

Nigerian Journal of Gastroenterology and Hepatology

A Publication of the Society for Gastroenterology and Hepatology in Nigeria(SOGHIN)

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The NIGERIAN JOURNAL OF GASTROENTEROLOGY AND HEPATOLOGY, abbreviated as *Nig. J. Gastroenterol. Hepatol.* is a quarterly publication of the Society for Gastroenterology and Hepatology in Nigeria(SOGHIN) which publishes original research on the biology and diseases of the Gut, Liver, Pancreas, Peritoneum and Spleen both in humans and experimental animal models.

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Editorial

THE CHALLENGES FACING THE LABORATORY DIAGNOSIS OF CHRONIC VIRAL HEPATITIS IN NIGERIA

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INTRODUCTION

Chronic hepatitis is a clinical and pathological syndrome characterized by varying degrees of hepatocellular necrosis and fibrous remodeling of the liver. By convention, it is defined as chronic inflammation of the liver continuing without improvement for at least 6 months. The entire world over, the major causes of chronic viral hepatitis are hepatitis C and B with or without hepatitis D.

Chronic viral hepatitis is highly prevalent globally, with some 500 million people estimated to be currently infected with hepatitis B or C. These two diseases are the cause of significant global mortality and morbidity with approximately 1 million deaths each year attributable to them and their sequelae, liver disease and primary liver cancer. The WHO estimates that about 130–170 million people are chronically infected with hepatitis C virus, and more than 350 000 people die from hepatitis C-related liver diseases each year while about 2 billion people worldwide have been infected with the hepatitis B virus and about 350 million live with chronic infection.

An estimated 600 000 persons die each year due to the acute or chronic consequences of hepatitis B. Endemicity of HBV infection is high in sub-Saharan Africa where almost all infections occur during the perinatal period or early in childhood. At least 8% of the population is chronically infected and 70–90% has serological evidence of previous HBV infection. The estimated overall prevalence of HCV in Sub-Saharan Africa is 3.0%. The central African region has the highest estimated prevalence of 6%, West Africa has an estimated prevalence of 2.4%, and southern and east Africa with the lowest estimated prevalence of 1.6%. In Nigeria, HBV infection has reached hyperendemic levels with the seroprevalence of HBsAg estimated to range from 10–40%. Studies have shown hepatitis C prevalence in Nigeria ranging from 4–5.8%. Chronic liver disease, mainly resulting from chronic hepatitis, is a major cause of significant morbidity and mortality in Nigeria comprising about 30% of clinical conditions seen at the gastroenterology medical outpatient unit in one tertiary health institution in Nigeria.

The Laboratory Diagnosis of Chronic Viral Hepatitis

Laboratory diagnosis of viral hepatitis continues to play a pivotal role in the management of chronic viral hepatitis. These tests include serological tests to identify viral markers, biochemical tests to assess presence and extent of hepatocyte injury, molecular biological methods for to quantify viral load in and histological examination of liver biopsy tissue. In viral hepatitis, both serologic and molecular assays are used to detect early infections at the asymptomatic phase, to differentiate acute from chronic infections, and detect persistence of viraemia or verify development of immunity.

Serology

Serological tests for viral antigens and antibodies are typically used for diagnostic screening and can be performed on either serum or plasma. Assays for HBsAg, anti-HBc (IgM, IgG), anti-HBs as well as antibody to hepatitis C virus (anti-HCV) can be used in the diagnosis of viral hepatitis infection.

Biochemical tests

Liver enzymes, especially the transaminases are usually elevated in chronic hepatitis. ALT levels are typically higher than AST levels. Persistent elevation of serum ALT for longer than 6 months is suggestive of progression to chronic hepatitis and is used as an important diagnostic criterion of the disease. Extremely high levels of ALT can be observed during exacerbation or reactivation of the disease and may be accompanied by impaired synthetic function of the liver (i.e. decreased albumin levels, increased bilirubin levels, and prolonged prothrombin time). Alkaline phosphatase levels may be elevated, but are usually less than 3 times the upper limit of normal. Patients with chronic active hepatitis have mild to moderate elevation of the aminotransferases (<5 times the upper limit of normal).

Molecular studies:

HBV DNA Testing offers the best indication of active viral replication and a high state of infectivity in the presence of HBV DNA in the serum. Branched DNA technology assays, hybrid capture assays, or more sensitive polymerase chain reaction (PCR) techniques are used to detect the viral genome in the serum. HBV DNA is useful to assess HBV status in patients with suspected false-positive results of serologic

studies and to evaluate the level of active replication in an HBV-infected patient. Quantitation of HBV DNA is helpful for predicting treatment response. Direct detection of the HCV genome has been made possible with RT-PCR and the branched DNA signal amplification assays. HCV RNA testing is essential in the diagnosis of chronic HCV infection because serologic testing cannot distinguish chronic infections from resolved acute infections.

Liver biops:

Liver biopsy and histologic appraisal is important not only to make a diagnosis but also to stage and grade the disease and to report any concomitant condition such as steatosis and pre-malignant changes which all have prognostic implications. An additional important role of liver biopsies is to help gauge the effectiveness of antiviral, anti-inflammatory, and/or anti-fibrotic therapy.

The Challenges Facing Laboratory Diagnosis of Chronic Viral Hepatitis in Nigeria

Non-recognition of chronic viral hepatitis as a major health problem by the Nigerian government

The HBV disease burden as outlined by the WHO is sufficiently startling to prompt a public health response. In Africa, there are few high-quality registries; and the majority of them only record cases in cities, whereas hepatitis B prevalence is often highest in rural areas. In Nigeria, the government has failed to appreciate the severity of viral hepatitis and consequently there has been a lack of budgetary provision for surveillance, diagnosis and management. This is a major setback for the laboratories diagnosis of chronic hepatitis.

Similarly, awareness among the general population is quite low in Nigeria as well as in most countries in sub-Saharan Africa. Of greater concern is the lack of proper education and awareness among health care providers, including doctors. This is because chronic hepatitis is a disease that requires adequate explanation, counseling, and individualized assessment for successful anti-HBV therapy. The Society for Gastroenterology and Hepatology in Nigeria (SOGHIN) identified this lack of knowledge among health care providers and took a positive step towards addressing the situation by publishing the first

edition of a treatment guideline for Hepatitis B and C in Nigeria in 2009 .

Probably owing to the official and private ignorance on the magnitude of the chronic hepatitis burden among the population, there is no government policy on diagnosis and management of chronic viral hepatitis other than the management guidelines produced by SOGHIN. Although more attention so far has been focused on HIV and AIDS, viral hepatitis is more obviously prevalent than HIV/AIDS in most parts of Sub-Saharan Africa. Most Sub-Saharan African governments do not provide funds for testing and treatment, which are very expensive. In Nigeria, according to the WHA/WHO study, testing for hepatitis B and/or hepatitis C is not easily accessible to more than 50% of the population and testing is not available free of charge to all citizens². It is, however, provided free of charge to some groups. These include infants of 0-11 months and healthcare workers. Testing is also not compulsory for any group, health workers inclusive. A major barrier to the diagnosis of the chronic hepatitis in Nigeria is the prohibitive cost of laboratory tests. Molecular studies for diagnosis of viral hepatitis are available in very few centers in the country. Currently, less than six centers are able to offer HBV DNA viral quantification. These inadequacies not only affect diagnosis but also affect research.

Systemic and institutional issues in Nigerian Hospitals and Laboratories

There is an acute shortage of necessary personnel for adequate management of chronic viral hepatitis. There a shortage of gastroenterologists and hepatologists as wells that of laboratory experts skilled in the laboratory evaluation of patients with the disease. For example, anatomical pathologists and adequately trained laboratory scientists in Nigeria are in short supply. Liver biopsy is a critical procedure in the evaluation of patients with CHB. Information obtained from this examination is very useful in making decisions regarding treatment as well as determining prognosis. The number of doctors trained in this procedure, and more importantly, the number of specialists trained to interpret the findings is very low in Nigeria. Newer modalities of investigation that can be used to non-invasively diagnose liver fibrosis are not yet available in most African countries, and where they are available, most physicians are not conversant

with the standard scoring systems used in reporting liver biopsies.

Many laboratories in Nigeria, including those in the teaching and specialist hospitals are poorly set up and can only conduct crude HBsAg screening. With less than 6 centers in Nigeria able to offer HBV DNA viral load measurements, patients must travel hundreds of kilometers to such centers in order to undergo the test. Quality assurance in medical laboratories is a major issue in resource-poor countries like Nigeria. Prolonged power outages are frequent in Nigeria, which adversely affects reagents stored in refrigerators.

Other infrastructural challenges include lack of adequate and timely equipment maintenance and unavailability of appropriately trained technical personnel for maintenance purposes. Problems also ensue from supply of substandard reagents and consumables.

THE WAY FORWARD

The challenges facing practicing hepatologists and patients in Nigeria are enormous, but not insurmountable if appropriate measures are put in place to solve these problems.

It is recommended that there should be a government policy and strategy on the surveillance and management of chronic viral hepatitis as it is with HIV/AIDS. There should be adequate budgetary provision made to backup this policy and surveillance program.

The government should provide support in the form of research/ educational grants and continuing medical education programs for primary care physicians, internists, and gastroenterologists in capacity building. The recommendations of the Global Hepatitis Policy should be implemented as much as is feasible. Health insurances should be strengthened in scope and content such that diagnostic procedures for diseases such as CHB are included. An adequate number of laboratories should be established and located in such a way that patients will not have to travel long distances for laboratory tests. Dedicated centers for the diagnosis and treatment of viral hepatitis should be established. In such centers, resources can be pooled for effective service delivery, research, and training.

Basic infrastructure including constant power supply and water should be provided and maintenance of equipment should be done on a preventive rather than a corrective basis.

The Society for Gastroenterology and Hepatology in Nigeria identified and took a positive step towards addressing the problems encountered in the management of viral hepatitis by publishing the first edition of a treatment guideline for Hepatitis B and C in Nigeria in 2009. The association should continue to engage in advocacy to bring awareness to the challenges facing the management of viral hepatitis in Nigeria.

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MANAGEMENT OF LIVER METASTASIS FROM COLO-RECTAL CARCINOMA WITH LAPAROSCOPY: A LITERATURE REVIEW

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ABSTRACT

Background: Worldwide, colo-rectal carcinoma is the second most common cancer with liver metastases as its major cause of mortality. This malignant condition is now seen more frequently in our environment typically at a late stage with distant metastasis especially to the liver. This study aims at highlighting the current use of laparoscopy in the management of liver metastases from colo-rectal cancer and its outcome.

Aims: To highlight the current use of laparoscopy in diagnosis, staging and treatment of liver metastasis from colorectal cancer with an evaluation of the outcome thus encouraging its practice in our subregion.

Method: Medline, Google, Highwire and Cochrane databases were searched. The search words were “metastatic colorectal cancer(MCC)” and “laparoscopic liver resection”. Review of relevant articles with literature in English language. Cross- referenced articles were also reviewed.

Results: Laparoscopy and intraoperative ultrasonography were shown to improve accuracy of diagnosis. Large multi-centre studies showed reduced blood loss, intra-operative/ post-operative morbidity and reduced length of hospital stay in laparoscopic liver resection for metastatic colorectal cancer. No large prospective randomised clinical trial comparing laparoscopic vs open hepatic resection was found. Laparoscopic ablative therapies were found to be useful in non-resectable liver metastasis.

Conclusion: Laparoscopic liver resection was found to be a favorable alternative to open resection in metastatic colorectal cancer and is associated with low morbidity and mortality in properly selected cases in specialized centres. There is however a steep learning curve required for such good outcome.

Keywords: Liver resection, Metastatic colorectal cancer MCC, Laparoscopy

INTRODUCTION

The liver is the most common site for blood-borne metastasis from colorectal cancer. About 25% of patients with colorectal cancer have synchronous hepatic metastases, and a similar percentage of patients will develop metachronous hepatic metastases.¹ It

has been documented that hepatic resection is beneficial to patients with colorectal metastases.²⁻⁴

The last three decades have witnessed the advent and progression of laparoscopic liver surgery from wedge resections to extensive segmental resections including extended hemihepatectomies⁵.

Currently, indication for liver resection has extended to include patients who would have previously been considered unresectable. Intraoperative ultrasonography, improvements in anesthesia and surgical techniques with increased knowledge of the surgical anatomy of the liver have been relevant to a favourable outcome. In liver surgery the laparoscopic use of the stapling devices, parenchymal transection tools such as the LigaSure and the harmonic scalpel, and hand-assisted technique⁶, have benefit of reduced blood loss, post-operative pain, shorter hospital stay, improved cosmesis and shorter time to adjuvant therapy compared with open resection.

Aims: This study aims at highlighting the current use of laparoscopy in the management of liver metastases from colorectal cancer and its outcome. This includes a review of the role of laparoscopy in diagnosis, staging and treatment of liver malignancy from MCC with an evaluation of the outcome.

Method: A review of available literature using the following sources: Medline, Google, Highwire and Cochrane databases. The search words were “metastatic colorectal cancer” and “laparoscopic liver resection”. Review was from articles with literature in English language. Cross- referenced articles were also reviewed.

FINDINGS

The extent of surgical resection to be undertaken is usually based on patient's condition, extent of the disease and liver function. A surgical resection with curative intent leaving no macroscopic residual disease (R_0 resection) is paramount.⁷ The goals of pre-operative assessment include the ability of the patient to tolerate hepatic resection, exclude the presence of non-resectable extrahepatic disease and also to delineate the tumour distribution with emphasis on number, location, size and relation to intrahepatic vascular or biliary structures. Such careful selection of patients influence the choice of treatment.

Patient fitness

Fitness for general anaesthesia (GA) is a precondition. Serious consideration is given to the cardiovascular status because of the possibility of

clamping manoeuvres and to the coagulation profile in view of bleeding diathesis. Standard preoperative investigations commonly carried out include liver imaging – helical computed tomography, magnetic resonance imaging and contrast ultrasonography, chest imaging -computed tomography or plain radiography, and clinical biochemistry including liver function test and carcino-embryonic antigen. Positron Emission Tomography (PET) and bone scans are not routine. Contraindications to surgery in synchronous liver metastasis include American Society of Anaesthesia score of >3 , intestinal obstruction, bowel perforation and non-feasible complete resection.⁸

Diagnostic laparoscopy

Liver metastases has been shown to be a major cause of death in colorectal cancer.⁹ Several reports have described the value of diagnostic laparoscopy in upper gastrointestinal malignancies.¹⁰⁻¹⁴ Laparoscopy can identify patients with previously undiagnosed extra-hepatic metastatic disease. The identification of these patients alters treatment plans sparing the morbidity of a non-therapeutic open laparotomy. Radiographically occult unresectable disease in patients considered for resection of malignant hepatic lesions are often diagnosed.¹⁰ Tumor adherence to major vascular structures and extensive biliary involvement by cancer is often difficult to determine using non-invasive radiology. John et al in a series of 50 patients with a variety of hepatobiliary tumors reported that laparoscopy and laparoscopic ultrasound spared 32 patients (64%) an unnecessary laparotomy.¹⁵ Likewise, Babineau et al. found unresectable disease in nearly half of a group of 29 patients with primary and metastatic liver tumors.¹⁶

Laparoscopic liver biopsy

Liver biopsy is the traditional gold standard for assessing liver disease and is indicated in MCC because it often reveals useful information not seen by imaging or blood tests that could help with patient management. The usefulness of this technique as a diagnostic index given the risks is currently being weighed. However, laparoscopic biopsy combines visualizing the entire liver, evaluation of extrahepatic spread of malignancy and the ability to obtain large biopsy material that dramatically upgrades the quality of staging disease severity.¹⁷ The major complications of liver biopsy include bleeding and bile leakage.

Intraoperative ultrasonography

Intraoperative ultrasonography (IOUS) has been found to be more sensitive (>90%) and more specific (>90%) than conventional ultrasonography, computed tomography and arterial portography in evaluating liver tumours.^{18,19} It can assess tumour load and reveal occult lesions as small as 2–3 mm in diameter defining their relationship to vital intrahepatic structures. This could therefore alter surgery-related treatment plan. Some factors found to influence resectability include: Patency of intrahepatic vessels, presence of tumour thrombus, metastatic lymph nodes in the porta hepatis and the coeliac region. IOUS can also guide fine needle biopsies and thus diagnose precisely the nature of the detected lesions. It is recommended that IOUS be performed in every case of liver resection for malignancy.²⁰

Laparoscopic liver resection

The goal of surgery is to remove all the metastatic sites regardless of size, number, distribution, or width of resection margin and where possible with a free clearance margin of not less than 1 cm while maintaining the vitality and quality of life of the patient by preserving a sufficient volume of functioning liver parenchyma. It was observed that patients who are fit, without unresectable extrahepatic disease and in whom at least 20–25% of functional hepatic parenchyma can be left after resection should be considered for surgery.²¹ Good results were seen amongst those with less than 4 lesions, less than 5 cm in size, without extrahepatic disease, that appeared more than 2 years after the resection of a stage I or II colorectal cancer and whose CEA level is less than 5 ng/ml.²²

Anatomic resections were associated with better haemostasis and control of bile leakage. According to the International Hepato-Pancreato-Biliary Association terminology derived from the Couinaud's classification, resection is considered "anatomic" when at least one entire segment was removed; all other resections were defined as non-anatomic or wedge resections while a major liver resection is defined as the resection of three or more hepatic segments (hemi-hepatectomy and extended hemi-hepatectomy).²³

In this review it was found that the type of liver resection depends on the size, number, location

of the metastases, as well as their relation to the main vascular/ biliary pedicles. These invariably determine the volume of the liver parenchyma that can be left in place after surgery. While small metastases located near the liver capsule can be resected by wedge resections, larger lesions often require major resections. Superficial or peripheral lesions have been found to be amenable to laparoscopic excision, however, tumours located in the posterior and superior segments of the liver - VII, VIII, IVa and 1, which require full mobilization of the liver are more difficult to resect laparoscopically.²⁴ On the whole segmental liver resection has been proposed as the preferred oncological procedure as it allows better clearance and is associated with less chance of intra-operative bleeding because fewer vessels lie in the interface between the segments.²⁵ There is a moderately increased operative time for anatomic resections while the removal of more liver parenchyma may lead to postoperative liver dysfunction. New surgical technology of ultrasonography (Cavitron Ultrasonic Aspirator CUSA) and coagulation-based parenchyma transection have increased the benefits of non-anatomic resection.²⁶

It has also been shown that in synchronous liver metastasis a simultaneous laparoscopic liver resection with that of the primary lesion is safe and feasible.^{27,28} In other cases it may be preferable to delay the hepatic resection for 2–3 months. During this period, systemic chemotherapy can also be given to the patient. This combined resection of both primary and liver metastases has been variously reported from specialized centres but are associated with increased mortality and morbidity.²⁹

Laparoscopic liver resection has been limited by difficulties in mobilisation, risks of bleeding and fear of compromising oncologic resection by tumoral cell seeding.³⁰ Hand-assisted laparoscopic technique is an alternative laparoscopic approach, in which the surgeon or his assistant inserts his hand/fingers through a planned mini-laparotomy incision while the pneumoperitoneum is maintained and the dissection maneuvers then performed under videoendoscopic control. The insertion of the hand is to restore the tactile feeling and the sensation of depth, and facilitates the exposure and manipulations. Single-incision laparoscopic liver resection in some selected cases has been found to be feasible with further improvement in cosmesis and metabolic response.

A major obstacle to routine laparoscopic liver surgery was found to be severe bleeding. Some documented techniques for reducing bleeding were use of ligature, metal clips, argon beam laser, fibrin glue, vascular stapler, harmonic scapel, LigaSure and saline-linked radio-frequency dissecting sealer (TissueLink)^{31,32}. Others were meticulous surgical technique, low central venous pressure (CVP) anaesthesia and vascular inflow and outflow control. High intra-abdominal pressure has been suggested to reduce amount of bleeding however with increased risk of air embolism.³³

Laparoscopic portal vein occlusion

In all this it has been shown that 20 to 30% of patients with liver metastases are amenable to surgery.³⁴ However, by laparoscopic portal vein ligation may induce ipsilateral atrophy and contralateral compensatory hypertrophy of the remnant liver by redirecting blood thus reducing postoperative liver failure.³⁵ A subsequent percutaneous portal vein embolism can be added if the degree of hypertrophy (DOH) is not satisfactory. Patients with liver remnant (< 1% of the body weight or less than two segments of the liver remnant on pre operative volumetric assessment) are considered as good candidates for portal vein occlusion.³⁶ This is expected to induce a 40–60% increase in the size of the non-embolized portion, but this could theoretically increase the risk of recurrence.³⁷ The outcome of this could be followed up by serial scan studies.³⁸

Ablation therapy

Ablation therapy is also currently being assessed and available techniques include cryotherapy, alcohol injection, radiofrequency, laser, and microwave energy.³⁹ Some workers are skeptical regarding the use of local therapies in patients with metastatic cancer in view of the likelihood of microscopic tumor cell deposits in a variety of other organs.⁴⁰ Probe placement for Radio Frequency Ablation (RFA) can be done laparoscopically under ultrasound guidance. Generally, lesions measuring less than 2.5 cm in diameter were reported to have a greater than 90% chance of being destroyed. For lesions measuring 2.5 to 3.5 cm, approximately 70% to 90% of these lesions can be completely treated with current RFA techniques and lesions measuring 3.5 to 5.0 cm, 50% to 70% have been completely treated.⁴¹ The commonly encountered

complaints following RFA include focal discomfort at the probe entry site(s), flu-like symptoms known as post ablation syndrome and hepatic abscesses.

RESULTS

It is now generally accepted that resection of colorectal cancer liver metastases could improve long-term survival. Untreated, survival is measured in months.⁴² The benefits of avoiding open laparotomy include reduced length of hospital stay, hospital cost, and earlier initiation of non-operative therapy. Problems identified with laparoscopic therapeutic modalities are related to the risks of tumour dissemination from pneumoperitoneum, from inadequate surgical margins and from the need for additional incisions to remove large specimens. Evidence from a large prospective randomised clinical trial comparing laparoscopic versus open liver resection is unavailable.

However an evaluation of 300 minimally invasive liver resections in a single centre with mixed pathology of benign /malignant conditions using purely laparoscopic, hand assisted and laparoscopic assisted techniques versus open resection showed a significant difference between the two groups. Operative time (99 mins vs. 182 mins), blood loss (102mls vs. 325mls), transfusion requirement (2 of 300 vs. 8 of 100) and length of hospital stay (1.9 vs. 5.4 days), in favour of the laparoscopic group.⁴³ Another large-volume single-center experience of laparoscopic liver resection for malignant tumors affecting either posterosuperior segments 1, 7, 8, and, 4a (group 1) or anterolateral segments 2, 3, 5, 6, and 4b (group 2) showed a low incidence of intra-operative (6.7%) and post-operative (12.6%) morbidities. The 30-day mortality was comparable to that of the open series (0.7%) and conversion rate to laparotomy was low (3.4%).⁴⁴ Complications are significant however low the rate. A comparison of outcomes of open versus laparoscopic liver resection is shown in Table 1.

Prognosis is predictable using the Clinical Risk Score calculated by assigning 1 point for each of the following adverse, disease-related factors: lymph node positive primary tumor, disease-free interval (time from discovery of the primary lesion to discovery of liver metastases) < 12 months, more than 1 hepatic tumor, hepatic tumor greater than 5 cm, and carcino-embryonic antigen level > 200 ng/mL (within 1 month of surgery).²

Table 1 Comparison of studies on laparoscopic versus open liver resection for metastatic colorectal cancer

Study	Year	Cases		Blood loss (mls)		Operation time		LOHS		Morbidity		Mortality		Conversion rate
		Lap	Open	LLR	OLR	LLR	OLR	LLR	OLR	LLR	OLR	LLR	OLR	
				(mins)		(days)		(%)		(%)		(%)		(%)
Morino <i>et al</i> ⁴⁵	2003	30	30	320	479	148	142	6.4	8.7	6.6	6.6	-	-	Nil
Koffron <i>et al</i> ⁴³	2007	300	100	102	325	99	182	1.9	5.4	9.3	22.0	-	-	7
Topal <i>et al</i> ⁴⁶	2008	76	76	150	300	95	179	6.0	8.0	7.8	28.9	-	-	6
Ito <i>et al</i> ⁴⁷	2009	65	65	100	200	170	140	4.0	6.0	13.8	44.6	-	-	20
Dagher <i>et al</i> ⁴⁸	2009	22	50	520	735	360	328	8.0	13.0	14.0	46.0	-	2	9
Abu Hilal <i>et al</i> ⁴⁹	2011	36	34	700	500	300	180	5.0	9.0	14.0	15.0	-	2	11

LOHS-Length of hospital stay

LLR-Laparoscopic liver resection

OLR-Open liver resection

Oncological follow-up consists of an abdominal ultrasound examination, tumour marker evaluation and chest x-ray every three months during the first, every month during the second and annually.⁵⁰ A CT-scan is performed annually. Recurrence occurs and if confined to the liver, a repeat resection can be performed.

CONCLUSION The yield of laparoscopy is greatest for detecting peritoneal metastases and additional hepatic tumors but often failed to identify nonresectability because of lymph node metastases, vascular involvement, or extensive biliary involvement without intraoperative ultrasonography. Hepatic resection remains a potentially curative therapy for metastatic colorectal cancer. With advances in technique, laparoscopic liver resection is seen as a favorable alternative to open resection for metastatic colorectal cancer associated with low morbidity and mortality in properly selected cases in specialized centres. However, there is a steep learning curve required for such good outcome.

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HELICOBACTER PYLORI: SEROLOGICAL TESTING AND TREATMENT IN UNINVESTIGATED DYSPEPSIA: RANDOMIZED CONTROL STUDY IN NORTHERN NIGERIA

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ABSTRACT

Purpose: *Helicobacter pylori* has been strongly associated with dyspepsia and eradication of *H. pylori* after a non-invasive testing is an integral part of most management guidelines. This study evaluated the benefit of serological testing and treatment of *H. pylori* in Nigerian patients presenting with uninvestigated dyspepsia

Methods: The study was a randomized double blinded controlled trial. 103 consecutive dyspeptic subjects aged between 18 and 50 years were recruited for *H. pylori* serology. Seropositive dyspeptic subjects were randomized to receive Lansoprazole with or without antibiotics (Clarithromycin 500mg and Metronidazole 400mg twice daily for 7 days). Seronegative dyspeptic subjects received Lansoprazole without antibiotics. Subjects were followed up at 2, 6 and 10 weeks from enrolment to assess dyspeptic symptoms using Global Overall Symptom Scale (GOSS).

Results: Of 103 cases enrolled, 23 were seropositive and 80 were seronegative. 10 (9.7%) seropositive were randomly assigned to receive triple therapy while 13 (12.6%) seropositive were randomly assigned to placebo group. The eighty (77.7%) seronegative were assigned to the placebo group. After two weeks of intervention, the mean GOSS for seropositive cases assigned eradication regimen dropped from 4.90 ± 1.66 at presentation to 1.11 ± 0.33 . There after to 1.38 ± 0.52 and 1.14 ± 0.38 at six and ten weeks respectively. The mean GOSS for seropositive cases assigned placebo group dropped from 5.00 ± 1.58 at presentation to 1.39 ± 0.65 by two weeks, this later became 1.60 ± 1.27 and 1.22 ± 0.67 at six weeks and ten weeks respectively. Seronegative cases were all assigned into placebo group, their mean GOSS dropped from 5.21 ± 1.48 at presentation to 1.48 ± 0.77 by two weeks after enrolment and subsequently, to mean scores of 1.53 ± 0.95 and 1.44 ± 0.56 at six weeks and ten weeks respectively. Hence, no significant benefit in treatment outcome when seropositive dyspeptics were treated with triple therapy compared with those treated with proton pump inhibitor only, up to 10 weeks after treatment ($p = 0.83$).

Conclusion: Antibiotic treatment for *H. pylori* offered no benefit over empirical use of proton pump inhibitor in uninvestigated dyspepsia. Proton pump inhibitor should be considered first in the management of uninvestigated dyspepsia.

Keywords: *Helicobacter pylori*, Dyspepsia, Nigeria

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INTRODUCTION

Dyspepsia is a term used to describe a range of symptoms arising from upper gastrointestinal tract.^{1, 2} At an international consensus meeting, dyspepsia was defined as discomfort or pain centered in the upper abdomen, excluding patients with predominantly heartburn or acute reflux as their main symptoms.³ Dyspepsia is a common condition affecting most populations globally and negatively affects the quality of life of affected individuals whose expectation from physicians to provide cure may not always be met.³

Helicobacter pylori (*H. pylori*) is strongly associated with gastritis, peptic ulcer disease, non ulcer (functional) dyspepsia, gastric cancer and mucosal associated lymphoid tissue (MALT) lymphoma^{4 - 6}

In primary care, the underlying pathology in patients with dyspepsia often is unknown and rather than recommending endoscopy for all patients, most national guidelines suggest a "test and treat" strategy.^{12, 13, 14} Several recent economic analyses show that the test and treat strategy improves symptoms and is cost effective compared with other strategies.^{15, 16 - 19} A long-term follow-up study comparing a test and treat strategy versus prompt endoscopy in patients with dyspepsia showed that the former reduced the number of endoscopies performed as well as the number of antisecretory medications administered.²⁰ We evaluated the benefit of serological testing and antibiotic treatment of *H. pylori* in Nigerian patients presenting with uninvestigated dyspepsia.

METHODS

This study was carried out in the General Outpatient Clinic of Aminu Kano Teaching Hospital (A.K.T.H), Kano, Kano state, Nigeria.

The study was a randomized double blinded controlled trial. Adult patients, aged 18 to 50 years presenting newly in the clinic were eligible for enrollment if they were presenting for the first time in the clinic with uninvestigated dyspepsia according to ROME II definition of dyspepsia and no other known gastrointestinal disease. Subjects were excluded if they had a history of endoscopy or barium study in the preceding 6 months; had been previously treated

with an antibiotic regimen for *H. pylori*; had been using non-steroidal anti-inflammatory drugs or aspirin in the preceding 30 days; had alarm symptoms of weight loss, anaemia, palpable abdominal mass, or supraclavicular lymphadenopathy; had a known allergy to the study drugs; or were pregnant. Patients with either heartburn or regurgitation were considered to have gastro-oesophageal reflux disease and were excluded

Ethical approval was obtained from Ethical committee of Aminu Kano Teaching Hospital. Voluntary written informed consent was obtained from each participant

After, interview based on pretested structured questionnaire including grading the severity of symptoms at presentation, using the Global Overall Symptom Scale (GOSS) was administered. Five milliliters (5mls) of venous blood were drawn from a peripheral vein, and plasma was screened for antibodies to *H. pylori* using '*H. pylori* One Step' (Grand Medical Diagnostic, Michigan U.S.A .LOT HP6030013, Expiry Date 2008-02), an ELISA-based test kit. This kit demonstrates an overall accuracy of 93.2% compared with culture/ histology.

Seropositive patients were randomized by lottery into two treatment groups of either lansoprazole (Lansozil, Fidson Healthcare Ltd., Nigeria) 30mg, metronidazole (Elagyl, Jopan Pharmaceutical, Nigeria) 400mg, clarithromycin (Klacid, Abbot, Switzerland) 500mg (*H.pylori* eradication group) or lansoprazole (Lansozil, Fidson Healthcare Ltd., Nigeria) 30mg, and two placebo starch-filled capsules that did not have an identical appearance to the active drugs (control group). Drugs in each treatment group were used twice daily for 7 days only. Seronegative patients received the same treatment as the control group. Both participants and investigator were blinded to the treatment allocation. Randomization was done by a trained assistant by lottery using green and red coloured beads, which participants drew from opaque container; green beads for eradication group while red beads are control group. The record of treatment assigned to each participant, which was documented against their study number was kept secret to the investigator till completion of the study.

Participants were seen in the clinic at four follow-up times: Day 2, Week 2, Week 6, and Week 10, after commencement of treatment. Those who could not make the follow up appointment had a telephone based follow up. Day 2 follow up was to identify the presence of any adverse event that might necessitate withdrawal of participant from the study, while subsequent follow ups ascertained the severity of symptoms at each visit using a 7 point Likert type scale, the Global Overall Symptom Scale (GOSS) ²¹

Participants with exacerbation that might require further intervention not part of the protocol were withdrawn from the study, at whatever stage this became necessary.

Data were entered, checked and analyzed in Epi Info 3.3.2 software (CDC, Atlanta, GA, USA). Treatment outcome was analysed using multiple linear regression with GOSS at follow up as the dependent variable and treatment group and seropositivity as independent variables. To control for the effect of baseline GOSS on outcome, this variable was included in the linear regression model as an independent variable. P value of 0.05 was considered significant.

RESULTS

Total of 103 dyspeptics were enrolled. Twenty three dyspeptic patients were seropositive for *H. pylori*, 10 (43.5%) of which were assigned to receive triple therapy (Treated Positive) and 13 (56.5%) were assigned

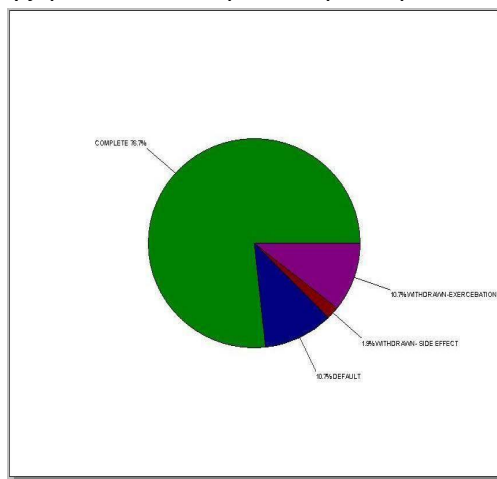


Fig1: Outcome of Treatment follow up among Cases

to the placebo group (Placebo Positive). The seronegative subjects (80) were assigned to receive lansoprazole (Placebo Negative).

A total of 79 (76.7%) subjects completed follow up, 11 (10.7%) defaulted, 2 (1.9%) were withdrawn due to symptoms of cramp like abdominal pain, nausea and vomiting which were not present at commencement of the study, and 11 (10.7%) were withdrawn due to exacerbation of dyspeptic symptoms while undergoing follow up. (Fig. 1)

After two weeks of follow up the mean GOSS of seropositive cases assigned to the *H. pylori* eradication regimen dropped from 4.90 ± 1.66 at presentation to 1.11 ± 0.33 . There after it became 1.38 ± 0.52 at six weeks and 1.14 ± 0.38 at ten weeks. The mean GOSS for seropositive cases assigned into placebo group dropped from 5.00 ± 1.58 at presentation to 1.39 ± 0.65 by two weeks, this later became 1.60 ± 1.27 and 1.22 ± 0.67 at six weeks and ten weeks respectively. For seronegative cases who received lansoprazole alone, the mean GOSS dropped from 5.21 ± 1.48 at presentation to 1.48 ± 0.77 by two weeks after enrolment. Subsequently, there was no significant change in GOSS, with mean scores of 1.53 ± 0.95 and 1.44 ± 0.56 at six weeks and ten weeks respectively (Figure 2).

Among patients with dyspepsia that were seropositive for *H.pylori*, multiple linear regression analysis of GOSS demonstrated no significant advantage of antibiotic treatment over lansoprazole

Table 1: Multiple linear regression analyses of the effect of treatment GOSS at 2, 6, and 10 weeks in 23 *H.pylori* seropositive subjects

Variable	Coefficient	Std. Error	P-value
Week 2:			
GOSSpresentation	0.098	0.072	0.1914
Treated (Yes/No)	-0.292	0.230	0.2206
Week 6:			
GOSSpresentation	0.139	0.149	0.3658
Treated (Yes/No)	-0.411	0.480	0.4072
Week 10:			
GOSSpresentation	-0.132	0.083	0.1388
Treated (Yes/No)	-0.059	0.269	0.8298

alone at any time point after treatment, after adjustment for baseline GOSS score (Table1).

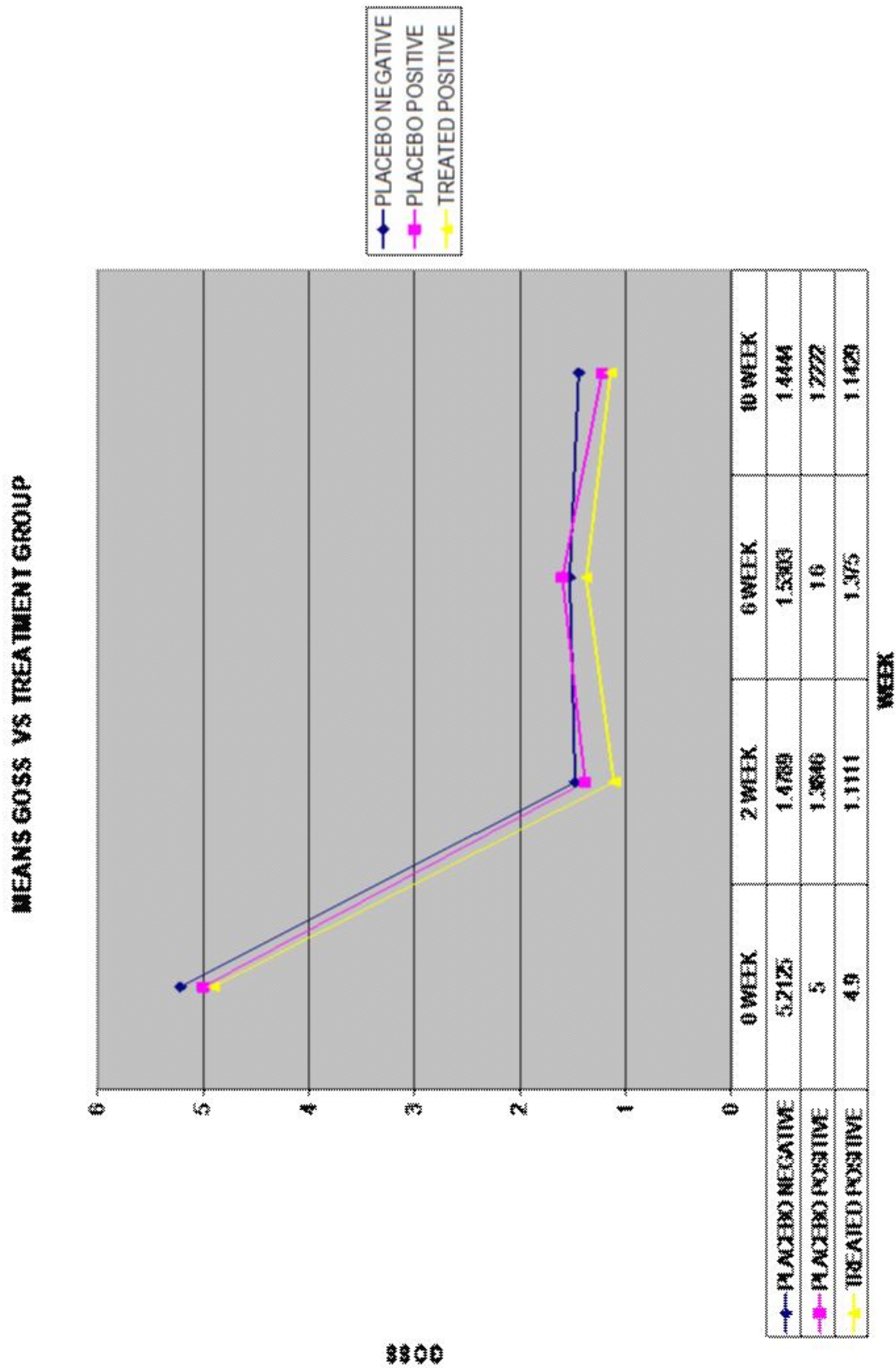


Figure 2 : Means GOSS vs. Treatment Group

Among all patients with dyspepsia, linear regression analysis of GOSS demonstrated no significant effect of *H. pylori* seropositivity on response at 2, 6 or 10 weeks after adjustment for baseline GOSS score (Table 2).

Table 2 : Multiple linear regression analyses of the effect of GOSS presentation, *H. pylori* seropositivity on GOSS at 2, 6, and 10 weeks in 23 dyspeptic subjects

Variable	Coefficient	Std. Error	P-value
Week 2:			
GOSS presentation	-0.035	0.050	0.4927
Seropositivity	-0.211	0.178	0.2401
Week 6:			
GOSS presentation	0.003	0.069	0.9605
Seropositivity	-0.030	0.256	0.9072
Week 10:			
GOSS presentation	-0.057	0.042	0.1798
Seropositivity	-0.275	0.156	0.0822

DISCUSSION

This study showed that in a General Outpatient Clinic in Northern Nigeria, there was no significant difference in the treatment outcome between dyspeptic subjects who were seropositive for *H. pylori* and had treatment and those who were seropositive who had proton pump inhibitor. Similarly, no significant difference was observed in short-term treatment outcome between those who were seropositive and seronegative for *H. pylori* who were treated with a proton pump inhibitor. Even though other studies reported significant benefit of non invasive testing and treatment for *H. pylori* in uninvestigated dyspepsia, the method of outcome measurement varied.^{6, 11} Our primary outcome measure was symptom score during scheduled at 2nd weeks, 6th weeks and 10th week follow up. A study conducted in Bristol measured outcome using consultation rate for epigastric pain (dyspepsia) with 35% fewer participants among eradication group consulted for dyspepsia over two years compared with the placebo group.¹¹ A Canadian study which measured successful intervention as minimal or no symptoms of dyspepsia at the end of one year, observed more patients in the eradication group were completely asymptomatic⁶

The difference in response to treatment between these studies and ours could be due to the fact that *H. pylori* infection was not found to be a significant risk factor for developing uninvestigated dyspepsia in our study, or because of the 'African enigma' in which it was observed that the presence of *H. pylori* presence does not correlate to occurrence of clinically important disease amongst Africa populations compared to those in the West.²² This has been thought to be due to difference in pattern of infection, age of acquisition, environmental, dietary and genetic influences which alter the pathological role and clinical relevance of the organism in Africa.^{21, 23}

We found no benefit in a test and treat approach in Nigerian outpatients with uninvestigated dyspepsia. Serological screening for *H. pylori* and antibiotic treatment offered no benefit over the empirical use of a proton pump inhibitor in management of uninvestigated dyspepsia. This observation could be as a result of the fact that *H. pylori* might not be aetiologically responsible for dyspepsia amongst the studied population considering; firstly the prevalence of those with *H. pylori* infection amongst the dyspeptic participants is small compare to those without. Secondly, there was no significant difference in the rate of abatement of symptoms between those seropositive dyspeptics who had triple therapy regimen, those seropositive dyspeptics who had proton pump alone and those seronegative dyspeptics who had proton pump inhibitors.

This study is limited by the small number of participants who were found to be seropositive, the short duration of follow up compared to other studies, even though use of ELISA method for *H. pylori* screening might be considered a limitation²², the low prevalence of seropositive participants in area where naturally high prevalence is expected might make this to be insignificant.

In conclusion, we recommend that patients with dyspepsia in resource-poor settings be given of proton pump inhibitor as first line therapy.

H. pylori testing and eradication should be considered only in those with dyspepsia who have had full course of proton pump inhibitor without abatement of symptoms.

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EVALUATION OF THE ANTIDIARRHOEAL PROPERTY AND SAFETY OF ETHANOLIC EXTRACT OF *FICUS BENJAMINA* 'VARIEGATA' FRUITS IN WISTAR RATS

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ABSTRACT

Background and Objectives: There is an age long folkloric claim that *Ficus benjamina* fruits could be used as an antidiarrhoeal agent. Up till this time, there has not been any scientific report on the acclaimed use. Therefore, the efficacy of the ethanolic extract of *Ficus benjamina* 'variegata' fruit as an antidiarrhoeal agent as well as the safety of the extract was evaluated in wistar rats.

Methods: Twenty albino rats were assigned into 4 groups: A - D (5 rats per group) in each of the experiment. Animals in group A were administered 1ml of distilled water while those in groups B,C, D were treated like the distilled water control except they received 2.5mg/kg Loperamide, 625 and 1250 mg/kg body weight of the extract respectively. The antidiarrhoeal activity of the extract was evaluated using two standard models: castor oil-induced diarrhoea and gastrointestinal transit motility. The safety/ toxicity risk was evaluated by determining the activity of some 'marker' enzymes of the small intestine, liver and serum of the animals.

Result: The ethanolic extract of *F. benjamina* significantly ($p < 0.05$) prolonged the time of diarrhoea induction and reduced the frequency of diarrhoea episodes in the castor oil induced diarrhoea model. Furthermore, there was significant decrease in the propulsion of charcoal meal through the gastrointestinal tract. These finding compared favourably ($P > 0.05$) with the reference drug (loperamide) – treated animals. Toxicological studies revealed that the extract significantly reduced the activities of Alkaline phosphatase (ALP) and Acid phosphatase (ACP) in both the small intestine and serum of the animals whereas the activities of Glutamate pyruvate transaminase (GPT), Glutamate oxaloacetate transaminase (GOT) and Gamma glutamyl transferase (GGT) in the liver and serum as well as the computed liver and small intestine – body weight ratio.

Conclusion: Overall, the ethanolic extract of *F. benjamina* fruit possesses antidiarrhoeal activity at the tested doses. However, the extract at the doses investigated may not be completely safe.

Keywords: Castor oil, Ethanolic extract, *Ficus benjamina* 'variegata', Gastrointestinal motility, Loperamide, Moraceae

INTRODUCTION

Diarrhoea can be described as the passage of three or more loose or liquid stools per day, or more frequently than is normal for the individual.¹ It is a major problem in Third world countries where it has been reported to cause 4-5 million deaths annually.^{2,3}

In Nigeria, the prevalence has been placed at 18.8% which is one of the worst in sub-Sahara Africa.⁴ The major cause of diarrhoea has been reported to be due to viral, bacterial (*Shigella flexneri*, *Staphylococcus aureus*, *Escherichia coli* and *Salmonella typhi*) and parasitic

infections.^{5,6} In addition, *Candida albicans* have also been reported to cause diarrhoea in humans.⁷ Other causes include malabsorption, inflammatory bowel disease and irritable bowel syndrome.⁸

The major management option is the oral rehydration therapy.¹ However, antibiotics, bismuth compounds and antimotility agents have also been used in the management of the disease.^{1,9,10} Apart from the modern medical therapy, the use of herbs and herbal preparations in the management of diarrhoea and other disease conditions is becoming a common practice in many countries of the world.¹¹

Ficus benjamina 'variegata' (family: Moraceae) commonly known as weeping fig or benjamina's fig (English) is native to the tropics of Central, South and West Africa as well as South East Africa and Australia.¹² It is an evergreen shrub or tree that grows up to 20-60 meters high and 70 meters wide, with dropping branches.¹² *Ficus benjamina* fruit has been claimed in the folklore medicine to be used in managing diarrhoeal conditions. This claim is however yet to be substantiated by scientific data. Therefore, the present study was aimed at evaluating the acclaimed antidiarrhoeal activity of ethanolic extract of *Ficus benjamina* fruits using standard models of castor oil – induced diarrhoea and gastrointestinal transit motility. The extract was also evaluated for its effects on some 'marker'enzymes of the liver and small intestine of Wistar rats.

MATERIALS AND METHODS

Plant Material

Ficus benjamina 'variegata' fruits were collected from Government Reservation Area, Ilorin, Kwara State, Nigeria and were identified at the Department of Plant Biology, University of Ilorin, Ilorin, Nigeria.

Laboratory animals

A total of forty albino rats (*Rattus norvegicus*) of both sexes weighing 100-150 g were obtained from the Animal Holding Unit of the Department of Biochemistry, University of Ilorin, Ilorin, Nigeria. They animals were fed on rat pellets (Bendel Feeds and Flour Mill, Ewu, Edo State, Nigeria) and water *ad libitum*.

Drug and Chemicals

Loperamide was a product of Sigma Chemical Co., Missouri, USA, while castor oil and charcoal meal (10% activated charcoal) were from Bell Sons and Co., Ltd, Southport, England.

Assay kits

The assay kits for Gamma glutamyl transferase (GGT), glutamate oxaloacetate transaminase (GOT) and glutamate pyruvate transaminase (GPT) were products of Randox Laboratory, Co-Antrim, United Kingdom while paranitrophenol phosphate and L- α -glutamyl – p-nitroanilide were from Sigma-Aldrich Inc., St. Louis, USA.

Preparation of extract

Ficus benjamina fruits were oven-dried at 40°C for 8 hours. The samples were thereafter pulverized using an electric blender. A known amount (100 g) of the powder was subjected to cold extraction in 100 ml of 70% ethanol in a screw-cap bottle. This was stirred intermittently for 72 hours after which it was filtered using Whatman No. 1 filter paper. The filtrate was concentrated at 40°C using rotary evaporator to give a yield of 20.06 g (% yield of 20.06).

Antidiarrhoeal studies

Castor-oil induction of diarrhoea in rats

The procedure described by Sunil *et al*¹³ was used with slight modifications to assess the antidiarrhoeal effect of the extract. A total of twenty experimental rats were weighed and randomly assigned into 4 groups (A – D). They animals then placed in a cage (the floor of which was lined with blotting paper) and fasted for 18 hours (without food but were given free access to water). Animals in group A received (po) 1 ml of distilled water while those in groups B, C and D were orally administered with the reference drug (2.5mg/kg body weight of loperamide), 625 and 1250 mg/kg body weight of the extract respectively. The doses of the fruit used for the study was calculated based on the information obtained from herb sellers within the locality of the authors. The rats were thereafter administered 1ml of castor oil (to induce diarrhoea), one hour after their initial treatment with distilled water, loperamide and the extract. The fecal parameters monitored for 6 hours include onset time of diarrhoea, total number of faeces, number of wet faeces, fresh weight of faeces and water content of faeces. The inhibition time of diarrhoeal faeces was computed using the expression:

$$\{100 - [(Total\ number\ of\ faeces - Number\ of\ wet\ faeces) / total\ number\ of\ faeces \times 100]\}.$$

Gastro intestinal motility test

The procedure described by Gerald *et al*¹⁴ with some modifications was used to evaluate the effect

of the extract on the propulsion of the charcoal meal through the gastrointestinal tract. Again, 20 experimental animals were weighed and randomly assigned into 4 groups (A – D). The animals were then placed in a cage and fasted for 18 hours (without food but were given free access to water). Animals in group A were orally administered 1 ml of distilled water while those in groups B, C and D received via the same route, 1ml corresponding to 2.5mg/kg body weight of loperamide, 625 and 1250 mg/kg body weight of the extract respectively. The rats which were weighed before the commencement of administration were orally administered 1ml of the charcoal meal, 30 minutes after the administration of reference drug and the extract. At the end of 30 minutes, the animals were sacrificed as described by Akanji and Yakubu¹⁵. Blood was collected into sample bottles and centrifuged at 503 x g for 15 mins to obtain the serum. The rats were thereafter quickly dissected and the section of the GIT covered by the charcoal meal was measured. The distance was expressed as a percentage of the length of the small intestine.

experiment, weighed and then immersed in 0.25M sucrose solutions. The liver was blotted in tissue paper while the small intestine was cleaned of metabolic waste. The organs were homogenized separately in 0.25 M sucrose solution. The homogenates were stored frozen for 24 hours before being used for the biochemical analyses.

Determination of biochemical parameters

The biochemical parameters determined were protein¹⁶, GGT¹⁷, ALP¹⁸, ACP¹⁹, GPT and GOT²⁰. The organ-body weight ratios were also computed using the expression described by Yakubu *et al*²¹.

Statistical analysis

The results were expressed as the mean $\pm$ SEM of five determinations. Data were evaluated for significance using one-way analysis of variance and Duncan Multiple Range Test at $p < 0.05$.

RESULTS

In the Castor oil induction of diarrhoea model, the extract significantly prolonged the onset time of

Table 1: Effect of the ethanolic fruit extract of *Ficus benjamina* 'variegata' on castor oil induction of diarrhoea in rats.

Parameters studied	Groups			
	Distilled Water	Loperamide (2.5 mg/kg)	Extract (625 mg /kg body weight)	Extract (1250 mg /kg body weight)
Onset time (min)	29.66 $\pm$ 0.34 ^a	59.67 $\pm$ 0.88 ^b	54.8 $\pm$ 1.25 ^c	58.1 $\pm$ 0.96 ^b
Total number of faeces	27.06 $\pm$ 0.22 ^a	8.21 $\pm$ 0.33 ^b	9.64 $\pm$ 0.58 ^b	8.32 $\pm$ 0.86 ^b
Number of wet faeces	21.34 $\pm$ 0.13 ^a	4.03 $\pm$ 0.11 ^b	4.63 $\pm$ 0.13 ^b	4.82 $\pm$ 0.38 ^b
Fresh weight of faeces	12.18 $\pm$ 0.62 ^a	2.70 $\pm$ 0.04 ^b	2.92 $\pm$ 0.13 ^b	2.21 $\pm$ 0.63 ^a
Water content of faeces (ml)	3.22 $\pm$ 0.32 ^a	0.71 $\pm$ 0.002 ^b	0.76 $\pm$ 0.001 ^b	0.73 $\pm$ 0.01 ^b
Inhibition of diarrhoea faeces (%)	78.86 $\pm$ 3.11 ^a	49.09 $\pm$ 2.15 ^b	48.03 $\pm$ 3.62 ^b	57.93 $\pm$ 2.11 ^c

Values are mean of 5 determinations $\pm$ SEM;

Test values carrying superscripts different from the control across the row for each parameter are significantly different ($P < 0.05$).

Toxicological Studies

Preparation of serum and tissue homogenates

The small intestine and liver were removed from the animals used in the gastrointestinal motility

diarrhoea with the value obtained for the animals treated with 1250 mg/kg body weight comparing favourably with those administered the reference drug (Table 1). Furthermore, the extract decreased all other fecal parameters (total number of faeces, number of

Table 2: Effect of the ethanolic extract of *Ficus benjamina* 'variegata' fruit on distance travelled by charcoal meal in the small intestine of rats

Groups	Distance travelled by charcoal (%)
Distilled water	77.06 ± 1.11 ^a
Loperamide (2.5 mg/kg body weight)	36.52 ± 1.28 ^b
Extract (625 mg/kg body weight)	66.73 ± 0.83 ^c
Extract (1250 mg/kg body weight)	45.86 ± 1.21 ^d

Values are mean of 5 determinations ± SEM;
Test values carrying superscripts different from the control are significantly different (P<0.05).

These reductions, although similar in pattern to the loperamide treated diarrhea induced rats did not compare favourably (p > 0.05) well with the animals treated with the loperamide (Table 2).

The extract dose dependently decreased the activities of ALP and ACP in the small intestine and serum of the animals when compared with the distilled water treated rats. The decrease in ALP was not significantly different from the rats administered loperamide whereas that of ACP was significantly different (p < 0.05) from the reference drug treated animals (Table 3). In contrast, the activities of GPT, GOT and GGT in the liver and serum of rats treated with the extract were not significantly different (p > 0.05) from the loperamide- and distilled water- treated rats (Table 4). Furthermore, the 625 and 1250 mg/kg body weight doses of the ethanolic extract did not significantly (p > 0.05) alter the computed small intestine- and liver- body weight ratios of the rats when compared with the distilled water treated rats. The

Table 3: Effect of the ethanolic extract of *figus benjamina* 'variegata' fruit on the activity of alkaline and acid phosphatase in the small intestine and serum of Wistar rats

Treatment	Enzyme activity (nm/min/mg protein)			
	Small intestine		Serum	
	ALP	ACP	ALP	ACP
Control				
Distilled water)	100.25 ± 1.23 ^a	118.32 ± 3.46 ^a	4.51 ± 0.11 ^a	3.62 ± 0.17 ^a
Loperamide(2.5 mg/kg body weight)	48.22 ± 1.42 ^b	65.42 ± 3.32 ^b	1.81 ± 0.07 ^b	2.75 ± 0.13 ^b
Extract(625 mg/kg body weight)	42.33 ± 1.98 ^b	37.36 ± 3.48 ^c	1.48 ± 0.06 ^b	1.12 ± 0.12 ^c
Extract(1250 mg/kg body weight)	40.49 ± 1.82 ^b	33.33 ± 3.42 ^c	1.35 ± 0.08 ^b	0.98 ± 0.11 ^c

Values are mean of 5 determinations ± SEM;
Test values carrying superscripts different from the control across the column for each parameter are significantly different (P<0.05)

wet faeces, fresh weight of faeces and water content of faeces) (P < 0.05) when compared with the distilled water treated rats (Table 1). The reductions in the fecal parameters by the extract compared favourably with the loperamide treated rats (Table 1).

In the gastrointestinal transit motility model, the extract significantly reduced the distance travelled by the charcoal in a dose dependent manner (Table 2).

trend was similar to the values obtained for the rats treated with the 2.5 mg/kg body weight of the loperamide (Table 5).

DISCUSSION

It is known that the active component of castor oil is the ricinoleic acid which is liberated by the

Table 4: Effect of ethanolic extract of *Ficus benjamina* 'variegata' fruit on selected enzyme activity of rat liver and serum

Treatment	Enzyme Activity (nm/min/mg protein)					
	Liver			Serum		
	GPT	GOT	GGT	GPT	GOT	GGT
Control (Distilled water)	125.21±0.20 ^a	139.02±2.11 ^a	8.42 ±0.68 ^a	9.02±0.81 ^a	39.04±3.36 ^a	1.11±0.06 ^a
Loperamide (2.5mg/kg body weight)	128.01±0.32 ^a	140.03±3.28 ^a	7.91±0.49 ^a	10.11±0.33 ^a	42.33±2.72 ^a	1.13± 0.09 ^a
Extract (625 mg/kg body weight)	124.22±0.38 ^a	140.18±3.02 ^a	8.79±0.36 ^a	9.32±0.22 ^a	38.72±3.65 ^a	1.18±0.07 ^a
Extract (1250 mg/kg body weight)	124.01±0.11 ^a	141.33±2.93 ^a	8.74±0.51 ^a	8.34±0.48 ^a	39.14±3.08 ^a	1.15±0.08 ^a

Values are mean of 5 determinations ± SEM;

Test values carry the same superscripts with the control across the column for each parameter indicating that they are not significantly different ($P>0.05$).

action of lipases on castor oil. The ricinoleic acid has been reported to produce irritating and inflammatory actions on the intestinal mucosa leading to the release

changes in electrolyte transport, which results in a hyper-secretory response (decreasing Na^+ and K^+ absorption), stimulating peristaltic activity and

Table 5: Effect of the ethanolic extract on the computed organ-body weight ratio of rats

Groups	Small Intestine: body weight ratio	Liver: body weight ratio
Control	0.026 ± 0.00 ^a	0.024 ± 0.002 ^a
Standard drug control	0.028 ± 0.00 ^a	0.026± 0.002 ^a
625 mg/kg body weight	0.026± 0.001 ^a	0.027± 0.002 ^a
1250 mg/kg body weight	0.027.± 0.00 ^a	0.025± 0.001 ^a

Values are mean of 5 determinations ± SEM;

Test values carrying superscripts different from the control for each organ are significantly different ($P<0.05$).

of prostaglandins.²² This condition stimulate an increase in the permeability of the mucosal cells and

diarrhoea.²³ Inhibitors of prostaglandin synthesis are known to delay diarrhoea induced with castor oil.¹⁴

The prolonged onset time of diarrhoea as well as the reduction in the fecal parameters following the administration of the extract in the present study indicated antidiarrhoeal activity. Furthermore, it is possible that the antidiarrhoeal effect of *Ficus benjamina* may be due to the inhibition of prostaglandin biosynthesis since many authors have also reported on the influence of botanicals on prostaglandin synthesis and activity.²⁴⁻²⁶ Charcoal was used in the gastrointestinal motility test to find out the effects of these extract on the peristaltic movement. It has been reported that activated charcoal avidly absorbs drugs and chemicals on the surface of the charcoal particles thereby preventing absorption. The results show that the extract suppressed the propulsion of charcoal meal thereby increasing the absorption of water and electrolytes. The mechanism of action of the extract may therefore be similar to the reference drug, loperamide used in the present study which primarily retards the intestinal transit, stimulates the anal sphincter pressure and increases the mucosal contact time allowing complete absorption of electrolytes and water.²⁷

Antidiarrhoeal activity of medicinal plants have been ascribed to the presence of various phytochemicals in a number of medicinal plants.²⁸ Therefore, the *in vivo* antidiarrhoeal activity of the ethanolic fruit extract of *Ficus benjamina* fruits might be due to the activity of the phytoconstituents.

The extract has produced enzyme specific effects in the animals by decreasing the activities of both ALP and ACP in the organs and serum of the animals whereas the activities of GOT, GPT and GGT remained unaltered. The reduction in the activities of the phosphatases (markers of plasma membrane and lysosomal membrane) in the small intestine of the animals may be attributed to inactivation or inhibitory effect of the enzymes by the extract since there was no corresponding increase in the serum enzyme. It is therefore possible that the extract possess compounds that either inhibited or inactivated the phosphatases investigated in the organ and serum of the animals. This however may adversely affect metabolic processes dependent on the enzymes. Interestingly, the other membrane bound enzyme, GGT and the cytosolic enzymes, GOT and GPT in the liver of the animals were not altered. The reason(s) for this is not immediately known but may not be unconnected with the small intestine being the most vulnerable organ in diarrhoea. Therefore, the results in the present study

with respect to safety evaluation suggest that the extract has exhibited selective toxicity only on the small intestine.

In conclusion, the results of this investigation revealed that the ethanolic extract of *Ficus benjamina* 'variegata' fruits possess antidiarrhoeal activity. The extract at the doses investigated is also not completely safe as an oral remedy.

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CLOSED HAEMORRHOIDECTOMY: A PRELIMINARY REPORT

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ABSTRACT

Introduction: The open haemorrhoidectomy has been criticized by various workers for its severe post-operative pains, slow wound healing and prolonged post operative care. This has led to a shift of interest to other methods of haemorrhoidectomy. Although, closed haemorrhoidectomy is not very popular in many centres in this country but commonly used in the United States of America, is obviously a dependable alternative. This study is set out to attest to the fact that closed haemorrhoidectomy is devoid of the above demerits and to join others in canvassing for its use as the main standard surgical procedure for 2nd and 3rd degree haemorrhoids.

Methodology: A prospective study of closed haemorrhoidectomy was carried out on all consecutive patients' that presented in our centre with late 2nd and 3rd degree haemorrhoids between 2007 – 2011; and by a visual observation technique (categorical rating scale); the patients' were closely monitored post-operatively while on admission.

Results: There were 12 males and 3 females in the study. Thirteen (13) of the patients' got discharged on the 3rd post-operative day while the rest 2 were discharged on the 5th post-operative day and were seen weekly at the surgical outpatient department (SOPD) weekly for further assessment and follow-up. The peak wound healing rate was 2 weeks, range 2 – 3 weeks. The post-operative pain score was mild in most of the patients; acute urinary retention, post-operative bleeding and faecal impaction were none existent. The only complication was a secondary haemorrhage in one male patient that occurred on the 8th post-operative day.

Conclusion: Closed haemorrhoidectomy is a safe alternative method, almost free of complications and has a faster healing rate so; it should be embraced by all workers.

Keywords: Closed haemorrhoidectomy, free of complication and faster healing rate.

INTRODUCTION

Haemorrhoids (Piles) are common disorders of dilated superior and or inferior haemorrhoidal plexuses of veins, occurring in relation to the anus. Such haemorrhoids may be external or internal to the

anal orifice¹. Epidemiological surveys have shown that the disorder has a worldwide distribution; with racial and regional variation². The surgical treatment of haemorrhoids was one of the earliest surgical procedures practiced in the ancient civilization³.

Ligation and excision haemorrhoidectomy, known as Milligan-Morgan Operation is considered the gold standard treatment for late 2nd and 3rd degree haemorrhoids and is most commonly used in Europe⁴ as well as in Nigeria. This age-long procedure has been variously criticized and modified for its post-operative pains, slow wound healing, haemorrhage, urinary retention and prolonged post-operative care^{5,6,7}.

The alternative methods, almost devoid of these complications include: closed,^{7,9} harmonic scapel¹⁰ and stapled haemorrhoidectomy⁸. This call for the appraisal of closed haemorrhoidectomy in modern times especially in a resource poor centre like ours. This study is carried out to verify the claims that a closed haemorrhoidectomy is actually almost pain free, has a rapid wound healing rate and early return to normal work. And also to call for its routine use in centres in Nigeria because of its socio-economic benefits to patients'.

PATIENTS AND METHODS

A prospective study of 15 consecutive patients with 2nd and 3rd degree haemorrhoids who had closed haemorrhoidectomy from Jan. 2007 to Dec. 2011 at the Federal Medical Centre, Ido-Ekiti, Ekiti State, Nigeria was documented. Ethical approval for the study was obtained from the hospital's Ethical Committee on Research. The patients' personal, clinical, operative and post-operative data were documented. They were clinically examined to rule out any cardiopulmonary, abdominal and genito urinary predisposing factors. Those patients' with complicated haemorrhoids, associated carcinoma, fissures, fistula-in-ano, debilitating medical conditions, like diabetes mellitus and immuno-compromised states that may affect normal healing processes, were all excluded from the study. There was no special bowel preparation in all the patients', save, an early morning disposable soap and water enema on the day of operation.

Dissection, ligation and excision of the principal haemorrhoids were done according to the classical St. Mark's Hospital London Method, under spinal anaesthesia. The anal sphincter was mildly stretched with the insertion of 2 fingers prior to the procedure and the piles were prolapsed by gently withdrawing a dry gauze which was inserted into the anus.

After the ligation and excision of the haemorrhoids, the mucosal defect from the base of the pedicle stump to the skin verge was then apposed completely with a continuous chronic 2/0 catgut suture. All patients had intramuscular dose of pentazocin (0.5mg/kg) eight (8) hourly for the first 24hrs post-operative day only. It was then substituted with a non-steroidal anti inflammatory drug (NSAID) ibuprofen only as from post operative day (POD) 1, per – os. Subsequent analgesic was based on the patients' pain assessment (Table 2)². Each patient was commenced on at least, twice daily warm sitz bath from the 1st post-operative day; until the wounds were judged healed (usually in 2 weeks time) when digital examination elicited no tenderness. While on admission, patients' were monitored daily for any complaints and were assessed accordingly. Bleeding was assessed using a bleeding assessment chart (Table 2)². They were discharged to the SOPD for follow up when the pain score became score 2 or less which usually occur at about 2 - 3 post-operative day (Table 1)² and were seen weekly for further assessment.

RESULTS

A total of forty (40) patients' were seen during this period of study. Of these, twenty two (22) had 1st degree haemorrhoids and were excluded. Of the eighteen (18) patients', 2 were excluded from the study due to associated Diabetes Mellitus and one (1) for Acquired Immune Deficiency. All 15 patients' had surgery, closed haemorrhoidectomy, (Excision and primary closure haemorrhoidectomy). Of these, 3 were females and 12 were males. Consultant Surgeons performed the operation in all patients'. The average length of hospital stay was 3 days, range 3 – 5 days.

The mean post-operative pain score showed that there was severe pain in the immediate post-operative period, but became moderate on the first post-operative day. The pain rapidly became mild from the 2nd post-operative day and subsequent days. The median daily post-operative pain score is as shown in table 1. There were no post-operative complications like urinary retention, reactionary haemorrhage and faecal impaction in all the patients. One of the patients', however, developed a secondary haemorrhage on the 8th post-operative day. He was re-admitted and managed conservatively as there were no overt site of

Table 1: Post-Haemorrhoidectomy pain score in the 15 patients.

DAYS	PAIN-SCORE	PATIENT	DRUGS
Immediate Post-op day	Grunting/screaming in pain	4	NSAID + Paracetamol + Pentazocin
1	Writhing in pain	3	NSAID + Paracetamol
2	Wincing to pain	2	NSAID
3	Wincing in pain	2	NSAID
4	Vocal complain due to pain	1	NSAID
5	Vocal complain due to pain	.1	NSAID

1 & 2 = Mild pain

3 = Moderate pain

4 = Severe pain

bleeding at proctoscopy in the accident and emergency (A & E).

The mean wound healing duration was 2 weeks with the highest peak rate at 3 weeks post-operative

Table 2: The chart used to assess post-haemorrhoidectomy bleeding.

Parameter	Grade of Haemorrhage
Streak of blood on toilet tissue	Type I
Frank bleeding at defecation	Type II
Overt bleeding requiring blood transfusion	Type III
Secondary haemorrhage	Type IV

day. Most patients' were lost to follow up after the 4th week of attending the surgical out-patient clinic. However, their wounds were already healed and elicited no tenderness on digital rectal examination done at the 2nd and 3rd week follow-up visit.

DISCUSSION

There has been a clarion call for a shift in the surgical treatment of haemorrhoids from the traditional open technique, to other techniques because of its significant post-operative pains, complications, slow wound healing and prolonged post-operative care^{5,6,7,8,9,10}. The severity of post-operative pain in open haemorrhoidectomy is real as seen by many workers in the field^{2,12,14}.

Parks in 1956 postulated that the pain in the open technique resulted from the low ligation and excision of the highly sensitive anal mucosa and the healing of a large area of denuded anal canal which leads to spasm and painful bowel action¹⁵. Hence, he "asserted that post-operative pain in open haemorrhoidectomy could be so severe that patients could conceal their haemorrhoids for fear of operation"¹⁴. For this reason, workers in the United States of America have modified closed haemorrhoidectomy with the use of harmonic scalpel and stapled technique to almost a painless procedure and improvement in recovery time^{8,9,10}.

In this study, 15 patients' had severe pains on the immediate post-operative period (6 – 8 hrs) which was adequately controlled with analgesics. The pain score improved rapidly thereafter to mild pains that enabled 13 of them to be discharged home by the 3rd operative day.

Only 2 patients' stayed for 5 days on admission as a result of poor resolution and delayed stability in their pain score. The above result compared favourably with Zanman *et al*⁷ who recorded 98.2% recovery in their study. There were no other notable complications like urinary retention, reactionary haemorrhage and faecal impaction in all the patients'.

It has been postulated that post-operative pain, acute urinary retention and faecal impaction have a causal relationship. Severe anal pain causes retention of urine and faecal impaction by reflexly inhibiting the voluntary relaxation of the perineal muscles which normally precede micturition and defecation. The use of anticholinergic drugs and other related agents have also been blamed¹⁷, but none of these drugs were

used in this study. As the pains were mild, well controlled with analgesics, the fear to micturate and defecate did not exist hence, no such complications were recorded.

We had one patient with secondary haemorrhage in our series. This contrasted with other workers who recorded mostly reactionary haemorrhage^{4,5,6,7} in their studies. However, it compared with Muhammed Sajid *et al*¹⁵ who recorded no post operative bleeding in their series. The reason for this is very clear in that once the haemorrhoidal vascular pedicles are properly ligated and the mucosal defects apposed by continuous suturing, there will be no raw sites, from which continuous oozes can occur.

The wound healing rate of 2 weeks and completed by 3 weeks, compared favourably with studies by other workers. Johannsons *et al*¹⁶ recorded that a complete healing was observed in 70% of cases in their closed haemorrhoidectomy patients' at 4 weeks follow up. Adna Aziz *et al*⁶, Zaman *et al*⁷, Porkharel N. *et al*⁴ and others have all attested to the faster healing rate of closed haemorrhoidectomy. Even the Newer modifications of the closed technique, such as Harmonic scalpel and stapled closed haemorrhoidectomy have made the technique not only painless but wounds sufficiently heal within 1 – 2 weeks for patient to return to normal work^{8,10}.

The reason for the faster healing rate found in closed haemorrhoidectomy is again due to the fact that all the incisions are sutured and the wounds heal by primary intention; in contrast to the traditional open haemorrhoidectomy in which after ligating the haemorrhoidal vascular pedicles, the incisions are left raw and allowed to heal by secondary intention..... the Achilles of the procedure. Closed haemorrhoidectomy therefore, with its reduced pain and faster healing rate, has immense socio-economic advantage to patients' worldwide especially in developing country like Nigeria where patients' pay for their hospital bills without any health insurance scheme. Early discharge from hospital, coupled with early return to normal work is therefore of immense economic benefit to patients'.

CONCLUSION

This short study has shown that closed haemorrhoidectomy is associated with less post-operative pain, quick wound healing rate, less bleeding and less complication. This technique, thus, has

advantage over open haemorrhoidectomy and should be embraced by all workers.

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ADVANCED HEPATOCELLULAR CARCINOMA IN 3RD TRIMESTER OF PREGNANCY —A CASE REPORT AND REVIEW OF LITERATURE

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ABSTRACT

Hepatocellular carcinoma is the commonest malignancy complicating chronic liver disease in the developing world. It could present with progressive right upper abdominal swelling and features of hepatic dysfunction. Pregnancy is associated with progressive abdominal distension and exerts increased physiological demand on the organ systems especially the liver. Hepatocellular carcinoma co-existing with 3rd trimester gestation (36 weeks) leading to sudden intra-uterine death and rapid deterioration of liver function and hepatic encephalopathy to the best of our knowledge has not been reported and is here presented.

Keywords: Hepatocellular carcinoma, Advanced, Third trimester, Pregnancy,

INTRODUCTION

Hepatocellular carcinoma (HCC) is the most common malignant tumour of the liver¹. It is the 5th most common cancer in men and the 8th in women². It is commoner in sub-saharan Africa than in western countries. In black African populations, the mean age of presentation is younger compared to patients from developed parts of the world³.

Hepatocellular carcinoma is rare in females of reproductive age, accounting for only 2.3% of cases

in Hong Kong⁴. Cancer generally is rare in pregnancy and HCC in pregnancy is even rarer⁴. The rarity of HCC in pregnancy results from a combination of three factors : the male predominance of HCC, the late age at which the tumour usually presents in women, and decreased fertility in women with advanced cirrhosis⁴.

We hereby present a case of HCC co-existing with 3rd trimester gestation (36 weeks) which led to

sudden intra-uterine foetal death, rapid deterioration of liver function and hepatic encephalopathy.

CASE REPORT

Mrs. O.G, a 37 year old Para 3+0 (2 alive) poultry farmer was referred from a peripheral hospital on account of an incidental finding of hepatic mass and gross ascites 4 days after she was delivered of a fresh still birth at gestational age (GA) of 36 weeks. She had received ante-natal care at the peripheral hospital from GA of 16 weeks and the pregnancy was said to have been developing well. There was no risk factor of chronic liver disease other than use of water based herbal remedies for febrile illness several years prior to this pregnancy.

She had noticed early satiety from the second trimester of her pregnancy but attributed it to the growing foetus hence did not seek medical help. There was no feature of liver disease or disease of other systems during the pregnancy.

Patient noticed reduced foetal movement a day before presenting at the referring hospital where she was delivered of a fresh still-birth via medical induction of labour (birth weight 2.6 kg). No excessive bleeding (Estimated Blood Loss was about 100mls) and procedure was uneventful. Four days after delivery, she noticed right upper abdominal swelling and was also found to have ascites necessitating referral to gastroenterologist.

There were no peripheral stigmata of chronic liver disease. Abdomen was distended, liver was hard, nodular and non-tender. Liver span was difficult to estimate due to the presence of ascites. Ascitic fluid was straw coloured. Other systems were essentially within normal limits.

Abdominal ultrasound scan showed enlarged nodular liver (span of 24cm) with completely distorted architecture and heterogeneous echogenicity. Ascitic fluid cytology yielded malignant epithelial neoplasm (HCC). Patient was being worked up for liver biopsy for histological confirmation before she finally died.

Alpha-fetoprotein was >500ku/l (normal range 0-10 ku/l). Screening for HBV, HCV and HIV was negative. Coagulation profile, renal and cardiologic investigations were not contributory. She

was managed for liver failure as evidenced by altered level of consciousness and the presence of flapping tremor, but succumbed to the illness after 2 weeks.

DISCUSSION

Hepatocellular carcinoma is a common malignancy in sub-Saharan Africa and this is linked to the high prevalence of hepatitis B virus infection, one of the major causes of HCC in this part of the world. Hepatitis B virus infection accounts for as much as 80% of the cases of HCC⁵.

Reported cases of HCC in pregnancy are largely isolated and highly scattered, with only 32 reports in the medical literature to the best of our knowledge⁶. These documented cases have been associated with poor maternal and foetal outcome. The median survival of this group of patients has been found to be shorter than that observed in non-pregnant patients with inoperable HCC, although, the impact of pregnancy on the prognosis of patients with different types of cancer remains controversial⁴.

In the analysis of 28 patients by Lau *et al*⁴, only 2 survived up to 1 year from diagnosis and live infants were delivered in just over half the cases. Increased levels of oestrogen and increased liver vascularity have been implicated in the abrupt progression of HCC during pregnancy⁷.

Hepatocellular carcinoma during pregnancy may be suggested by the detection of high alpha-fetoprotein levels during screening higher than the modest elevations usually associated with pregnancy⁴.

Oral contraceptive steroid is one of the minor risk factors for HCC, and this group of patients constitutes a small proportion of all patients with hepatocellular carcinoma⁸.

In our patient, HCC was suspected as a result of incidental finding of hepatic mass and gross ascites, although she had complained of early satiety during the second trimester which was attributed to the pregnancy. This shows that we should not attribute all symptoms to pregnancy alone and that a high index of suspicion is required when there is exaggerated abdominal distension. If an abdominal USS had been done earlier, probably the diagnosis would have been made. The ascitic fluid cytology and markedly elevated alpha-fetoprotein supported the diagnosis. Although,

biopsy ought to have been done for histological confirmation. This was not possible because, the patient was already in hepatic encephalopathy while she was been prepared for the liver biopsy and died few days later.

The exact risk factor in this patient was not known as she was negative for both hepatitis B and C, and there was no oral contraceptive pill use, because oral contraceptive pill is a minor risk factor for HCC. This case has demonstrated that HCC can coexist with pregnancy even till late pregnancy, therefore proper investigations, like abdominal Ultrasonographic scan, not only obstetric scan will go a long way to diagnose HCC early in pregnancy. Alpha fetoprotein may not be very useful as an initial screening tool because, it is generally elevated in pregnancy, unless there is a marked elevation as we have seen in our patient. Entezami *et al*⁹ have described a case in which a massive increase of alpha-fetoprotein was found during a routine screening for neural tube defects in the 17th week of gestation. The diagnosis of HCC was confirmed in this case by magnetic resonance imaging and fine needle aspiration.

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GASTRIC SCHISTOSOMIASIS MIMICKING GASTRIC CANCER - A CASE REPORT

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ABSTRACT

Schistosoma species especially *S. mansoni* and *S. Japonicum* cause significant disease in the gastrointestinal tract and liver. These parasites cause hepatosplenic and hepatointestinal schistosomiasis associated with significant morbidity and mortality especially in children and young people. We report a case of middle aged northern Nigerian farmer who had gastric schistosomiasis that mimicked an ulcerated gastric tumor at endoscopy with good response to chemotherapy with praziquantel.

Keywords: Gastric, *Schistosomiasis*, Gastric cancer

INTRODUCTION

First described in ancient Egypt in approximately 1550 BC¹, and in 1851, Theodor Bilharz described a parasitic infection (bilharzia) that was later termed Schistosomiasis (bilharziasis) caused by parasites belonging to the *Schistosoma* group. About 250 million people in over 76 countries worldwide are affected by the disease². Laughlin estimated that about 1.5 billion people live in endemic areas, while the World Health Organization (WHO) quotes 600 million people who are in constant threat of acquiring this protean disease. Several types of schistosoma are human pathogens, and *Schistosoma mansoni* (*S. Mansoni*) mostly affects the gastrointestinal tract and the liver. *S. mansoni* is mainly found in Central Africa and South America, *S. haematobium* in Africa, *S. Japonicum* in Far East and the Philippines and *S. mekongi*/*S. intercalatum* in Africa and Indonesia.^{3,4,5} Schistosomiasis is therefore

one of the most threatening parasitic diseases of warm countries with estimated morbidity and mortality of 20,000/year and 500-1,000/year respectively⁶.

Hepatosplenic schistosomiasis and hepatointestinal schistosomiasis from portal and mesenteric veins affection are well documented in literature but gastric schistosomiasis is not as common. De Cock in a study in Kenya has shown that Praziquantel is effective against all major schistosome species and is well tolerated in advanced disease. Praziquantel damages the schistosome integument and interferes with inorganic ion transport and glucose metabolism. Side effects are rare and not serious. They include skin rash, fever, pruritus, abdominal discomfort, nausea, headache, and dizziness. This drug is currently the treatment of choice for all forms of schistosomiasis⁷.

CASE REPORT

IB is a 45 year old farmer from Bella, Minjibir LGA of Kano State. He was first seen in the Medical Outpatient Department (MOPD) of Aminu Kano

or jaundice and never received blood transfusion. Patient is not a known diabetic or hypertensive and he never smoked cigarette nor drank alcohol.

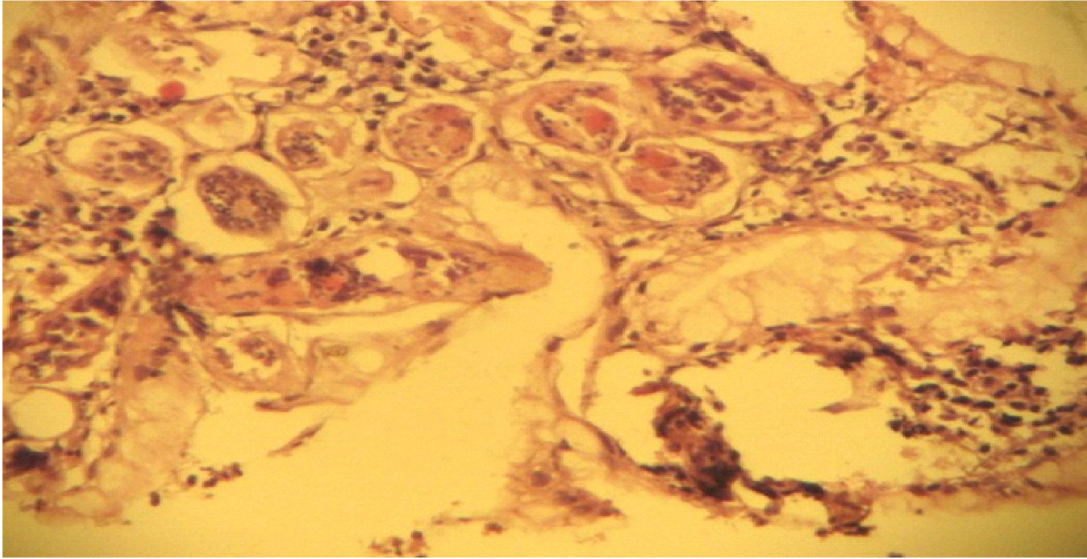


Figure 1: Section shows gastric mucosa infiltrated by schistosoma ova and mononuclear infiltrate. H and E x 40

Teaching Hospital (AKTH), Kano, northwestern, Nigeria in September 2008 with 5 months history of generalized body weakness, abdominal swelling,

Significant findings on physical examination were those of wasting, pallor and moderate hepatosplenomegaly. He had hypochromic microcytic

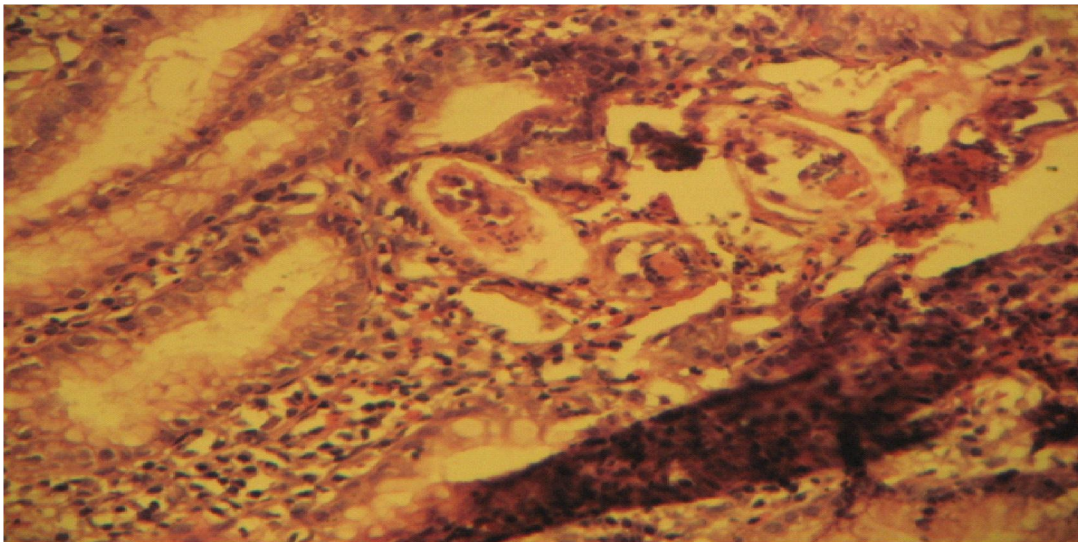


Figure 2: Section shows gastric tissue with viable schistosomal ova and lamina propria infiltrated by eosinophils, lymphocytes and accompanying fibrosis. H and E x 20.

progressive weight loss, recurrent mucoid non-bloody diarrhea and Vomiting. No past history of terminal haematuria. No history of bone pains or bleeding from any orifice. No history of cough, fever, night sweats

anemia, normal urine and stool microscopy but rectal snip revealed numerous ova of *S. mansoni*. Upper GIT endoscopy revealed a huge irregular, lesser curve gastric tumor and gastric biopsy histology showed ulcerated

mucosa with few glands supported by lamina propria which is expanded by several *S. mansoni* ova and infiltrates of lymphoplasmic cells and eosinophils (Figures 1 & 2).

Liver biopsy also showed chronic schistosoma hepatitis with granulomas, mononuclear cell infiltrations

3 & 4). A diagnosis of gastric schistosomiasis was then made and was given oral Praziquantel of 40mg/Kg body weight in two divided doses 4 hours apart with significant clinical improvement and complete resolution of gastric mass at repeat endoscopy after 8 weeks. It is a routine practice in the unit to repeat

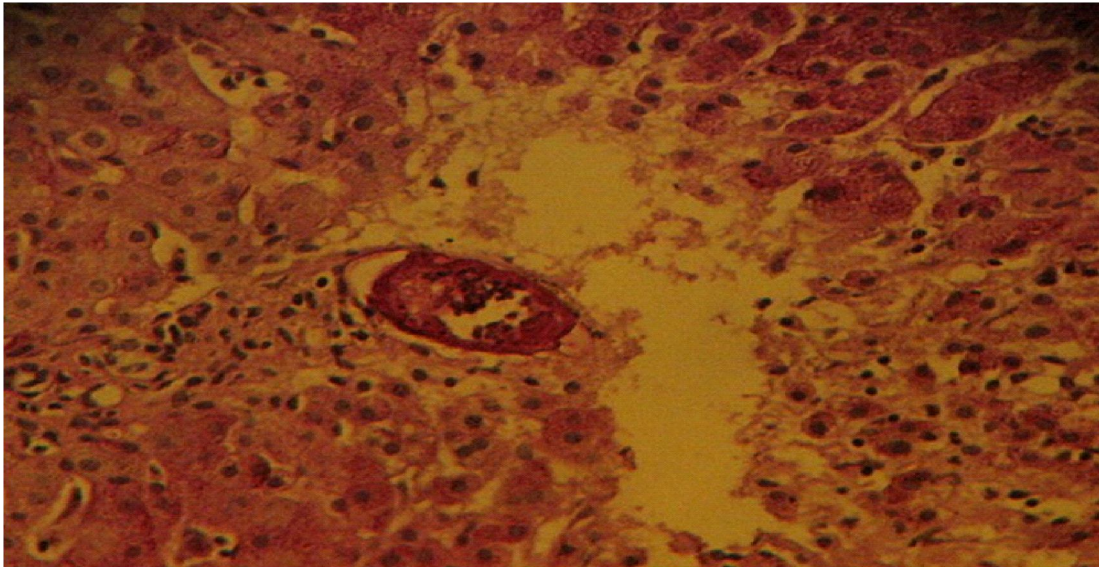


Figure 3: Section shows moderately preserved architecture with focal areas of granulomatous inflammation + multinucleated giant cells, eosinophils and schistosoma ova. Areas of portal fibrosis with lymphocytic infiltrates also present.

with multinucleated giant cells, mild periportal fibrosis and relatively preserved hepatic architecture (Figures

endoscopy in all non-NSAIDs induced gastric ulcers to assess healing and rule out malignancy. Repeat

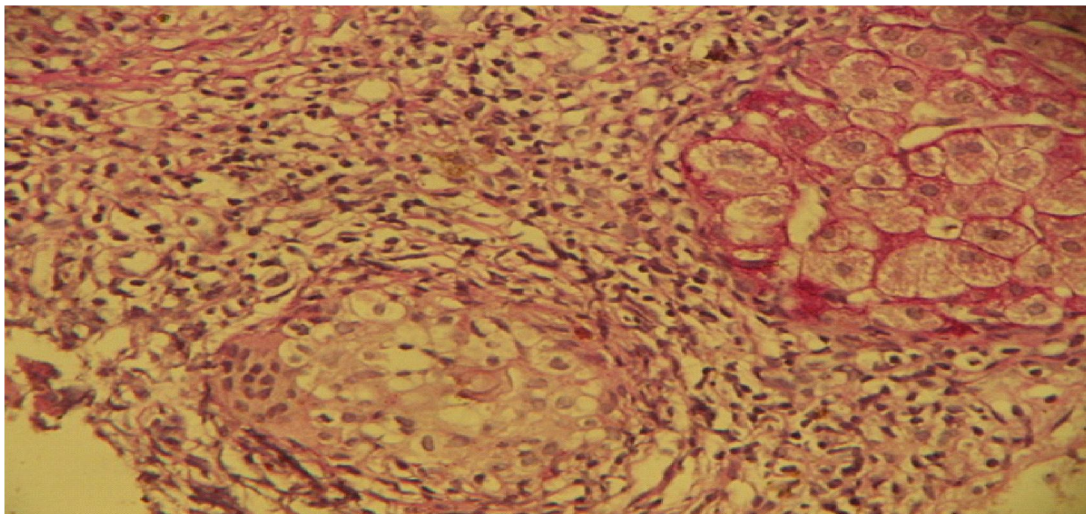


Figure 4: Section shows hepatic tissue cirrhotic nodules surrounded by fibrotic stroma with eosinophilic and lymphocytic infiltrates. One of the nodules shows a central calcified ovum with surrounding multinucleated giant cells. H and E x 20

biopsy was however not taken at second endoscopy because of near complete resolution of the gastric lesion.

He is now stable with no residual complaints and he is being followed up in the Gastroenterology and Liver Clinic of AKTH.

DISCUSSION

Schistosomiasis results from the immune response mounted by the infected host to schistosome eggs and the granulomatous reaction evoked by the antigens they secrete. The clinical course of the disease is determined by the amount of antigen released and the severity of the chronic fibrosis. Most granulomas develop at sites of maximal egg accumulation- the intestine and liver in the case of *S. mansoni* and *S. japonicum*. However, all species of this blood fluke infecting humans have the capacity to cause gastrointestinal and liver disease regardless of their primary target tissue.

Gastric schistosomiasis which is reported in this case is not only uncommon but has not been reported as a recognized cause of gastric ulcer or gastric tumor. This patient presented with an ulcerated gastric tumor-like growth prompting the initial suspicion of a malignant gastric ulcer (gastric cancer). The histology was reported as gastric schistosomiasis, which was the first time in our centre after more than a decade of active endoscopy services.

Capdevielle P and others have reported a similar case of pre-pyloric ulcer associated with gastric schistosomiasis from Tananarive in Madagascar.⁸ Gastric carcinoma has also been found arising from schistosomiasis in the endemic area of south China and this chronic inflammation has been linked to the development of gastric cancer in China⁹. Praziquantel was effective in treating the gastric schistosoma lesion in our patient as there was complete resolution of gastric lesion at repeat endoscopy 8 weeks after receiving praziquantel and a repeat rectal snip at the same time showed marked improvement in ova density in the snipped rectal mucosa.

Physicians practising in schistosomiasis endemic zones therefore, should always consider schistosomiasis

as a differential diagnosis in gastric ulcers and even gastric tumours, since when diagnosed early, treatment could be very rewarding as was the case in our patient.

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ANNOUNCEMENT

CONFERENCE ANNOUNCEMENT

The African Middle East Association of Gastroenterology (AMAGE), an affiliate of the World Organization of Gastroenterology (WGO), is honored to hold its sixth congress in Nigeria in collaboration with the Society of Gastroenterology and Hepatology in Nigeria (SOGHIN).

This is the first time for AMAGE to visit sub-Saharan Africa and we believe it would not be the last. A part of our mission, besides education and training, is to bring gastroenterologist from all over the world together in a friendly atmosphere irrespective of color, ethnicity and religion.

Nigeria is definitely one of the important gates for sub-Saharan Africa as it has a good scientific infrastructure and good organizational abilities. I am sure we all shall have a good time in a peaceful place like Tinapa Resort, Calabar, Nigeria.

Calabar, with its serene and beautiful looks is an idyllic setting for the 6th AMAGE Congress and Tinapa, the Congress venue, has purpose-built modern conferencing facilities. In addition, there are many interesting tourist attractions that would give the attendees of the Congress a memorable visit to this old national capital of Nigeria.

Welcome to Nigeria, Welcome to Tinapa, Calabar
Welcome to the 6th AMAGE Congress **November 22-24, 2012**

AMAGE President

Invitation for Abstracts

Abstracts are invited from all and sundry addressing either the main theme or any of the sub-themes of the 6th AMAGE Congress.

An Abstract must be between 250 and 300 words long and structured as follows: Title, Authors (The presenting author to be asterisked), Background / Objective, Method, Results and Conclusion. The final deadline for abstract submission is August 31, 2012.

Abstracts must be uploaded at the website: <http://www.sixthamagecongress-calabar.com>

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- (2.) From your "Dashboard", select **Submit or manage your abstract** option from the list.
- (3.) On the Abstract submission page (Section A), supply your abstract's **title, author(s), and content**.
- (4.) You can optionally upload a Portable Document Format (pdf) or Microsoft Word document of the same abstract (Section B).

OPERATIONAL GUIDELINES

Manuscript Submission

Submission of manuscript could be by either electronic and/or surface mails. Electronic submission shall be by e-mail, flash drive or CD rom.

Manuscripts should be sent with a cover letter to the Editorial Office. The cover letter should include a declaration that the work is original, is not under consideration for publication elsewhere and that all authors participated in the publication and agreed to submission to the Nigerian Journal of Gastroenterology and Hepatology.

A processing and Acceptance fee shall be charged as determined by the Editorial Committee. A sum of N2,500.00 shall be charged as processing fee when manuscripts are submitted, while authors whose manuscripts are accepted shall pay a sum of N5,000.00 for now.

Types of Manuscripts

Only the following manuscript type shall be considered for publication:

Original Research Work

This should have a maximum length of 5,000 words, including references, a structured abstract of not more than 300 words and a title with not more than 15 words.

Research Letters

These shall be brief, definitive reports of unusual interest and should not exceed 1000 words including references.

Review Article

This shall normally be solicited for from an expert in the area of interest. Unsolicited reviews shall not be accepted for publication. Reviews may be on both basic and clinical topics and should not exceed 5,000 words including references. However, authors who are interested in contributing reviews are requested to first contact the Editor to agree on the topic and outline of the proposed article.

Letters to the Editor

This should not be longer than 500 words and include not more than 5 references and one figure.

Conference Abstracts and Proceedings

Abstracts for this purpose shall be structured and should not exceed 350 words (Background and Objectives, Methodology, Results and Conclusion). Proceedings shall be in the format of original articles.

Case Reports/Brief Reports

This shall be unusual reports of interest to the readership and not a mere repeat of what has been described earlier. It should not exceed 1000 words divided into abstract, introduction, Case report, discussion, references and figures/table. References should not exceed 10, and tables and figures should be limited to two each.

NB: Manuscripts that exceed the word limits as stated above will be returned to the authors for shortening before a full review.

Advertisements

Drugs, meetings and other advertisements will be published for a token amount as shall be decided by the Editorial Committee, provided they are in line with the vision and mission of the Journal.

Other Publications

Events, such as conferences, workshops and job openings/vacancies as well as profile of medical pioneers deemed relevant to members shall be published from time to time.

Submission Check List

1. Complete manuscript consisting of: Title page with Authors' names and affiliations/addresses, Abstract, Introduction, Materials and Methods, Results, Discussion, References, Acknowledgement, Tables and Figures as Microsoft Word document. Tables and Figures should be submitted separately with one Table/Figure on separate pages.

2. Cover letter
3. A description of any commercial affiliation or consultancy that could be construed as conflict of interest.
4. An author agreement/Transfer of copyright form signed by all listed authors.
5. Letter of ethical approval for the study.
6. Payment of processing fee.

Manuscript Organization

Text of manuscript should be type written in word format, double-spaced in Times News Roman font 12, and all pages must be numbered in the upper right corner, starting with the title page. Manuscripts describing original research should contain, in this order, the following:

Title Page

Title

No more than 15 words, with at least one running title. The use of acronyms and abbreviations should be avoided. The species used for work with experimental animals must be indicated in the title.

Author Names

The full name (SURNAME LAST), institutional affiliation and e-mail of all authors must be included. In a multi-authored work involving more than a single institution, indicate individual affiliation by means of a superscript Arabic number. Correspondence author should be indicated.

Financial Support

List of grants and other financial support.

Abstract

A structured abstract is required as follows: Background and Objectives, Methods, Results and Conclusion. Abbreviations must be defined in the abstract to allow the abstract to stand alone. Abstract should not exceed 300 words.

Keywords

Five keywords for the purpose of indexing.

Introduction

This shall contain an introduction, mini literature review and a clear objective stated in the last paragraph.

Materials and Methods

This shall contain the essentials of materials used and the methodology as well as statistical methods.

Results

Relevant findings from the study shall be reported in this section. Graphical illustrations, figures and images should be labelled in the order in which they appear in the text and should be placed after the Acknowledgement section.

Discussion

The results of the study shall be discussed in this section with review of relevant literature.

References

Authors should cite only articles that are relevant. References, which shall be in Vancouver style, should be numbered in the order in which they are cited as Arabic numerals in the text, in superscript at the end of the sentence. Cited references must have been published in literature or in press (with the name of the Journal and date of acceptance or in press with date). Abstracts and letters to the editor may also be cited. Manuscripts submitted, unpublished data, personal communications may not be cited. Consult Index Medicus for guide for Journal abbreviations. Up to six authors must be listed. When more than six authors are involved, list the first six and "et al." EndNote is recommended to authors to help in this regard. When books are cited, the name of authors, title of publication, In (title of book), chapter, edition, editors, publishers, city and year of publication and pages must be cited in order.

The following examples are provided for guidance:

Journal article

AA Adesanya, JT da Rocha-Afodu. Colorectal cancer in Lagos-a critical review of 100 cases. Nigeria Postgrad. Med J, 2000; 7: 129-136.

Articles in Press

FB Abdulkareem, Abudu EK, NA Awolola, SO Elesha, O Rotimi, OR Akinde *et al.* Colorectal carcinoma in Lagos and Sagamu, Southwest Nigeria: A histopathological review. *World J Gastroenterol* Accepted Sept. 2008. In Press

Books

V Kumar, AK. Abbas. Inflammation. In : F. Nelson (Ed) *Robins and Cotran Pathologic basis of disease*. Chapter 4, Elsevier Saunders Inc, Philadelphia. 2005, 864-865.

Acknowledgment

Due acknowledgement of personal assistance and provision of special reagents etc. if any should be documented.

Tables, Figure and Legends

Tables and figures should be numbered in the order they appeared in the text

Permission

Quotations, tables, or illustrations taken from copyrighted materials must be accompanied by written permission for their use from the publisher and the original author.

Abbreviations

Abbreviations should be spelt out, in parentheses, in its first use in the text. Abbreviations used in figures or tables should be defined in the legend.

Drug Names

Generic names shall be used as much as possible, while proprietary names may be mentioned in parentheses. Batch numbers of drugs used should be stated.

Peer Review and Publishing

There shall be initial Editorial review to determine suitability of article for publication. At least two experts in the relevant field will review each article. Discordant comments will warrant further review outside the initial reviewers. Only recommended manuscripts will be published after meeting relevant conditions. At the initial stage, two editions will be published annually (May/November) and subsequently four editions per year. The Association shall be the Publisher of the Journal. The ISSN number will be obtained and shall be in the custody of the Editor-In-Chief.

Galley Proofs of accepted papers shall be sent to the corresponding author for final correction before publication. Proofs should be returned within 72 hours by the fastest possible means to the Editorial Office.

Conflict of Interest

Any conflict of interest must be stated by authors.

Contribution of Authors

The contribution of each author to the manuscript, stating clearly the role performed, should be well enunciated in the cover letter to the Editor.

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