intake while 17 (63.4%) did not take alcohol. (Fig. 2). Anatomical discription of tumour location revealed that lateral wall and tonsil tumours constituted 15 (55.6%) of the total; followed by base of the tongue tumours 7 (27.3%), and soft palatal tumours 5 (18.2%). None in the posterior pharyngeal wall.(Table2).Invasive SCC was the most common histology type; 22 (81.5%) followed by salivary malignancies; carcinoma ex-pleumophic 2 (7.4%) and adenoid cystic carcinoma 1 (3.7%) (Table: 3, Fig. 3 and 4).Seven patients (26.0%) had surgery followed by chemo-radiation, 3(11.1%) had chemo-radiation only, while 17 (63.4%) either declined surgery or defaulted from clinic follow-up. (Table 4).Two of the patients (7.4%) had associated HIV infection.

Discussion

This study found a female preponderance in the occurrence of oropharyngeal tumour with a male to female ratio of 1:1.7 which contradict the common pattern of higher incidence in males in the literature and previous studies in this country.[4,7,820-24] This finding suggest a probable changing trend in the epidemiology of oropharyngeal cancers as the female gender is no

Table 1: Age Distribution of Patients

AGE GROUP OF PATIENTS	n(%)
20-40	7(27)
40-60	15(55)
61-80	5(18)

Table 2: Distribution of Tumour by Subsite

Subsite	n(%)
Tonsil/ Lateral Pharyngeal Wall	15(55)
Base Of Tongue	7(27)
Soft Palate	5(18)
Posterior Pharyngeal Wall	0(0)

Table 3: Histological diagnosis of oropharyngeal tumour

Histology types	Frequency	Percent
Invasive Squamous Cell Carcinoma	22	81.5
Carcinoma expleumophic	2	7.4
Adenoidcystic carcinoma	1	3.7
Anaplastic carcinoma	1	3.7
Burkits Lymphoma-	1	3.7

Table 4: Treatment offered to patients

Treatment	n(%)
Surgery only	Nil (0%)
Surgery followed by chemoradiation	7 (26.0%)
Chemoradiotherapy only	3 (11.1%)
Declined treatment	17(63.0%)

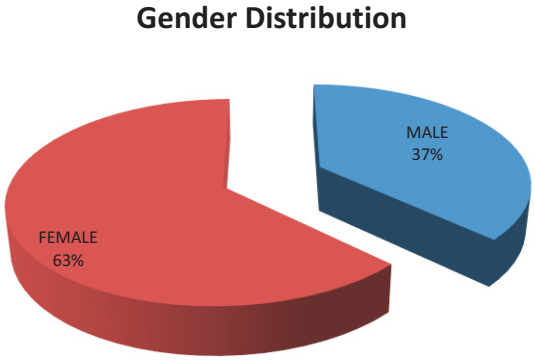

Fig. 1: Gender distribution of patients

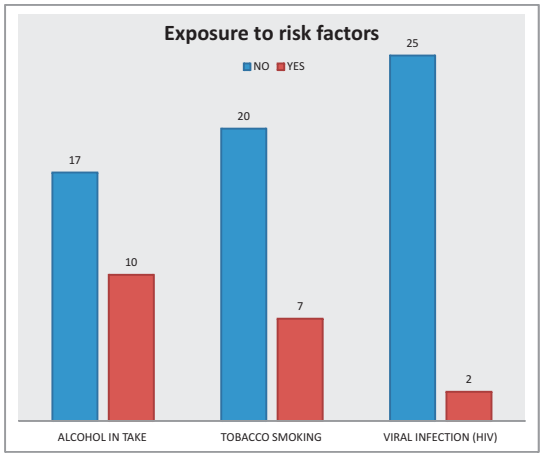

Fig. 2: Bar chart showing frequency ofexposure to risk factors

less exposed to known predisposing factors than the male counterpart.(Fig. 1). Alcohol use and tobacco smoking is rampant among the females than documented but most women do not often divulge information about their habits for socio-cultural reasons. Besides, the female gender bears high risk of orogenital infections predisposing to cancers.

Peak incident was in the 40-60 age group (Table 1), this is similar to the pattern in earlier studies in Ilorin [22, 23] and consistent with findings in other part of the country.[20]

Majority 72.7% (20/27) of the patient in this study were non-smokers while 27.3% (7/27) of patients indulged in cigarette smoking. Similarly, many of the patients 63.0% (17/27) had never consumed alcohol, while 37.0% (10/27) disclosed history of alcohol consumption.(Fig. 2). This finding suggests possibilities of other risk factors at play. Other forms of tobacco use other than active smoking were not inquired from the patient. Moreover, use of traditional concoctions, locally brewed spirit (Berukutu and Ogogoro) were missed out in the documentation and some of these may have carcinogenic potentials.[25]

Another important factor is viral infection; history of oro-genital sexual practices and exposure to HPV infection which most patient will not readily admit because of cultural and religious reasons. Besides, serological test for HPV is not routinely done for Head and Neck cancer patients in this environment. A retrospective study of 45 cases of oropharyngeal cancers in North Eastern Nigeriareported SCC as the most common histological type 73.4% (33/45) and found 2 of the patients (4.4%) with Kaposi's Sarcoma; these findings tallies with that documented in previous studies.[4, 20, 21] Similarly, our study found invasive SCCas the most common histology type; 22 (81.5%) followed by salivary malignancy (carcinoma ex-pleumophic and adenoid cystic carcinoma) 3(11.1%). (Table: 3). However, the two cases of HIV positive patient in this study had no documented evidence of kaposi sarcoma.

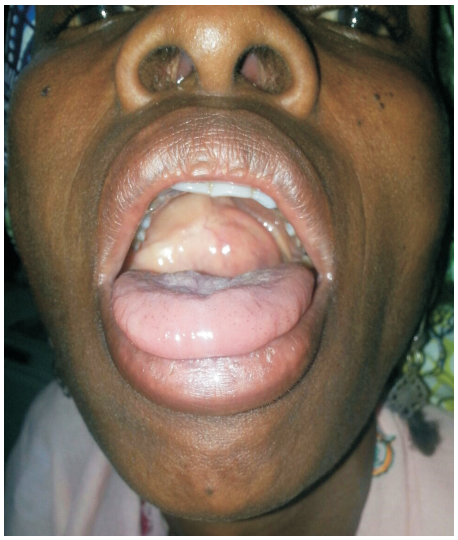

Fig. 3: Adenocystic carcinoma of the soft palate, Excision and reconstruction done followed with radiotherapy

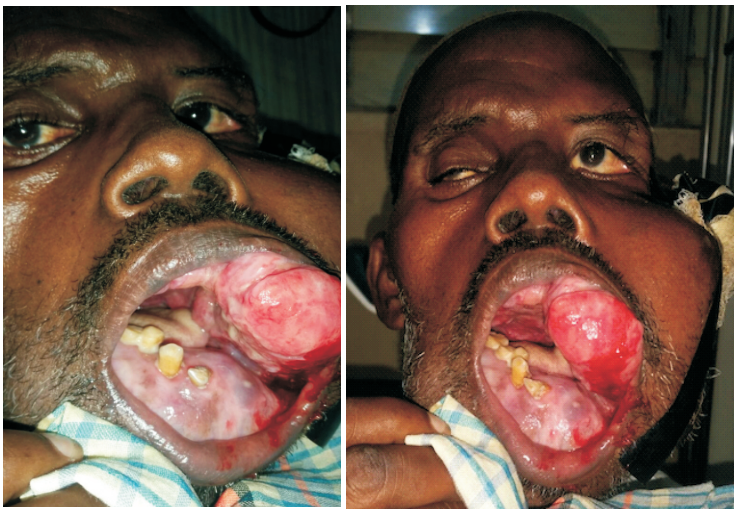

Fig. 4a and b: Advanced cancer of left tonsil with invasion of adjacent structures; mandible, hard palate and pterigoid muscles.

Lateral pharyngeal wall (tonsils) tumours constituted the most common site in this study, followed by base of the tongue and soft palatal tumours; but none of the patient in this series had posterior pharyngeal wall tumour.(Table 2).This is at variance with the findings of Garandawa et al in Maiduguri, Nigeria[20] which reported lateral pharyngeal wall as the commonest site 71.1% (32/45), followed by posterior pharyngeal wall 11.1% (5/45), soft palate and tongue base 8.9%(4/45) each. In the same study, 37/45(82.2%) patients took treatment for oropharyngeal cancers, and 8/45(17.8%) had no treatment.[20] Our study recorded poor treatment uptake by patients; 17/27 with (63.4%) patients either declined surgery or defaulted clinic follow-up, while 10/27 (36.4%) had surgery and/or chemo-radiation (table 3). This may be due to financial constraints, as most of the patients are indigents who could not afford hospital bills. Moreover, existing socio-cultural believes in this part of the country still favours traditional and spiritual healing for cancers over orthodox medicines. Further awareness about the efficacy of orthodox medicine in cancer management will improve early hospital presentation and acceptance of treatment by patients in this part of the world.

Conclusion

There is a relatively high incidence of oropharyngeal tumours in young and middle aged females; who are non-alcohol drinking and non-smokers. Incidental finding of HIV infection in some of the patients is a pointer to the possible role of sexually transmitted viral infections in the epidemiology of oropharyngeal cancers and a focus for preventive measures. There is need to create awareness on the value of early presentation and prompt consent for treatment.

Recommendations

Evaluation of oropharyngeal cancer patients should dwell extensively on environmental risk factors; including social habits, alcohol and sexual behaviours in addition to tobacco use. Screening for associated viral infections such as Human Immuno-deficiency Virus infection and Human Papiloma Virus should be routine for all cases of Head and Neck cancers.

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Non-galactorrhoeic Hyperprolactinaemia in Subfertile Female Patients: A Nigerian Tertiary Hospital's Experience.

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Abstract:

Non-galactorrhoeic hyperprolactinaemia is one of the major causes of infertility, usually overlooked worldwide. Observed increasing incidence and prevalence, result in high medical cost and poor outcome of infertility treatment. The high possibility of missing this clinical entity which is usually a biochemical diagnosis need to be critically looked into as there is paucity of data in this aspect thus necessitating this study.

A cross sectional study of eighty-seven (87) sub-fertile females with age range of 31 and 42 years attending the Assisted Reproductive Unit of the University of Ilorin Teaching Hospital (U.I.T.H) Ilorin, Nigeria were recruited for the study. Their descriptive parameters and information were extracted from their hospital folders.

Forty-eight (55.2%) of the 87 of the subfertile females had hyperprolactinaemia without galactorrhoea while thirty-nine (44.8%) had galactorrhoeic hyperprolactinaemia. Mean ages of galactorrhoeic and non-galactorrhoeic hyperprolactinaemia patients were 39.2±6.1 and 37.3±6.9 respectively, and when they were compared there was no statistically significant difference with p-value of 0.194. There was significant positive correlation between age, duration and serum level of prolactin in both galactorrhoeic and non-galactorrhoeic hyperprolactinaemia.

We concluded that non-galactorrhoeic hyperprolactinaemia is an hidden common cause of infertility and an appraisal of this clinical entity is important more so that it is the major presentation of hyperprolactinaemia in our study. The import of the study therefore is that person with suspected case of infertility should be investigated for hyperprolactinaemia even in the absence of galactorrhea as well as holistic interpretation of hormonal profile as prompt and proper treatment will yield a fruitful result.

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Keywords: Non-galactorrhoeic Hyperprolactinaemia, Subfertile females, Assisted Reproductive Unit.

Introduction

Infertility is a global health issue that is affecting 12 to 14% of the couples worldwide and remains stable in recent years.[1] World Health Organization estimated that 60-80 million couples worldwide currently suffer from infertility.[2] In Nigeria as well as most parts of sub-Saharan Africa, where the main reason for marriage is to have children irrespective of whether the couple is in love or not, infertility is a serious social stigma.[3]

Infertility, generally speaking is due to male factor (30%), female factor (35%), combination for the two sexes (20%) while idiopathic infertility accounts for (15%).[4] About 10% of couples of reproductive age have infertility, and ranges from 20 to 46% in some parts of West Africa.

Hyperprolactinaemia is one of the most common endocrine disorders of the hypothalamo-pituitary-ovarian axis affecting the reproductive functions.[5] It is present in as high as 9-17% of women with reproductive disorders.[6]

Generally speaking, patients with hyperprolactinaemia are usually believed to present with galactorrhoea. Galactorrhoea can be defined as inappropriate secretion of breast milk and may be intermittent or continuous, free-flowing or expressible, and unilateral or bilateral and is one of the complaints often associated with infertility.

In recent years, it has been demonstrated that hyperprolactinaemia may not only be associated with galactorrhoea but with numerous ovulatory disorders such as amenorrhea, anovulation, oligo-ovulation, luteal phase defect, luteinized unruptured follicle syndrome, and perhaps unexplained infertility.[7] Hyperprolactinaemia may have a direct effect on the ovary.[8] Suggested mechanisms include atresia of a developing dominant follicle, interruption of ovulation and normal corpus luteum development and premature involution of the corpus luteum. Coincubation of follicles with high levels of prolactin, 100ng/ml and above reduces aromatase activity in vitro by antagonizing the effect of FSH.[9]

The four most common causes of hyperprolactinaemia are central dopamine metabolism disturbance (functional hyperprolactinaemia), prolactinomas, hypothyroidism, and drug ingestion.[10]

Patients with hypothyroidism deserve special comment. These patients present with compensated primary hypothyroidism and may demonstrate a normal thyroxin level with markedly elevated TSH levels. They often have pituitary enlargement mimicking an adenoma and may have visual impairment.[11] In addition to the above most common causes of hyperprolactinaemia, numerous types of trauma and pathology have been associated with increased prolactin production. These include head trauma, obstetric accident, intracranial tumour, encephalitis, meningitis, histiocytosis X, syphilis, tuberculosis, cavernous sinus thrombosis, temporal arteritis, chest trauma, chest surgery, breast augmentation, herpes zoster, oophorectomy, hysterectomy, and renal failure.[12]

After pathologic nipple discharge is ruled out, patients with galactorrhea should be evaluated by measurement of their prolactin level. Those with hyperprolactinaemia should have pregnancy ruled out, and thyroid and renal function assessed. Brain magnetic resonance imaging should be performed if no other cause of hyperprolactinaemia is detected. No cause is found in about a third of all cases of hyperprolactinaemia. In men, high prolactin levels can cause galactorrhea, impotence (inability to have an erection during sex), reduced desire for sex, and infertility. A man with untreated Hyperprolactinaemia may make less sperm or no sperm at all.

Galactorrhea may be intermittent or continuous, bilateral or unilateral, and free-flowing or expressible.[13] In humans, prolactin appears to play a key role in the maintenance of lactation because bromocriptine administration blocks lactogenesis.[14]

Although galactorrhea is a common sign of hyperprolactinaemia, adolescent and teenage patients often present with prolactin levels in the range of 2,000–3,000 ng/mL with no galactorrhea.[15] Hyperprolactinaemia has been shown to result in the inhibition of pubertal development and occasionally presents as primary amenorrhea after normal pubarche and adrenarche. Hyperprolactinaemia is often associated with large macroadenomas that could be classified as invasive. These lesions are not spherical, grow along dural planes, and histologically closely resemble meningiomas.[16] Children presenting with galactorrhea or menstrual dysfunction should be aggressively evaluated and treated to prevent both loss of reproductive capacity and visual impairment.

In clinical practice, more emphasis is placed on galactorrhoeic patients as major cause of hyperprolactinaemia, and hence infertility. Owing to the magnitude of hyperprolactinaemia in relation to subfertility, it becomes imperative to also know the proportion of the subfertile patients that are having hyperprolactinaemia without galactorrhoea, hence this study.

Materials and Methods

The study was a retrospective one done at a North-Central Nigerian Assisted Reproductive Unit (precisely at University of Ilorin Teaching Hospital, Ilorin, Kwara state; Nigeria. A total of 87 hyperprolactinaemic female patients that constitutes a subset of sub-fertile patients attending the facility were recruited for the study. Their age ranges between 31 and 42 years. Of these 87, non-galactorrhoeic were 48 while 39 were galactorrhoeic in number. The subjects' results of serum prolactin which was analyzed using Accubind ELISA kits and other descriptive parameters and information were extracted from their hospital folders. Ethical approval was gotten from the Ethical committee of the hospital.

Statistical Analysis

Data extracted includes age, serum prolactin level, duration of infertility, types of infertility as well as galactorrhoemic state. These data were analyzed using SPSS version 20. Comparison between galactorrhoeic and non- galactorrhoeic groups' parameters were done using Student's t-test. Correlation studies were also done for parameters within each group. Statistical significance was taken at $p<0.05$. Simple frequency charts and cross tabulations were generated and compared.

Results

A cross sectional study of eighty-seven (87) subfertile females between ages of 31 and 42 years attending the Assisted Reproductive Unit of the University of Ilorin Teaching Hospital (U.I.T.H) Ilorin,

Table 1: Descriptive Statistics of all Hyperprolactinaemic Patients (Galactorrhoeic and Non-galactorrhoeic)

Characteristics	All Hyperprolactinaemic Patients	Galactorrhoeic Hyperprolactinaemic Patients	Non-galactorrhoeic Hyperprolactinaemic Patients
No of Patients	87(100%)	39(44.8%)	48(55.2%)
Mean Age(Years) ±SD	38.1±6.3	39.2±6.1	37.3±6.9
Mean Duration of Infertility(Years) ±SD	8.8±5.9	10.4±5.5	7.6±5.9
Mean Serum Prolactin Level(ng/ml) ±SD	33.8±17.1	37.2±18.0	31.1±16.1

Table 2: Types of Infertility among the Hyperprolactinaemic Patients

Types of Hyperprolactinaemia	Primary Infertility	Secondary Infertility	Total
All Hyperpro-lactinaemic Patients Galactorrhoeic	33	54	87
Hyperprolactinaemic Patients	12	27	39
Non-galactorrhoeic Hyperprolactinaemic Patients	21	27	48

Table 3: Comparing some Characteristics between Galactorrhoeic and Non-galactorrhoeic Hyperprolactinaemic Patients

Characteristics	Galactorrhoeic Hyper-prolactinaemic Patients	Non-galactorrhoeic Hyper-prolactinaemic Patients	p-value
Mean Age(Years) ±SD	39.2±6.1	37.3±6.9	0.194
Mean Duration of Infertility(Years) ±SD	10.4±5.5	7.6±5.9	0.002*
Mean Serum Prolactin Level(ng/ml) ±SD	37.2±18.0	31.1±16.1	0.026*

Table 4: Correlation Study of Parameters in all Hyperprolactinaemic Patients

Parameters	'r'	p-value
Age and Duration	0.666	0.000*
Age and Serum Prolactin	0.406	0.000*
Duration of Infertility and Prolactin	0.307	0.004*

Table 5: Correlation Study of Parameters in Galactorrhoeic and Non-galactorrhoeic Hyperprolactinaemic Patients

Parameters	Galactorrhoeic Hyperprolactinaemic		Non-galactorrhoeic Hyperprolactinaemic	
	'r'	p-value	'r'	p-value
Age and Duration	0.572	0.000*	0.717	0.000*
Age and Serum Prolactin	0.316	0.050*	0.457	0.001*
Duration of Infertility and Prolactin	-0.033	0.841*	0.539	0.000*

Nigeria based on the availability of their serum prolactin results. This are as shown in Table 1.

Table 2 shows that 48 (55.2%) of the 87 of the subfertile females had hyperprolactinaemia without galactorrhoea while thirty-nine (44.8%) had galactorrhoeic hyperprolactinaemia. Mean ages of galactorrhoeic and non-galactorrhoeic hyperprolactinaemia patients were 39.2±6.1 and 37.3±6.9 respectively and there was no statistically significant difference when they were compared and p-value was 0.194 (Table 3).

There was significant positive correlation between age, duration and serum level of prolactin in both galactorrhoeic and non-galactorrhoeic hyperprolactinaemia. However there was however a non-significant negative correlation between duration of infertility and serum prolactin level females with galactorrhoeic hyperprolactinaemia (Tables 4 and 5).

Discussion

It has come to stay at least for now, that infertility is a global health issue that is affecting 12 to 14% of the couples worldwide and remains stable in recent years.[1] World Health Organization estimated that 60-80 million couples worldwide currently suffer from infertility.[2] In Nigeria as well as most parts of sub-Saharan Africa, where the main reason for marriage is to have children irrespective of whether the couple is in

love or not, infertility is a serious social stigma.[3]

Elevated serum prolactin level and galactorrhoea is a common finding in reproductive disorders.[17] Hyperprolactinaemia does not only cause galactorrhoea but also gonadal dysfunction and infertility which has led to wider use serum estimation of serum prolactin. The import or the significance non-galactorrhoeic hyperprolactinaemia is usually under-emphasized or under-estimated in most gynaecologic settings.

In this study, 37.9% of the patients had primary infertility while 62.1% had secondary infertility. This appears a little bit higher as against a previous study done by Israel J et al which reported 19% of primary infertility and 81% of secondary infertility.[18] This might not be unconnected with elitist awareness amongst clients attending the fertility center.

This study reveals that hyperprolactinaemia, whether galactorrheoic or non-galactorrhoeic is more in females with secondary infertility. This might be connected with the fact that they have been in position of prolactin hypersecretion before. However, it was discovered in this study that majority (55.2%) of subfertile women attending the Assisted Reproductive Unit of the University of Ilorin Teaching Hospital have non-galactorrhoeic hyperprolactinaemia. Galactorrhoeic hyperprolactinaemia accounts for only 44.8% of the total women (30.8% had primary infertility while 69.2% had secondary infertility).[18,19,20] This is higher than findings in previous studies.[19,21]

Although, there was significant positive correlation between age, duration and serum level of prolactin in both galactorrhoeic and non-galactorrhoeic hyperprolactinaemia, younger age and shorter duration of infertility tends to tilt the patients towards having non-galactorrhoeic hyperprolactinaemia. This might not be unconnected with the fact they also have lower serum prolactin when compared with that of women with galactorrhoeic hyperprolactinaemia. There was negative correlation between duration of infertility and serum prolactin level in females with galactorrhoeic hyperprolactinaemia though not significant. This negative correlation between duration of infertility and serum prolactin level might not be unconnected with possible physiologic adaptability to previous experience of hypersecretory exposure to prolactin probably from previous pregnancy or even lactation.

Conclusion

From this study, we concluded that non-galactorrhoeic hyperprolactinaemia is an hidden common cause of infertility and an appraisal of this clinical entity is important more-so that it is the major presentation of hyperprolactinaemia in our study. The import of the study is that anyone with suspected case of infertility should be investigated for hyperprolactinaemia even in the absence of galactorrhoea as well as holistic interpretation of hormonal profile as prompt and proper treatment will hopefully yield a fruitful result.

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Massive Bleeding From Colonic Diverticular Disease In An Elderly Nigerian: A Case Report

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Abstract

Colonic diverticular disease is one of the most common and costly gastrointestinal disorders among industrialized countries. The disease was thought to be rare in the African population, but is being increasingly diagnosed with the advent of modern imaging techniques and colonoscopy. Diverticular bleeding is a common cause of lower gastrointestinal (GI) haemorrhage and patients typically present with massive and painless rectal haemorrhage. Reports of massive bleeding from colonic diverticular disease are rare in Nigeria. We report a case of massive bleeding from multiple colonic diverticuli in a 70 year old Nigerian male who was admitted due to haematochezia and dizziness and was transfused with 8 units of blood. There was spontaneous resolution of bleeding in spite of the absence of facilities for therapeutic intervention at our institution.

Key words: Colonic diverticular disease, colonoscopy, haematochezia, massive bleeding, gastrointestinal disorders

Introduction:

Diverticular disease of the colon refers to herniation(s) of the mucosa and submucosa through weak points in the muscular walls of the colon to form narrow necked pouches.[1] Diverticular disease of the colon is common in developed nations.[1] Early reports noted its prominence in the USA, Europe and Australia and its rarity in Asia and Africa but the disease is now being increasingly reported in Africa.[2-4]The pathogenesis of this disease process is likely multi-factorial involving dietary habits, changes in colonic pressures and motility, colon wall structural changes associated with aging, increase in type III collagen and deposition of elastin and genetic factors.[5] Diverticula develop at sites of weaknesses in the colonic wall that occur where the vasa recta penetrate the circular muscle layer. As a diverticulum herniates, the vasa recta drape over the dome of the diverticulum and become susceptible to trauma and disruption.[5]

Lower GI haemorrhage is a recognized complication of colonic diverticular disease and usually presents as massive and painless rectal haemorrhage that is often self limiting. Although diverticula typically occur throughout the colon, diverticular bleeding tends to occur in the thinner-walled ascending (right) colon and results from rupture of the vasa recta.[6] In adults older than 65 years, diverticular haemorrhage can lead to significant morbidity, especially in those with haemodynamic instability and co-morbid conditions, including systemic hypertension, diabetes mellitus, chronic obstructive pulmonary disease, chronic renal insufficiency, and coronary artery disease.[7] Other recognized complications of colonic diverticular disease are diverticulitis, abscess and fistula formation, perforation and peritonitis.[8] A definite diagnosis of diverticulosis as the source of bleeding requires the finding of one of the following after vigorous irrigation of diverticula: active bleeding, a non-bleeding visible vessel, or an adherent clot. Two other types of diverticulosis have also been defined: incidental diverticulosis, in which diverticulosis was present but the bleeding originated from another lesion or lesions, and presumptive diverticular haemorrhage, in which diverticula had no evidence of bleeding but no other major colonic lesions or bleeding sites were identified on colonoscopy.[9]

Treatment mainly involves resuscitation of the patient with urgent blood transfusions and conservative management with antibiotics, bowel rest, pain control and dietary advice since most cases of bleeding resolve spontaneously. However, there have been case reports of treatment of diverticular haemorrhage with colonoscopy.[10-13]Surgery may also be indicated in some cases of severe bleeding .[14]

Case Report:

A 70 year-old Nigerian retired male engineer, was admitted to the emergency ward following a referral on account of massive per rectal bleeding which started about 3 days prior to his presentation. He had had eight to ten episodes of passing fresh blood and clots per rectum and the estimated volume of blood loss per episode was about 200–250 ml of blood. He gave a history of postural dizziness and severe generalized body weakness. There was no associated

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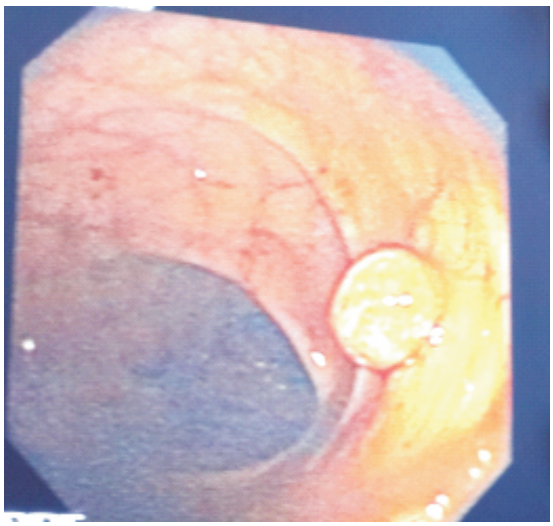

Figure 1: Solitary polyp in the sigmoid colon

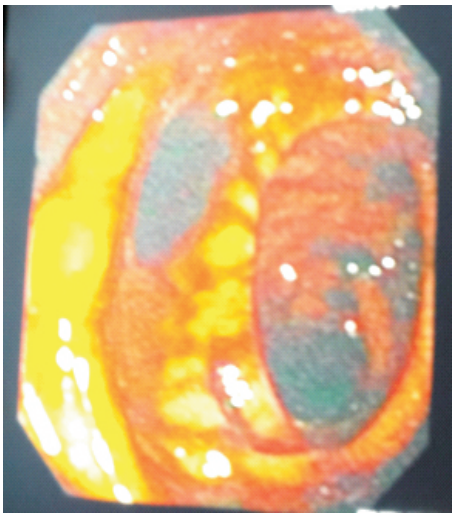

Figure 2: Multiple diverticuli with blood clots in situ

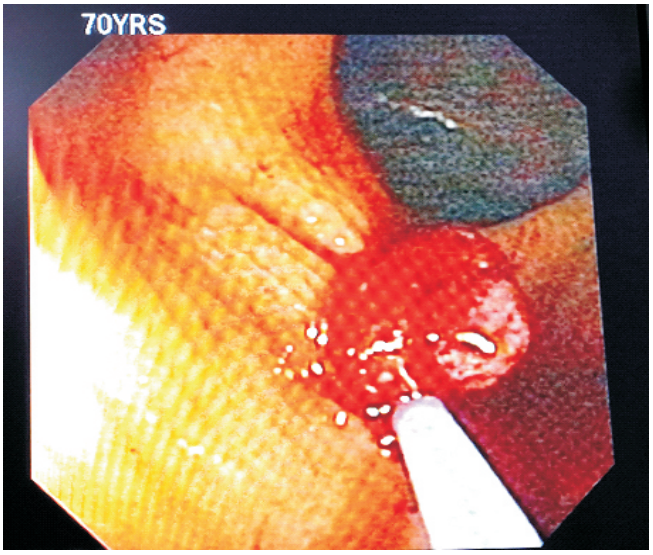

Figure 3a: Removal of the polyp with a snare polyp

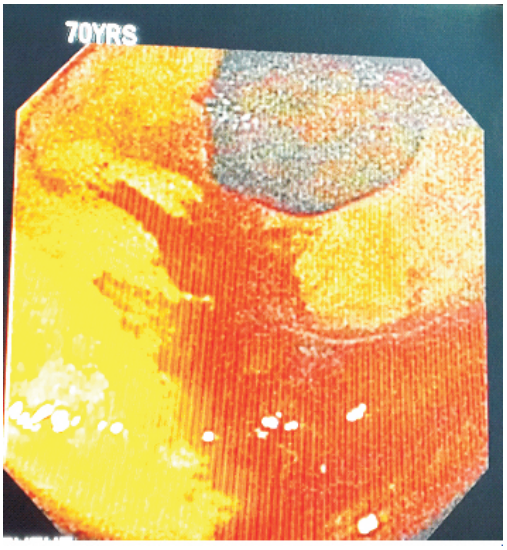

Figure 3b: Post polypectomy image showing the complete removal of the

abdominal pain and no history of bleeding from the other body orifices. A known patient with systemic hypertension, type II diabetes mellitus and lentiviral infection, who was on low dose anti-platelet (aspirin 75mg daily) and other medications. He was well controlled on his medications and had no history of bleeding tendency. A private practitioner had transfused him with 4 units of blood prior to his admission in our hospital but the bleeding per rectum persisted.

On examination, he was pale, anicteric, afebrile (T=36.8^{0}C), had no finger clubbing and no pedal oedema. His pulse rate was 112 beats per minute and blood pressure reading in supine position was 110/70mmHg but the reading in erect position could not be measured because he became dizzy upon standing. The first and second heart sounds were normal but a haemic murmur was heard. There were no other positive findings except for the examining gloved finger that was stained by bright red blood on digital rectal examination. His packed cell volume (PCV) was 18% and he was transfused with additional 4 units of blood. Colonoscopy was performed within 48 hours using the Olympus CF-180 Exera II Colonoscope and the findings were: a solitary pedunculated polyp in the sigmoid colon (see Figure 1), multiple diverticuli in the sigmoid, descending and transverse colon with blood clots seen in some of them (see Figure 2). The polyp was removed completely with a snare (see Figures 3a and 3b). Histology revealed that it was a benign polyp. The lower GI bleeding resolved completely with conservative management comprising discontinuation of the low dose aspirin, bowel rest and the use of antibiotics (ciprofloxacin and metronidazole). He had a total of 8 units of blood transfused (the 4 pints received at the private hospital inclusive) and was discharged home on haematinics and his routine medications with a PCV of 28%. The patient is being followed up in the GI clinic and he is currently doing well. As at his last visit

to the GI clinic, he was stable and had not had any repeat rectal bleeding since the past 5 months. Stool for occult blood was negative and his PCV was 42%.

Discussion:

Diverticular disease, an acquired disease, is one of the most common disorders of the colon in the elderly in the Western society.[1] Colonic diverticular disease is now being increasingly reported in developing nations with the change in dietary habits of these nations towards that of the western diet.[2] Colonic diverticula occur more commonly after the age of 60 years and affect both sexes equally. Though asymptomatic in most cases, in 10-20% of the cases affected patients present with symptoms of abdominal pain, change in bowel habits, bleeding or perforation.[5] Bleeding is a common complication and it can be life threatening like in the case reported where the patient had a PCV of 18% at presentation and had massive blood transfusion with 8 units of blood. Our patient had a definite diagnosis of diverticulosis being the source of bleeding since adherent clot was seen in some of the diverticuli at colonoscopy and there was no evidence of bleeding from the polyp. Other possible causes of lower GI bleeding in our patient such as haemorrhoids, solitary rectal ulcer, inflammatory bowel disease, angiodysplasia and colorectal malignancy were excluded at colonoscopy. The regular and consistent use of low dose aspirin, a non-steroidal anti-inflammatory drug (NSAID), was believed to have triggered the massive bleeding in this patient since the regular use of aspirin or NSAIDs generally has been reported to be associated with an increased risk of diverticular bleeding.[10] The use of aspirin was discontinued in this patient to prevent a recurrence but the decision was made after careful consideration of the potential risks and benefits of the medication. No therapeutic endoscopic intervention was offered with respect to the bleeding diverticuli because of non-availability of the necessary accessories unlike in some reports by some authors where a variety of therapeutic options were tried. Johnston and Sones described four patients who were treated with an endoscopic heater probe.[11]Three of the patients had active bleeding, and one had a sentinel clot in a diverticulum. Kim and Marcon reported the successful treatment of active diverticular haemorrhage with injection of epinephrine in one patient.[12] Savides and Jensen described three patients with severe, recurrent lower GI bleeding in whom non-bleeding visible vessels were successfully treated with bipolar coagulation.[13] Hokama *et al*, described three patients with diverticular bleeding that was controlled by an endoscopic haemoclip.[14] Neither complications nor recurrent bleeding in the short or long term was reported in these series. Our patient responded well to conservative management with bowel rest, use of antibiotics and the discontinuation of aspirin resulting in spontaneous resolution of the bleeding and he was lucky to have escaped the rigors of surgery which may be indicated in some cases to stop bleeding.[15] Colonic diverticular bleeding can be prevented by performing screening colonoscopies or barium enemas among the population at risk (elderly, males, individuals on NSAIDs and or anticoagulants) in order to ensure early detection of colonic diverticular disease and elimination of modifiable risk factors, particularly the use of NSAIDs and anticoagulants.

Conclusion:

Colonic diverticular disease should be considered as a possible cause of bleeding in elderly patients in Nigeria presenting with massive lower GI bleeding.

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An Unusual Case of Intestinal Perforation by Peritoneal Dialysis Catheter: Case Report

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Abstract

Peritoneal dialysis is a life saving intervention in children with impaired kidney function. Children on this intervention experience various complications, though bowel perforation is rare.

We report case of a 15 year old paraplegic child that was on peritoneal dialysis on account of renal failure secondary to neurogenic bladder who had bowel perforation. We concluded that peritoneal dialysis catheters could migrate into the intestine. A high index of suspicion is required to make a diagnosis of this condition towards so that prompt intervention can be applied to save life.

Keywords: Peritoneal dialysis, Intestinal perforation, Continuous ambulatory peritoneal dialysis

Introduction

Peritoneal dialysis (PD) is a procedure which serves to replace kidney function. Continuous ambulatory peritoneal dialysis (CAPD) is now widely used as a method of renal replacement therapy. It has the advantages of improving quality of life, cost effectiveness, less dietary restrictions than haemodialysis (HD) and better clearance of middle molecules to mention a few[1]. Catheter placement is cardinal in the administration of peritoneal dialysis but it is associated with complications such as pain, hernias, infections, catheter leaks, obstruction, and visceral perforation[2]. Bowel perforation is rare, especially when catheter placements are done under laparoscopic guidance or open surgical implantation. However, when it does occur, it is a dangerous complication and mortality as a consequence of bowel perforation has been reported in the literature[3].

We report an unusual case of colonic perforation by peritoneal catheter in a 15 year old paraplegic child.

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Case Report

A 15 year old paraplegic male with chronic renal failure secondary to neurogenic bladder was admitted for investigation and management after presenting with short history of right flank pain and pus draining from his urethral catheter.

He had been born with a myelomeningocoele and paraplegia. He was referred to our unit at the age of 12 years in Stage 4 Chronic Kidney Disease due to obstructive uropathy secondary to neurogenic bladder. He had been on long term self-intermittent clean catherization (SICC) at the time presentation in our unit. He was eventually placed on CAPD at the age of thirteen years, on account of his deteriorating renal function.

He developed peritonitis four months after commencement of CAPD complicated by a blocked PD catheter. The PD catheter was removed and the patient was placed on haemodialysis (HD) to allow the peritoneum to recover. The PD catheter was then reinserted after 6 weeks but had to be revised 2 days later, again due to PD catheter obstruction. At this revision an adhesiolysis was performed via the mini-laparotomy site, the PD catheter was flushed and then replaced under peritoneoscopic vision back into the peritoneal pelvis.

Six months after his last surgery, although clinically asymptomatic, brownish faeculent material was noticed in the dialysate effluent. His mother, despite extensive counseling and pleading to reconsider, repeatedly declined admission for investigation and management.

Dialysate culture performed at the time yielded *Escherichia coli*, *Escherichia faecium*, *Klebsiella pneumonia* and *Enterobacter spp*. He was started on Ertapenem and Amikacin as out-patient based on the organism sensitivity pattern and his mother was encouraged to return to the clinic immediately should any symptoms of peritonitis or sepsis develop. The child remained stable for the next two years, all the way until this admission, with no undue worsening in his renal function (Table I) or clinical condition. During this period some faeculent material was noticed intermittently and outpatient clinic attendance was fairly regular.

During this presentation, he presented in the clinic with a short history of progressive worsening pain over the PD catheter insertion site and cloudiness

of his urine. On examination he was noted to have a weight of 21 kg (41% of expected), pallor and mild pedal oedema. He was cheerful and apyrexial and, although there was some tenderness around the peritoneal catheter insertion site, no abdominal masses could be palpated and he had no clinical signs of peritonism. Frank purulent material was noted to be draining from his urethral catheter and his dialysate effluent was, once again, faeculent in nature.

The working diagnosis was acute urinary tract infection secondary to poor compliance with SICC and likely chronic migration of the PD catheter into the large bowel. He had lost his mother a month before this presentation and was been cared for by his brother who consented along with the patient for admission for treatment of the UTI and for investigation of the faeculent dialysate effluent. Based on prior urine sensitivity patterns, he was placed onto Ertapenem and Amikacin. In hospital, although never previously reported by his family, PD fluid was noted to be draining per rectum.

A peritoneal dialysis catheterogram suggested that the Tenckoff catheter had eroded into the rectum (Figure 1), and this was confirmed on abdominal CT (Figure 2).

The findings at exploratory laparotomy showed the sigmoid colon adherent to the anterior abdominal wall, with the perforated tip of the PD catheter in the colon with soft adhesions around the catheter (Figure 3). The peritoneal cavity was clean and not communicating with the catheter lumen. The catheter was removed and the bowel perforation repaired.

A new PD catheter was placed into the peritoneal cavity and a temporary subclavian HD line was inserted to allow dialysis while the surgical site healed. His urine cleared with regular SICC and a course of intravenous Imipenem and Amikacin. Unfortunately, due to repeated PD catheter malfunction, obstruction and eventually membrane failure, we were unable to re-establish CAPD and a decision was taken to convert the child onto chronic HD. He was discharged home and remains well on permanent HD.

Table 1: Renal function indices while on CAPD

Renal Indices	Weight	Bld Press	Hb	Na+	K+	Urea	Creat	Albumin
Date								
10/04/2013	24	130/70	11.8	145	6.6	26.9	279	46
11/06/2013	24	110/70	12.8	143	5.6	26.9	244	40
27/08/2013	23	110/70	10.6	144	5.1	42.2	343	42
25/09/2013	23	105/65	10.9	144	5.0	31.7	316	38
19/11/2013	23.5	110/70	13.8	143	4.7	28.2	356	42
18/02/2014	25	120/80	12.7	138	5.3	36.8	319	43
15/04/2014	24.3	120/80	10.0	139	5.3	19.9	343	38
09/06/2014	23.7	120/70	10.5	137	4.4	37.9	302	40

Figure 1: Peritoneal dialysis catheterogram showing catheter eroding into the rectum.

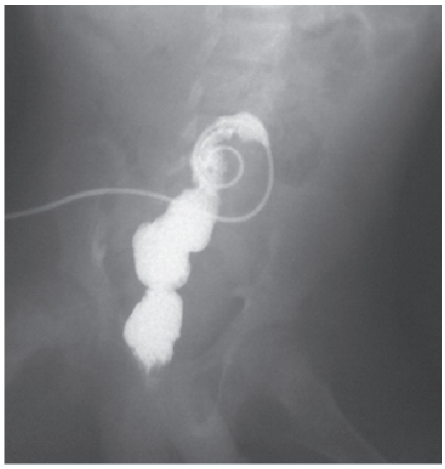


Figure 2: Abdominal CT- scan confirming Tenckoff catheter eroding into rectum

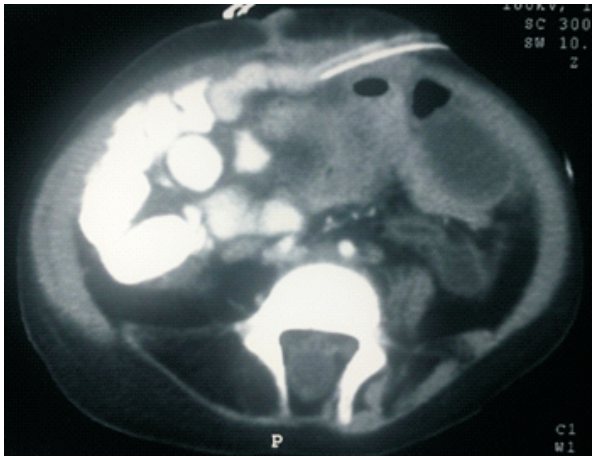
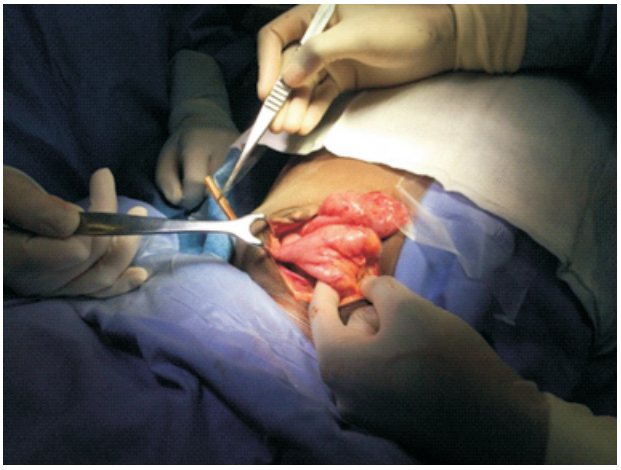


Figure 3: Perforated tip of PD catheter in the colon on exploratory laparotomy.



Discussion

Acute bowel injury at the time of peritoneal catheter insertion is a well described complication[4, 5, 6]. It is most commonly seen in cases of blind insertion via a puncture technique when compared to open insertion via a mini laparotomy. The incidence of acute intestinal perforation in children on PD is up to 3.2%[4, 5]. The mortality recorded in such cases is high and these children are usually toxic, manifesting features of peritonitis and septic shock[3]. Case reports of intestinal asymptomatic migration are described in adults with little consequence[6]. In our patient the peritoneum did not show any gastrointestinal contamination and he never manifested any features of severe sepsis or peritonitis in the period between his first presentation of faeculent PD fluid and this admission.

Catheter malfunction may be expected as a feature of intestinal perforation although more common reasons for catheter malfunction are migration out of the pelvis, omental wrapping of the catheter, blockage, infection, adhesions and peritoneal membrane failure[7]. The catheter in our patient never gave any sign of malfunction and his renal function remained stable throughout (Table I).

The initial incident, 15 months before this admission, of the finding of faecal-like material in his dialysate raised the suspicion of migration of his catheter. Passing peritoneal fluid per rectum also strengthened the possibility that the catheter had remained in the colon for that duration.

The colon is made up of simple columnar epithelium and consists of numerous goblet cells making it appropriate to absorb the remnant fluid in the chyme. However, it does not possess the vascularity and lymphatic drainage reminiscent of the peritoneum and neither does it have the peculiar mesothelium and multiple microvilli characteristic of the peritoneum which are some of the features that facilitate the diffusion and osmotic processes that occur in peritoneal dialysis[8]. The sigmoid colon is known to be a mobile part of the large bowel probably explaining the intraoperative finding of adherence to the anterior abdominal wall. The lack of peritoneal contamination suggests a slow erosion of the catheter into the bowel lumen. A similar situation may be seen in patients with chronic ventriculo-peritoneal shunts that occasionally erode into bowel[9]. It remains an enigma how his renal function did not deteriorate during this period and more research is required on the possibility of the colon having some anatomic and physiological properties similar to the peritoneum with regards to dialysis.

The organisms cultured from the dialysate could raise the suspicion of intestinal perforation. Culture results revealing multiple organisms, especially the enterobactereacae and anaerobic organisms, may be suggestive of a perforation, although finding multiple organisms has also been reported in 10% of cases of peritonitis accompanying PD[10]. The suspicion is increased if these organisms are not responsive to antimicrobial therapy[10]. Our patient had features consistent with the above and would probably have benefitted from a PD catheter change earlier, however South African law gives absolute right on a minor to the parents. Having a legal input during the first admission would have benefitted the child but this was not considered at the time.

Conclusion And Recommendation

Intestinal perforation can complicate peritoneal dialysis catheter placement. A high index of suspicion is required to make a diagnosis of intestinal perforation from a PD catheter especially in the presence of multiple organisms in dialysate culture. Our findings also suggest that the sigmoid colon may be able to sub serve some peritoneal function as far as dialysis is concerned but sepsis is a serious concern. Further study is needed to investigate this hypothesis.

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