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TOPIC:

IS IT ALL ABOUT THE DEAD? NAY! IT IS THE LIVING THAT BENEFITS

By

PROFESSOR FATIMAH BIADE ABDULKAREEM

IS IT ALL ABOUT THE DEAD? NAY! IT IS THE LIVING THAT BENEFITS

An Inaugural Lecture Delivered at the University of Lagos Main Auditorium on Wednesday, 18th February 2015

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Members of Senate, University of Lagos;
Heads of Departments;
Traditional rulers her present;
Gentlemen of the Press;
All invited guests;
My esteemed audience, ladies and gentlemen.

Preamble

The Vice Chancellor sir, I hereby express my appreciation for giving me the opportunity to deliver my inaugural lecture today the 18th of February 2015, which coincides exactly with my 51st birthday. I feel highly honoured and I thank you sincerely for bearing with me to perform this obligatory assignment 7 years after I was made a Professor of Anatomic Pathology at the University of Lagos, University of first choice, the Nation's pride. Thank you for your understanding.

Why specialise in pathology?

To the layman, a pathologist is erroneously believed to be 'doctor of the dead', so, when people heard that I wanted to become a pathologist after graduating from Medical School, they wondered why? I was asked: Do you want to deal with the dead for the rest of your life? Even doctor colleagues sometimes remark: "your

patients don't complain" and some people actually believe that we have been 'cooked from home' because they believe we deal ONLY with the dead. Some of my brothers and sisters in Islam feel it is contradictory to my faith-Islam- because of the autopsy part of it.

Pathology, to me, was an easy and interesting subject when I was in medical school. I had a distinction in it at my Part 2 professional examinations and I was encouraged and motivated by my teacher, Prof Edward B. Attah and also supported by my husband, to both, I am eternally grateful.

What is Pathology?

According to the Royal College of Pathologists, Pathology is the hidden Science at the heart of modern medicine, vital for the diagnosis and clinical management of disease. It is defined as the science that is behind the cure in Medicine; the science that deals with the study of diseases and the body's responses to them. The discipline is the link between basic medical sciences and clinical practice.

Pathology can further be divided into four major areas:

1. Haematology-that deals with diseases of blood and blood components
2. Microbiology-the study of micro-organisms that cause diseases
3. Chemical Pathology-studies changes that occur in body chemistry during diseases
4. Anatomic Pathology-studies the changes that occur in structure and function in disease.

At the College of Medicine of the University of Lagos, all these departments exist but they are in different faculties. Anatomic Pathology and Microbiology are domiciled in

Faculty of Basic sciences while Haematology and Chemical Pathology are in clinical sciences. The practice now is to have all these departments together under the same faculty because they are similar; being a link between basic and clinical. Pathology is strictly not a basic science because basic science deals with normal body structure and function while pathology deals with diseases.

Who is An Anatomic Pathologist?

An Anatomic Pathologist is one who is involved in making diagnoses of diseases (or a lack of) from a patient's tissue. He or she is first and foremost a medical doctor who then undertakes an extra five years or more of postgraduate training in laboratory medicine and may sub-specialise. He or she examines tissues by the use of macroscopic (gross or naked eye appearance), light microscopic and molecular techniques such as immunohistochemistry to make a diagnosis. He or she is responsible for the accuracy of laboratory tests and may also undergo additional training (fellowship) to sub-specialise. He/she in addition teaches medical and paramedical students, trains resident doctors and carries out research to improve knowledge about diseases.

The major areas of practice of an academic anatomic pathologist are:

For every academic, the major function is basically Teaching, Research and Service.

- Teaching of Medical Students and training of specialists
- Research and service can be in all or any of these areas:
  - Surgical pathology,
  - Cytopathology and
  - Autopsy pathology.

Surgical pathology (histopathology) involves examination of tissue samples removed from patients by surgeons and non-surgeons such as dermatologists, radiologists etc. Tissue samples can be biopsies wherein a small piece of tissue is taken from the patient while resection involves complete or partial removal of a whole organ as a therapeutic measure (form of treatment). Example of the latter is mastectomy (removal of the breast for treatment of breast cancer) and colectomy (removal of the large bowel to treat colon cancer). A biopsy may be incisional biopsy where a bite of the suspicious lesion is removed by the use of a large gauge needle or excisional where the entire lesion suspected to be abnormal is removed.

Cytopathology studies individual cell characteristics to make a diagnosis. It includes: Fine Needle Aspiration Cytology (FNAC) of solid masses, gynaecological cytopathology-Pap smear and exfoliative cytology – examination of fluids from the abdomen (ascites), chest cavity (pleural effusion), brain (cerebrospinal fluid) or joint space.

Autopsy pathology is examination of the body after death (surgery after death), usually for the purpose of determining the cause and circumstances of death. It may be partial or full dissection and consists of external and internal examination, sometimes involves imaging of the body and review of medical records and collection of appropriate specimens. It is divided into hospital autopsy or forensic (medico-legal) autopsy. Hospital or clinical autopsy is one in which it is the attending physician that makes the request if he or she could not make a diagnosis before death or even when diagnosis has been made, circumstances surrounding the death is unknown. It usually requires the consent of the next of kin of the diseased. Forensic autopsyon the other hand is

examination performed under the law with the order of the coroner, consent from the next of kin is not required.

Uses/Benefits of autopsy:

- To determine cause of death;
- Teaching of medical students and paramedics;
- Training of specialists;
- For clinical audit in the hospital;
- For research purpose;
- Discover "disease of unknown cause"- e.g. Severe Respiratory Distress Syndrome (SARS), HIV-AIDS;
- Medico-legal cases: to establish justice in the law court or to claim insurance benefit, a definite cause of death has to be found.

Cases categorised under Medico-legal autopsy are:

- Unknown cases;
- Sudden unexpected and unnatural deaths;
- Deaths from a reasonable suspicion of criminal activity;
- Accidental Death or Death by misadventure;
- Death due to self –neglect or negligence by others;
- Death due to industrial disease, accident at work or industrial poisoning;
- Death due to negligent medical intervention;
- Death occurring within 24hours of admission in the hospital;
- Death occurring after surgical operation;
- Death as a result of non-conventional medical procedure or medication;
- Suicide, suspected suicide or assisted suicide;
- Death occurring in custody or circumstances related to recent custody;
- Death of a child in care in circumstances that raise prima facie maltreatment.

Thus, performance of autopsy generally achieves the following whether by coroner or otherwise:

- Knowing circumstances surrounding death→ allows for institution of justice
- Knowing cause of death→
  - peace of mind to relatives
  - Precautions can be taken in case of hereditary disease
- Education(training & research)→
  - Training of medical personnel
  - Understanding and studying the nature of diseases,
  - Medical audit-the physician learns if a mistake has been made: i.e., 'learning from the dead to help the living'

In terms of the load of samples processed in the laboratory, autopsy pathology constitutes less than 10% of the routine work of an anatomic pathologist. Some pathologists after sub-specialisation may not even get to do autopsy at all.

Is Autopsy contradictory to Islamic belief?

As a Muslim, it is essential that I talk about this because I get questioned very often. From the above, it is clear that autopsy is to achieve 2 main purposes: 'institution of justice and acquisition of knowledge from the dead that will help the living'.

In Islam, Allah (SWT) frowns at taking of life for unjust reasons as stated in the holy Qur'an.

▸ ---if someone kills another person unless it is for murder or for spreading mischief in the land, it will be as if he murdered all mankind. And if any one saves life it will be as if he saved the life of entire mankind (Qur'an 5 verse 32).

▸ Nor take life which God has made sacred except for just cause. And if anyone is slain wrongfully, we have

his heir authority {to demand Qisas (law of equality in punishment) or to forgive}, but let him not exceed bounds in the matter of taking life; for he is helped {by the law}. (Quran 17 verse 33).

Prophet Muhammad (PBOH) was quoted to have said: 'There is always a leeway to escape for all crimes that might have been committed except for when there is blood in his hands'—i.e. commit murder (Ibn Majah, 1953 vol 2:873, Sahih al-Bukhari-1994:1011). He also said: "The worst of Allah's enemies is a murderer"—(Ash-Shafi'i,al –Umm,1993,vol 6-7).

Islam is a religion that makes institution of justice and fair-play an obligatory duty on individuals and the authority:

- Allah commands justice, the doing of good, and liberality to kith and kin, He forbids all shameful deeds and injustice and rebellion: He instructs you that ye may receive admonition'. {Quran 16verse 90}.
- We sent aforetime our apostles with clear signs and sent down with them the book and the balance that men may stand forth in justice' {Quran 57 verse 25}.

Islam also is the only known religion that places great emphasis on knowledge and has made acquisition of it compulsory.

- "Those without knowledge are not equal to those who have" – Qur'an 39 verse 9
- "Whosoever is given knowledge has indeed been given abundant good" – Qur'an 2 verse 269
- "In fact, Allah enjoins Muslims to pray: "O my Lord, advance me in knowledge" – Qur'an 20 verse 114.

Prophet Muhammad (PBOH)) encourages Muslims to seek for knowledge in the following hadiths:

"The seeking of knowledge is obligatory for every Muslim male or female" and
"That knowledge is the lost property of Muslims, wherever he finds it, he should grab it".
"He who leaves home in search of knowledge, to him Allah shows the way to paradise".

According to the Fatwa issued by the Council of Senior Scholars in the Kingdom of Saudi Arabia (Al-Buhooth al-'Ilmiyyah, 2/83-84) on dissection or autopsy for criminal investigation, investigation into an infectious disease so that precautions may be taken to protect others and dissection for scientific purposes for learning and teaching, it was unanimously agreed that it is generally permissible to carry out autopsy/dissection on human bodies.

In all cases however, bodies must be treated with dignity and respect because Islam pays emphasis on the dignity of the Muslim body during life and at death and we believe that the dead also feel pain even though they do not complain. Aa'ishah (may Allaah be pleased with her) reported that the Prophet (peace and blessings of Allaah be upon him) said: "Breaking the bone of the deceased is like breaking it when he was alive"(Imam Ahmad, Abu Dawood and Ibn Maajah).

Subspecialties in Pathology

Sub-specialisation exists in pathology wherein a pathologist undergoes further training or fellowship to develop skill and expertise and then focuses his or her practice and research work in an area particularly in academics. There are numerous recognised sub-specialties of surgical pathology including: gastrointestinal & liver pathology, renal pathology, bone pathology, neuropathology, pulmonary, hemato-pathology, gynaecological, genitourinary, soft tissue etc.

The Vice chancellor sir, my area of research interest or specialisation is gastrointestinal and liver pathology but I have not lost track of my beginning which is renal pathology and of course my association with the National Orthopaedic Hospital as the only Consultant Histopathologist (Part time) for over 15yrs has compelled me into the area of bone and soft tissue pathology.

I shall therefore let you into the work that I have been doing in the last 18years of my sojourn at the University of Lagos; particularly with regards to the significant contribution and impact on the health of Nigerians. In this discussion titled "Is it just about the Dead? Nay, it is The Living That Benefits". I will educate and demonstrate to you through my various academic and research works that there is more to pathology than 'just the dead'.

MY CONTRIBUTIONS

Vice Chancellor sir, I will follow this outline in stating my contributions:

1. Studying the dead for the benefit of the Living
    a. Cerebral Malaria
    b. Common causes of death in childhood
    c. Changing Pattern of Tuberculosis
    d. Emergency room deaths
2. Renal pathology
    a. Renal transplant pathology
    b. Renal neoplasms in Childhood
3. Gastrointestinal (GI) Pathology
    a. Acute Appendicitis
    b. Cancer Diagnosis/research–a major bulk of Pathologist's burden
    c. Colorectal carcinoma

d. Gastric cancer and the role of Helicobacter pylori infection
e. Gastrointestinal stromal tumour

4. Liver pathology
   a. Hepatocellular carcinoma, liver cirrhosis and chronic hepatitis
   b. Role of the pathologist in diagnosis and management
5. Challenges of GI pathology in Nigeria and my role in training of Medical students and specialist pathologists.

STUDYING THE DEAD FOR THE BENEFIT OF THE LIVING

Cerebral malaria

The pathologist studies the dead for the benefit of the living. My first publication was a study on cerebral malaria which was carried out during my postgraduate (residency) training. Malaria is a very common life-threatening parasitic infection that is endemic in Nigeria but mortality is highest in children under 5years. It is transmitted by anopheles mosquitoes and according to the latest data from World Health Organisation (WHO); malaria kills one child every minute in Africa1[1].

Several complications can occur that result in death but cerebral malaria is rare in adults. Cerebral malaria is a complication in which the malaria parasite infects the brain and blocks the small blood vessels in the brain thus resulting in unconsciousness, convulsion with very high fever and other symptoms/signs. We noticed that several adults who were treated during life for malaria were discovered to be dying from cerebral malaria at autopsy. This prompted us to do a prospective study of all cases diagnosed as malaria at autopsy over 4years[2]. Of the 117 malarial deaths, cerebral malaria (Figure 1) was the most common cause of death accounting for 45.6% and

children 1-5yrs were the most vulnerable (Tables 1 &2). Other causes of death in malaria such as anaemia/anaemic heart failure, enteric malaria etc are listed in Table 1. Seven adults were recorded, one of whom was a Caucasian. The common presenting symptoms were: fever only, fever with convulsions and or coma and fever with gastrointestinal symptoms such as vomiting and diarrhoea. Five of the 7 adults were comatose without fever on admission. If not promptly recognised and treated, mortality approaches 100%[3]. Outcome is dependent on the speed at which appropriate therapy is instituted. All the cases in our series reported late to hospital and died within 24hours of admission.

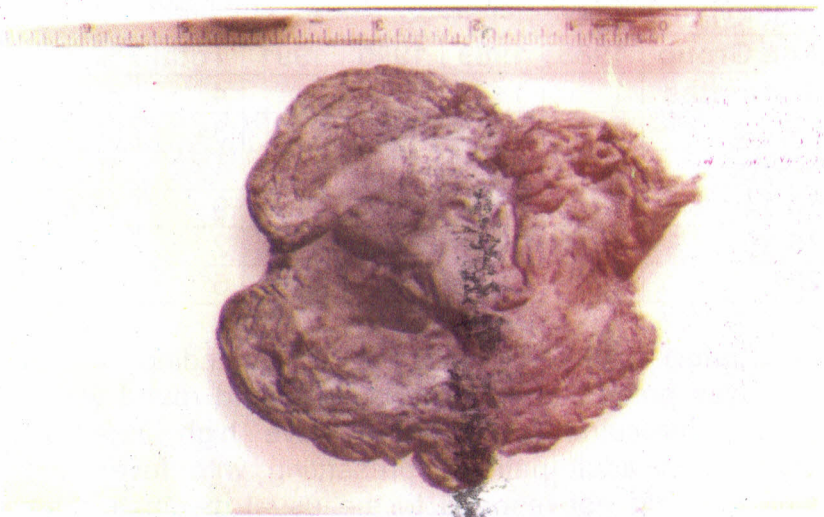


Figure 1: Gross photograph of Malaria involving the Cerebellum showing Petechial heamorrhages in the white matter.

Table 1: Common Causes of Death in 117 cases of Acute Malaria Fever (1988-91)

Causes of Death	Number	%
Cerebral Malaria	67	45.6
Anaemia/anaemic heart failure	27	18.4
Enteric Malaria (enterocolitis &hepatosplenomegaly)	22	14.9
Cerebral oedema	12	8.2
Aspiration/bronchopneumonia	10	6.8
Dehydration/shock	9	6.1

Table 2: Age Distribution of 67 cases of Cerebral Malaria (1988-91)

Age Group	1988	1989	1990	1991	Total	%
0-11mnths	1	1	2	0	4	6
1-5yrs	12	8	9	5	34	50.7
6-9yrs	3	5	4	1	13	19.4
10-14yrs	1	5	0	3	9	13.4
15-19yrs	0	0	2	0	2	3
20+	1	0	2	2	5	7.5

Conclusion and Message: The initial finding of this study was presented at the hospital grand round which alerted physicians to begin to have high index of suspicion in adult patients presenting with fever and coma who did not respond to the usual medication for malaria. This study also further highlighted the issue of chloroquine resistant malaria and fake-drug syndrome.

Common Causes of Death in childhood

Another autopsy study was to determine common causes of death in children 0-14yrs; this was part of my dissertation for the award of fellowship of the National Postgraduate Medical College of Pathologists. The study

revealed that 608 of 4,500 children admitted to Lagos University teaching hospital (LUTH) died (death rate 13.5%)[4]. Of the 151 paediatric autopsies, 50% of death occurred in children less than 1 year and male gender were more vulnerable (male to female ratio of 1.6:1). The risk of dying reduces with increasing age (from 28.4% in neonates to 13.2% at school age (Table 3). As shown in Table 4, infections accounted for 39.7% of all deaths and were the leading causes of death in all age groups. Other causes of death are anaemia, accidental injuries, birth trauma and malnutrition. Birth trauma commonly associated with prematurity can result in death through intracranial haemorrhage as depicted in Figure 2. The common infections were: tetanus, typhoid enteritis, tuberculosis, malaria (Table5).

Table 3:Age and Sex Distribution of Childhood Deaths in LUTH) (1993-1994)

AGE GROUP	MALE	FEMALE	TOTAL	%
NEONATES (1st 4 weeks of life)	26	17	43	28.47
INFANTS (1-11months)	23	13	36	23.84
PRESCHOOL (1-4 years)	19	12	31	20.53
SCHOOL (5-9 years)	13	8	21	13.91
(10-14 years)	13	7	20	13.24
TOTAL	**94**	**57**	**151**	**100**

Table 4: Causes of Childhood Mortality in Lagos University Teaching Hospital (LUTH), 1993-1994 (Classified According to Modified International Classification of Diseases)

DISEASE CLASS	MALE	FEMALE	TOTAL	%
1. Infective (specific)	18	12	30	19.0
2. Respiratory system	18	5	23	15.2
3. Digestive system	12	6	18	11.9
4. Blood related disorders	8	7	15	9.9
5. Congenital malformations	7	7	14	9.3
6. Accidental injury (road traffic accident and burns)	8	3	11	7.3
7. Birth trauma	6	4	10	6.6
8. Nutritional/metabolic	5	5	10	6.6
9. Nervous system disorders	4	4	7	4.6
10. Genitourinary system	5	2	7	4.6
11. Neoplastic	3	2	5	3.3
12. Circulatory system disorders	-	-	-	-
TOTAL	**94**	**57**	**151**	**100%**

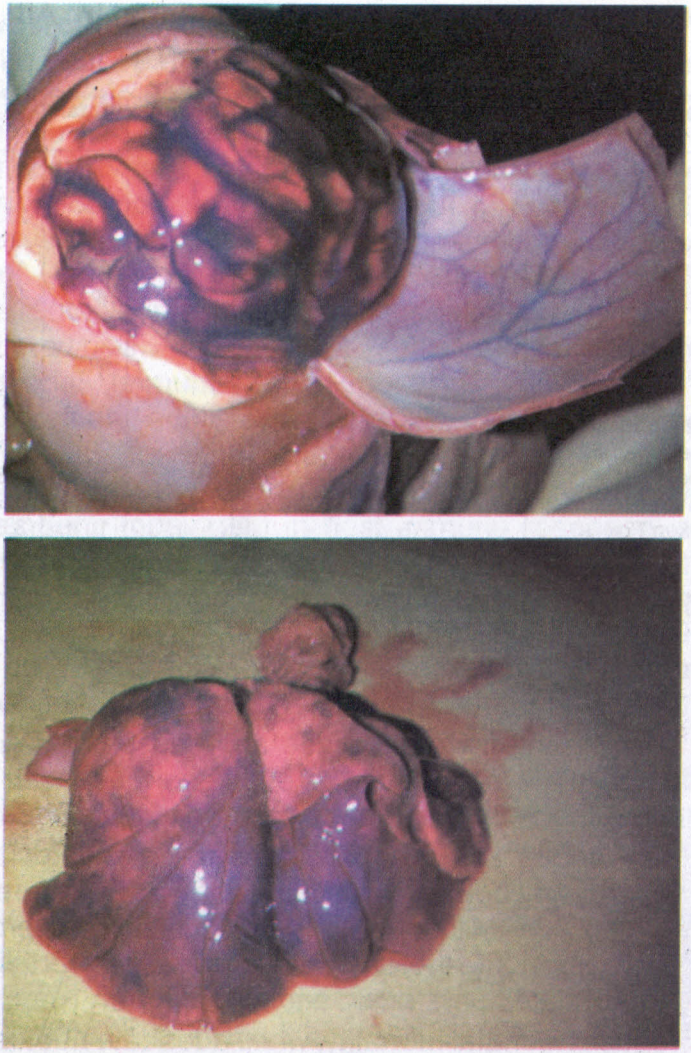


Figure 2: Subarachnoid haemorrhage(Left) and Lung Collapse (right) in a neonatal death

Table 5: Common Causes of Infections in All Age Groups (0-14 Years) at LUTH (1993-1994)

Type of Infection	Neo-nate	Infants	Pre-school	School	Total	%
Bacterial (66.7%)						
Tetanus	5	-	1	1	7	23.3
Typhoid Enteritis	-	-	1	4	5	16.7
Tuberculosis	-	1	1	2	4	13.3
Septicemia	3	-	-	1	4	13.3
Parasitic (16.7%)						
Malaria (Cerebral)	-	-	1	4	5	16.7
Viral (16.7%)						
Measles	-	-	2	-	2	6.7
Rabies	-	-	-	1	1	3.3
Viral Hepatitis	-	-	-	1	1	3.3
Chicken Pox	-	1	-	1	1	3.3
TOTAL	**8**	**2**	**6**	**14**	**30**	**100%**

Conclusion and Message:

- This study further confirmed that majority of deaths occur in the first year of life and causes of death in children are mostly due to preventable diseases.
- Also, the knowledge of common causes of death in the various age groups guides the paediatrician in considering common conditions first in the differential diagnosis of childhood illness and institution of prompt and appropriate therapy, thereby reducing mortality.
- Appropriate antenatal and intrapartum care will reduce neonatal mortality, while adequate nutrition by strict adherence to exclusive breastfeeding, immunization against major childhood diseases and improvement in environmental hygiene and provision of potable water by government will reduce mortality in older children.

Tuberculosis-Changing Pattern

With our earlier study showing that infection was responsible for most childhood deaths and the increasing number of cases of tuberculosis that we diagnosed at autopsy even in healthy looking patients who are not from the typical poor socio-economic background, we decided to carry out a survey of cases diagnosed both at autopsy and from surgical biopsies. Tuberculosis (TB) is a worldwide, preventable infectious disease caused by *mycobacterium tuberculosis*. Despite the acclaimed success of the National Immunization Programme in Nigeria, many children and adults still die from it. Apart from the impact of HIV-AIDS, the rising incidence has been attributed in Africa to poor efficacy of the BCG vaccine, malnutrition with attendant impairment in host immune response, poverty and poor environmental hygiene. Non-availability and accessibility of the drugs coupled with non-compliance to drug regimen on the part of patients as well as emergence of drug resistant tuberculosis have all contributed to the endemic nature of this infection.

One hundred and thirteen cases were diagnosed at autopsy while 54 cases were diagnosed from surgical biopsy samples over the 5year study period (Abdulkareem et al 2000). Majority of deaths occurred in persons under 10years and pulmonary tuberculosis was the main cause of death in 55% of cases diagnosed at autopsy followed by disseminated tuberculosis (Table 6)[6]. Of the surgical biopsy samples, tuberculous lymphadenitis was the commonest and cervical lymph node in the neck region (also known as Scrofula) was the most involved and accounted for 70% of childhood TB diagnosed from surgical biopsies (Table7). Confirmation of diagnosis often requires the use of Ziehl Nielson stain to identify the acid fast bacilli (Figure 3).

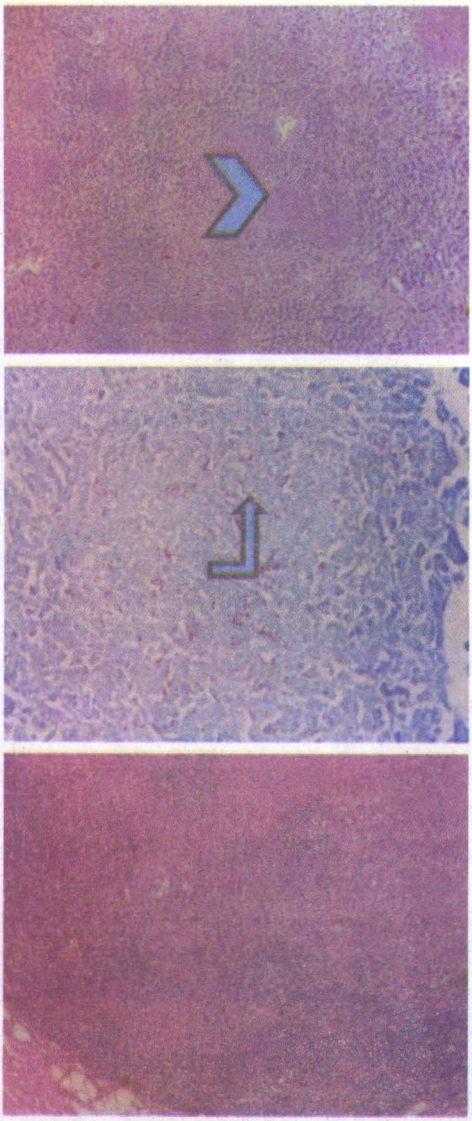


Figure 3: Photomicrographs of liver (left) and cervical lymph node (far right) showing characteristic caseating granulomatous lesions. The liver is in an HIV positive patient, showing positive acid fast bacilli in tuberculosis using Ziehl Nielson stain (center)

Table 6: Organ Distribution of Cases of Tuberculosis Diagnosed at Autopsy

Organ Diagnosis	Male	Female	Total
Pulmonary tuberculosis	19	11	30 (55%)
Disseminated tuberculosis	13	3	16 (30%)
Pulmonary TB with TB meningitis	3	2	5 (9%)
Primary TB meningitis	2	-	2 (4%)
Primary Abdominal TB	-	1	1 (2%)
Total	37	17	54 (100%)

Table 7: Tuberculosis Revisited –Age Distribution of Cases Diagnosed from Surgical Biopsies

Age Group (year)	Total	Percentage
0-9	11	10
10-19	31	28
20-29	26	23
30-39	14	13
40-49	14	13
50-59	2	2
60-69	-	-
70 and above	2	2
Age not stated	10	9
Total	100	100

Conclusion and Message:

- Our study concurs with previous studies which have shown that in the tropics, cervical node is the commonest site of clinically apparent TB.
- TB of the breast and reproductive organs such as ovary, epididymis and testes we rerecorded. Thus, some cases of TB mastitis may be misdiagnosed as breast cancer. Also, screening for TB should be part of investigations for male and female infertility.

Emergency room deaths in LUTH

We carried out a 5-year retrospective analysis of 427 acute medical deaths in our emergency department at

LUTH between 2005 and 2009 and determined the medical causes and mechanisms of death at post-mortem (Ajuluchukwu et al, 2012)[7]. We found that more males died compared to females in the ratio of 1.4:1 and >70% were ≤ 49 years of age. The common presentations were unconsciousness (36%), breathlessness (10%), body swelling (19%), fever (10%), cough (4%) and the symptoms had lasted for less than four days (Table 8, 9). About 23% died after 10pm, 16% were dead on arrival at the hospital and 40% died within the first 6hours of admission. Post-mortem Examination revealed that cardiovascular disease such as hypertension and heart failure constituted the major causes of death accounting for 36%, infections such as HIV, septicaemia, malaria and tuberculosis accounted for 18% followed by cancer (8.4%) particularly of the breast (Figures 4 &5).

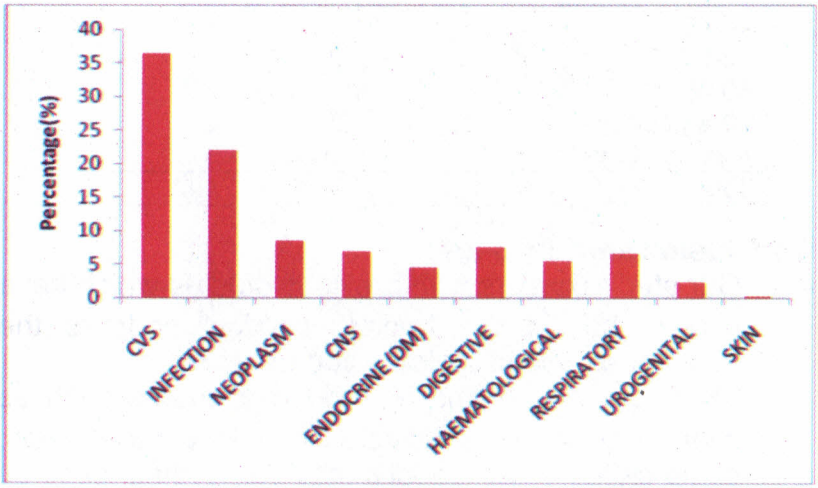


Figure 4: Distribution of causes of death among Acute Deaths in the Emergency Room (CVS=Cardiovascular diseases consisting mainly of cardiac and cerebrovascular disease; CNS=central nervous system diseases, such as meningitis and encephalitis)

Table 8: Major presentation and their range of duration Among Emergency Room Deaths

Major presentation	No Total=427	% 100	Range of duration
Dead on arrival	68	15.9	Nil (0)
Altered level of consciousness	151	35.6	4hours to 3 days
Body swelling Fever	83 45	19.4 10.5	14 days -5 months 4 days-6weeks
Breathlessness	42	9.7	3hoursto 3weeks
Cough	17	4.0	1 month to 1.5 years
Others**	39	9.1	3hours to 24 hours

**=Others: numbers with characteristic seizures (10), gastrointestinal bleed (14), chest pain (5), headache (10). Some patients had more than one symptom.

Table 9: General Characteristics of Patients who Died Acutely in the Emergency Room

Parameters	Number (Percentage)
[Age in years	43.2 +-16]
<20	26 (6.8%)
<49	281 (65%)
<60	79 (22%)
Males	250(58.5%)
Females	177 (41.5%)
Referred	170 (40.4%)
Time of arrival	
8am-4pm	215 (50.4%)
4pm-10pm	112 (26.2%)
10pm-8am	100 (23.4%)
Cause of death	
Cardiovascular disease	155 (36.3%)
Infections	77 (18.0%)
Others	195 (45.7%)
Mechanisms of death	
Cerebral	127 (29.7%)
Heart failure	81 (19.0%0)
Infections/Septicaemia	63 (14.8%)
Others	156 (36.5%)

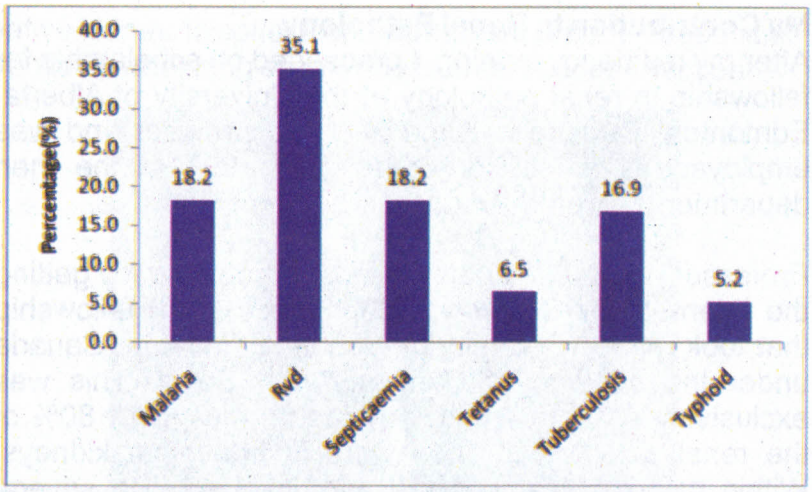


Figure 5: Pattern of Infections among Acute Medical deaths

Conclusion and Message:

- Majority of deaths are preventable medically –hypertension, diabetes, infections, cancer;
- Late presentation is a major factor and sometimes, there is delay in referring to specialists from primary healthcare settings;
- Non- compliance with prescribed treatment is another major factor especially in cases of hypertension and diabetes;
- Mean age at death in this study corroborates that life expectancy in Nigeria is less than 50years and that males are more likely to die earlier than females;
- The problem of late presentation can be minimised by health education to modify lifestyle, improving access to health facilities, raising awareness concerning the asymptomatic, silent phase of non-communicable disease;
- Furthermore, medical officers at the peripheral health facilities should recognise their limitations and avoid delay in referral.

My Contribution to Renal Pathology

After my residency training, I proceeded on scholarship for fellowship in renal pathology at the University of Alberta, Edmonton, Canada. I came back a year later and was employed as a lecturer grade 1 in 1997 at the then department of Morbid Anatomy, College of Medicine.

Professor A.F.B. Mabadeje was instrumental to my getting the International Society of Nephrology (ISN) fellowship that took me to University of Alberta, Edmonton, Canada under the tutelage of Professor Kim Solez. This was exclusively a Renal Transplant centre; thus, over 80% of the renal pathologies seen were in transplant kidneys. Within the one year period I was involved with several research studies two of which materialised into journal publications[8,9]. Generally, diseases in transplanted kidney may be related to a rejection reaction or it may be a recurrence of the disease present in the patient that necessitated the transplant.

Renal Transplant Pathology

One of such studies carried out was a case I presented at one of the clinicopathologic sessions in a patient who had recurrence of anti-Glomerular Basement Membrane disease (Anti-GBM) nephropathy (Trypkov et al, 1998)[9]. This patient had anti-GBM nephropathy and it was the primary disease that necessitated the transplant. He started to show symptoms of recurrence after 12years of uneventful post-transplant course. He was a 41-year old male who presented with features consistent with rapidly progressive glomerulonephritis (GN) and positive serology for anti-Glomerular basement membrane (Goodpastures's syndrome). Histology of the renal biopsy showed recurrent crescentic GN at almost end stage with co-existing IgA nephropathy which was not present in the

native kidney. In spite of appropriate treatment, patient died from overwhelming sepsis due to enterococus infection.

Figure 6: Photomicrograph of the kidney showing crescentic lesion in a Glomerulus

Renal Neoplasm's in Childhood

My experience in Edmonton was such an interesting and memorable one because I had to take the electron microscopic pictures as well as the immunofluorescence on my own and I also prepared the slides. It was such an unfortunate situation I found myself coming back with no tools to work with. Pathology of the kidney can only be unravelled with a combination of light microscopy, immunofluorescence and electron microscopy. No journal will accept to publish any research work that lacks this except in few conditions such as renal neoplasm and straight forward rejection reaction.

Thus, I started from this, when I came back, we studied renal neoplasms in childhood. This was a '28years' retrospective study to review renal cancer in children (Elesha & Abdulkareem, 1999)[10]. Of the 131 nephrectomise received during the period, 63 cases representing 48% were in children whose ages ranged

between 6weeks and 11years. Majority of them (75%) were less than 5years and there was no gender preference. All except 3 were nephroblastoma (Figure 7) which has been reported in most studies as the commonest type of renal cancer in children. In another study, we documented that majority present at advanced stage (Akinsulie et al, 2005)[11]. Surgery (nephrectomy) combined with chemotherapy and radiotherapy is the main stay of treatment. Unfortunately, many patients do not complete the therapy before seeking discharge against medical advice and are lost to follow up.

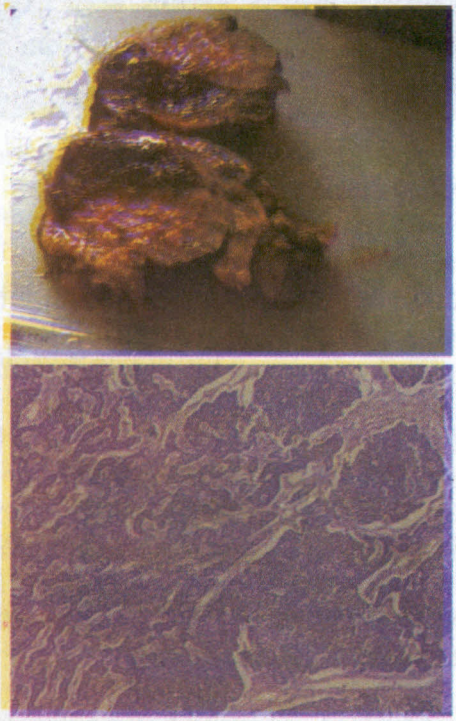


Figure 7: Gross photograph (left) and photomicrograph of nephroblastoma in a 2years old male

While being interviewed for lecturer appointment in 1997, I was asked how much of renal pathology I knew and how much I could achieve in terms of research output

without electron microscopy and immunofluorescence by my then HOD, Professor SO Elesha. He asked if I was not going to get frustrated and will be ready to explore other areas if it happened that research tools were not available. I answered to the affirmative. Yours truly, this was exactly what happened. Then, I remembered that my dissertation for the West African Postgraduate Medical College Fellowship was on the liver; thus I started to do a re-think. This however did not materialise until I was invited to be Secretary to the Local Organising Committee to plan a conference for the National Association for the Study of the Liver in Lagos. This eventually landed me in gastrointestinal and liver pathology. I had to attend several short courses in and outside Nigeria; one of which was as at the Histopathology and Molecular Pathology department of the University of Leeds Teaching Hospital, United Kingdom under Dr. Olorunda Rotimi, a Nigerian, practicing in the United Kingdom.

GASTROINTESINAL RESEARCH

The gastrointestinal tract (GIT) includes all the organs involved in the digestion of food starting from the mouth through the oesophagus that conducts food to the stomach and intestines; where the food is digested and absorbed and the large intestine from which the remnant is excreted (Figure 8). It traditionally also includes the liver which receives all materials from the GIT, modifies it before discharging it into the blood to be transported to the other parts of the body. The appendix, although the blind end of the GIT is also very essential and in disease conditions can result in great morbidity and sometimes mortality if not recognised early.

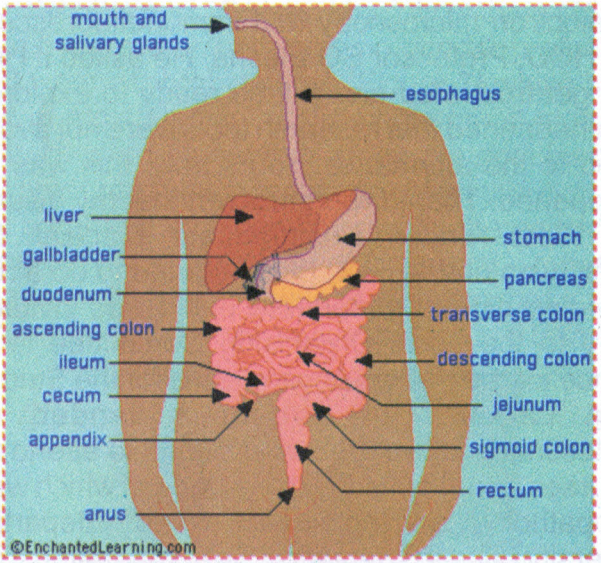


Figure 8: Showing Parts of the Gastrointestinal Tract and the accessory Organs

Acute Appendicitis

Appendicitis (Figure 9) is a very common surgical condition and the most common cause of acute abdomen. We carried out a retrospective histopathological review of 299 consecutive appendicectomy samples received in our department over an eight year period, 266 cases of which were removed for clinically suspected acute appendicitis (Abdulkareem & Awelimobor, 2009)[12]. The age group 20-29syear was the most vulnerable with mean age of 24years (Figure 10). The various diagnoses are shown in Table 11. Diagnostic accuracy rate was 70.3%. This concurs with 64.6% and 77% reported in two separate studies from the United Kingdom[13,14]. The rate of perforation in acute appendicitis was (30.5%) and children 10-19years were more vulnerable (Table 12). Negative appendicectomy rate (cases in which there was

no histological evidence) of 10.2% recorded in the study was within the range of 10-20% considered to be acceptable. Unsuspected but significant pathologies were recorded in such as schistosomiasis, tuberculosis, mucocele of the appendix, adenocarcinoid tumour and a case of tubulo-villous adenoma with severe dysplasia.

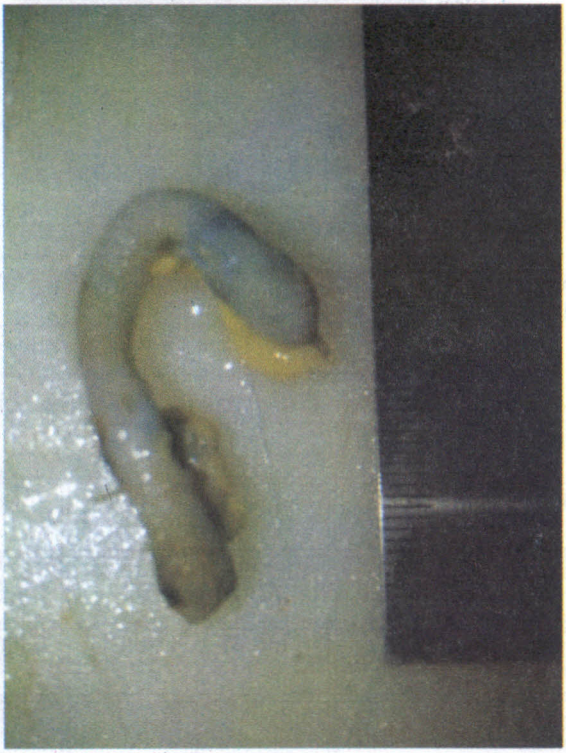


Figure 9: Gross Photograph of an appendix removed for suspected Appendicitis

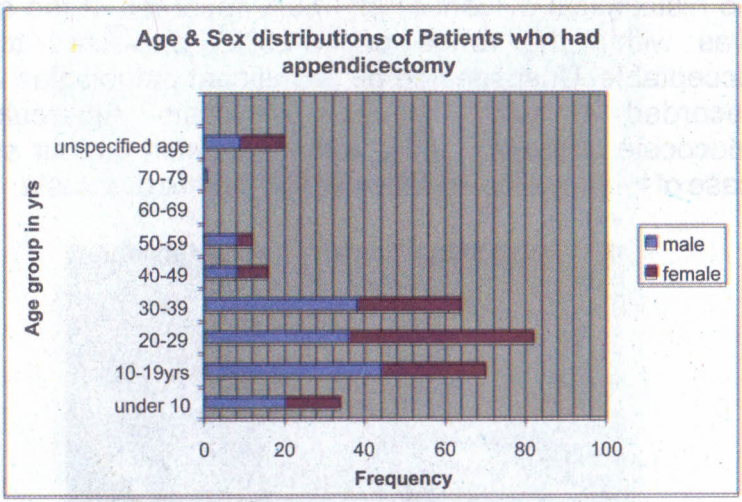


Figure 10: Age and Gender distribution of 299 Patients who had Appendicectomy

Table 11: Histological Diagnoses in 299 cases of Appendicectomies

Histological Diagnosis	Male (%)	Female (%)	Total (%)
Acute appendicitis	123(75)	64(47.4)	187(62.5)
Appendix with hyperplasia	17(10.4)	41(30.4)	58(19.4)
Extra-appendiceal peritonitis	5(3)	6(4.4)	11(3.7)
Normal appendix	16(9.8)	21(15.6)	37(12.4)
Granulomatous Inflammation	2(1.2)	1(0.7)	3(1.0)
Neoplastic lesions	1((0.6)	2(1.5)	3(1.0)
TOTAL	164	135	299(100)

Table 12: Age and Sex Distribution of Patients with Acute Appendicitis with or without Peritonitis

Age Group in Years	Male (%)	Female (%)	Total (%)	Perforation with peritonitis (%)
under 10	6(4.9)	4(6.3)	10(5.3)	5(8.8)
10-19yrs	34(27.6)	12(18.7)	46(24.6)	20(35.1)
20-29	30(24.4)	24(37.5)	54(28.9)	11(19.3)
30-39	29(23.6)	12(18.7)	41(21.9)	12(21)
40-49	8(6.5)	6(9.4)	14(7.5)	5(8.8)
50-59	8(6.5)	0(0)	8(4.3)	1(1.7)
60-69	0(0)	0(0)	0(0)	0(0)
70-79	0(0)	1(1.6)	1(0.5)	0(0)
Unspecified	8(6.5)	5(7.8)	13(7)	3(5.2)
	123(65.8)	64(34.2)	187(100)	57(M:F=43:14)

Conclusion/Message:

- To improve the diagnostic accuracy and decrease negative appendicectomy rate, other investigative modalities such as ultrasound scan, elevated C-reactive protein and total white blood cell count with relative neutrophilia should be combined with clinical symptoms and signs.
- High index of suspicion should be entertained in younger children as they are more likely to perforate because of unusual symptoms.
- Due to the possibility of presence of unusual pathologies and the fact that mere normal appearance of appendix cannot predict the histologic diagnosis, all appendices should be submitted for histopathological examination. **Appendix should no longer be thrown away.**

Cancer Diagnosis/Research–major bulk of Pathologist's burden

Cancer is a non-communicable disease and constitutes a major public health problem affecting all categories of persons. It is the second most common cause of death in developed countries and among the three leading causes of death in developing countries. In our study, it was the 3rd most common cause of death recorded in the emergency room after cardiovascular diseases and infection[7]. The 2012 Global Cancer Statistics published in 2014 showed that there were 32.6 million people living with cancer (within 5years of diagnosis) with 14.1million new cancer cases and 8.2million cancer deaths worldwide in 2012. Of the new cases, 57% occurred in the less developed regions such as Nigeria (globocan.iarc.fr).

Increasing incidence has been reported from Nigeria and yet it is still under-reported. A study reported that only 1% of reports from Cancer Registries worldwide emanated from Africa compared to 34% and 42% from Europe and Asia respectively (Moore M)[15]. This under-reporting has been attributed to:

- Inaccurate population statistics which makes age specific incidence rates impossible or if available, inaccurate;
- Poor health seeking attitude of Africans; large proportion still seek unorthodox medical care and so are not recorded;
- inadequate diagnostic facilities;
- limited access to care;
- Inadequate technical manpower and infrastructure as well as quality of cancer data systems all contribute to inaccurate data on cancer burden.

The Lagos Cancer Registry is located at the Lagos University Teaching Hospital and is one of the 11 cancer

registries in Nigeria. Although, this is not population based, it constitutes a major source of statistics regarding cancer burden in Nigeria. Of the six most common cancers in Nigeria, our analysis of the literature shows colorectal and liver cancers to be 4th and 5th respectively; this is corroborated by the latest figure from Global Cancer Data (2012). Majority of diseases that we diagnose from the GIT are malignancies; and these account for about 5.4% of all cancers (Abdulkareem et al 2009)[16]. We have carried out studies on cancers of the colorectum, stomach, liver, oesophagus which are all parts/accessory organs of the GIT.

Gastrointestinal tumours constitute one of the major tumour burden to man. Earlier studies from Africa showed lower incidence compared to other parts of the world[17,18,19] In Nigeria, earlier studies showed lower incidence of bowel cancer with figures of 3% and 5.7% reported from Ibadan and Benin respectively[20,21]. This is in contrast to the finding of 29.3% of the total cancer burden recorded for example in a study in Saudi Arabia[22]. We studied the pattern, age and sex distribution as well as histopathological characteristics of 713 malignant tumours of the gastro-intestinal system in Lagos and Sagamu in South West Nigeria (Abdulkareem et al 2009)[16]. **The results are shown in** Figures 7 and 8 below.

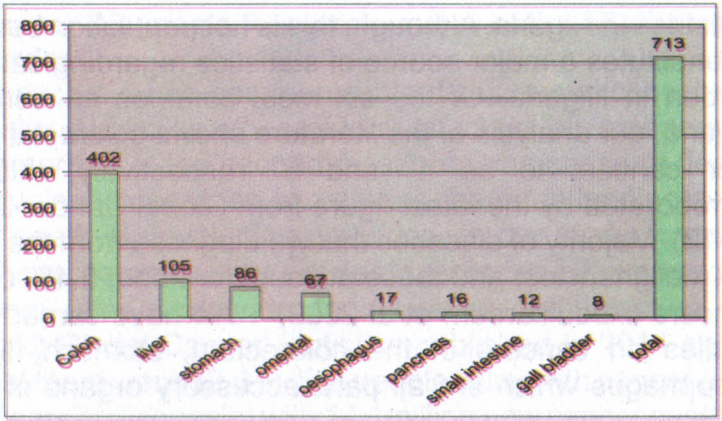
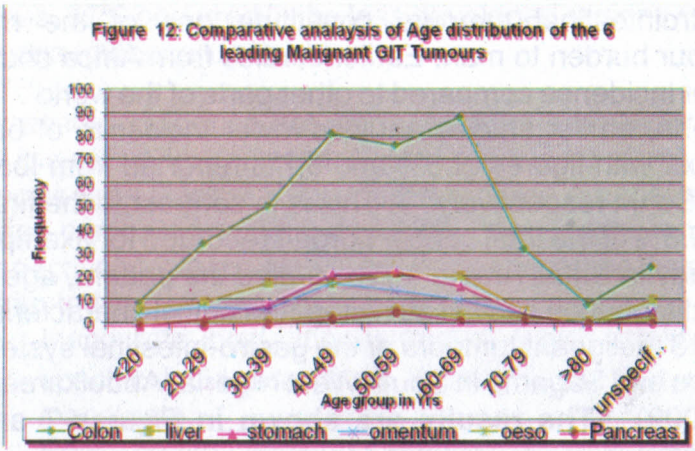


Figure 11: Site distribution of Malignant Gastrointestinal Tumours



Colorectal Cancer Research

The Vice Chancellor Sir, here lies my main interest. As a follow up on the last study of gastrointestinal cancers, my team further carried out a review of 420 colorectal cancer cases diagnosed from 5 laboratories in Lagos and Sagamu (Abdulkareem et al 2008)[23]. The mean age was 50.7years, M: F ratio 1.3:1 with 23% occurring below 40years of age. The majority was well to moderately differentiated adenocarcinoma 321 (76.4%), mucinous carcinoma 45 (10.7%) and signet ring

carcinoma 5(1.2%) were more common in patients under 40yrs compared to well differentiated tumours. The recto-sigmoid colon was the commonest site (58.6%). About 51% and 34% of cases presented at TNM stages II and III respectively. The age and sex prevalence and histopathological features concur with reports from other parts of the world.

Due to late presentation of CRC, screening, proven to be effective in reducing disease mortality, has been advocated in Nigeria. We carried out a study to review the practice of CRC screening among medical practitioners in Nigeria (Onyekwere et al 2009)[24]. Most respondents, 265 (87.8%), agreed that CRC was worth screening for while over half of the respondents employed one of the screening methods such as: faecal occult blood test (FOBT), double contrast barium enema (DCBE), flexible sigmoidoscopy. The study advocated the need to improve the practice of CRC screening through sensitisation of medical practitioners and provision of necessary diagnostic resources and possible formulation of effective local guidelines.

Table 13: Site Distribution and Histological types of Colorectal Carcinoma in patients >40years and above compared with <40years

	≥40years	< 40years
Site	Frequency (%)	Frequency (%)
Caecum	23(7.14)	11(11)
Ascending colon	20(6.21)	4(4)
Transverse colon	13(4.04)	6(6)
Descending colon	13(4.04)	2(2)
Recto sigmoid	194(60.25)	52(53)
Unspecified	59(18.32)	23(23)
Total	322(100)	98(100)
	≥40years	<40years
Histological Grade	Frequency (%)	Frequency (%)
Well Differentiated adenocarcinoma	191(59.3)	42(43)
Moderately Differentiated adenocarcinoma	63(19.6)	25(26)
Poorly Differentiated adenocarcinoma	38(11.8)	7(7)
Mucinous carcinoma	15(4.7)	19(19)
Signet Ring carcinoma	2(0.6)	3(3)
Undifferentiated	13(4)	2(2)
Total	322(100)	98(100
M:F Ratio	**1.3:1**	**1.2:1**

Legend: Patients below 40years had more tumours located in the proximal colon and there are more mucinous and signet ring carcinomas in them compared to those above 40years.

Table 14: Pathological staging of 123 cases of colorectal carcinoma

Duke 's Stage		%	TNM Staging		%
A	17	14	Stage I	17	14
B	64	52	Stage II A	54	43
C	41	33	Stage II B	10	8
D	1	1	Stage III A	13	11
			Stage III B	28	23
			Stage IV	1	1

Table legend: Majority of colorectal cancer cases presented in TNM Stages II and III (85%).

53years of reporting colorectal cancer in Nigeria: a systematic review of the Literature

The available literature has shown a disparity in the clinicopathological features of colorectal cancer in Africans compared with the Caucasian. Particularly, the younger age of presentation in Africans has been shown to be at least a decade lower. Most of the publications from various centers in Nigeria are not population based studies, thus, it is difficult to know the national picture of CRC. One review looked at 40 years of reporting CRC in Nigerians but this was not a systematic review and had

several overlaps and multiple reports of the same cohort of patients from the same center[25].

We therefore carried out a detailed systematic review of all the available published data on CRC in Nigerians over a period of 53years (1954 and 2007) as a proximate indication of the burden of the disease in Nigeria (Rotimi & Abdulkareem 2014)[26] .All published studies on histologically confirmed CRC in Nigerians constituted the materials. A total of 2497 cases reported in the 19 publications that met the criteria constituted the materials utilised for the review.

Results:

- The study showed increasing incidence as evident by increase in annual frequency from 18.2/annum in the period 1954-1969 to 86.8/annum in the period 1991-2007(Figure 10).

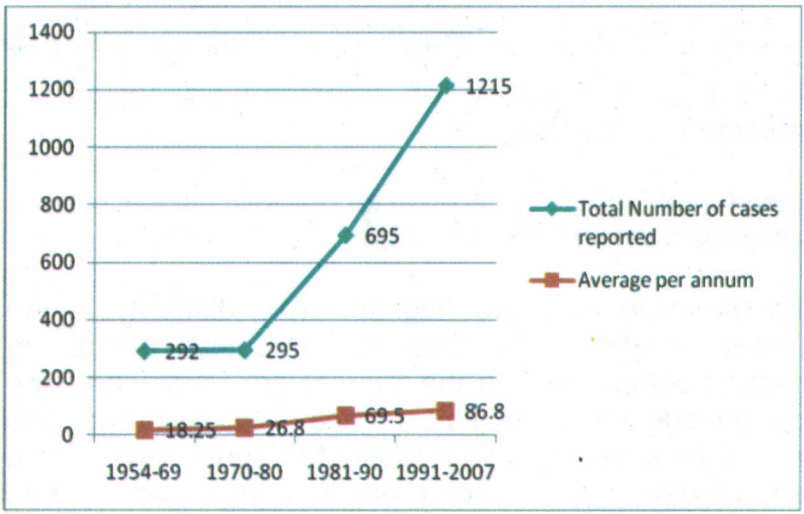


Figure 13: Line graph showing Increasing Number of Colorectal Cases Reported in Nigerian Literature from 1954 to 2007

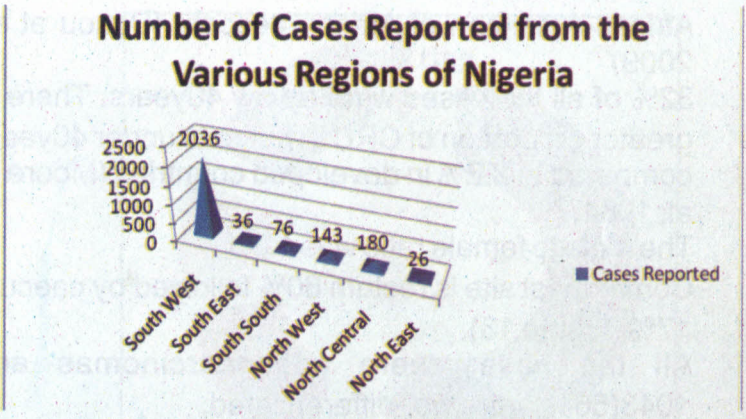


Figure 14: Bar Chart Showing Regional Distribution of 2497 Cases of CRC reported from Nigeria(1954-2007)

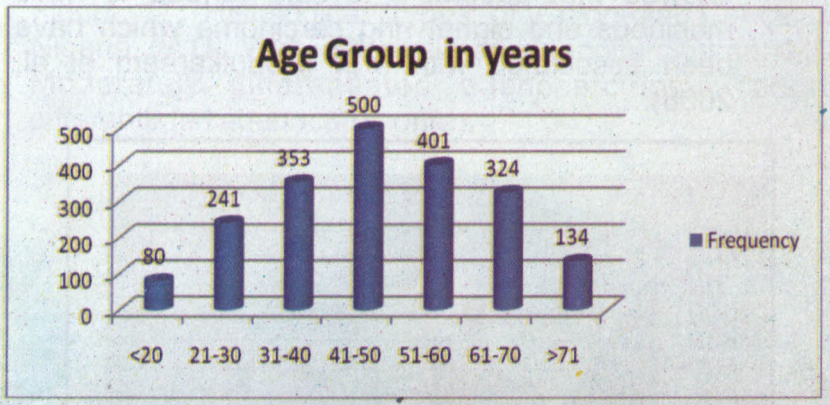


Figure 15: Bar chart showing reported age-groups, n=2033.

- Most cases are reported from South West Nigeria
- The mean age incidence of 46years is far lower than the mean in Caucasians which is said to be in the 7th decade of life. Although, this may in part be explained by low life expectancy in Nigerians (<50years), this lower age incidence has been alluded to in several studies including study on

African-American of African descent (Dimou et al, 2009)[27].

- 32% of all the cases were below 40years. There is greater proportion of CRC in patients under 40years compared to 3.2% in developed countries (Moore et al, 1084)[28].
- The male to female ratio was 1.3:1.
- Commonest site is rectum 60% followed by caecum 17% (Figure 13).
- All the cases were adenocarcinomas and 1043(56%) were well differentiated.
- Mucinous carcinoma and signet ring type accounted for 17% and 2% respectively. We had earlier showed that patients <40years tended to have mucinous and signet ring carcinoma which have been associated with MSI (Abdulkareem et al, 2008).

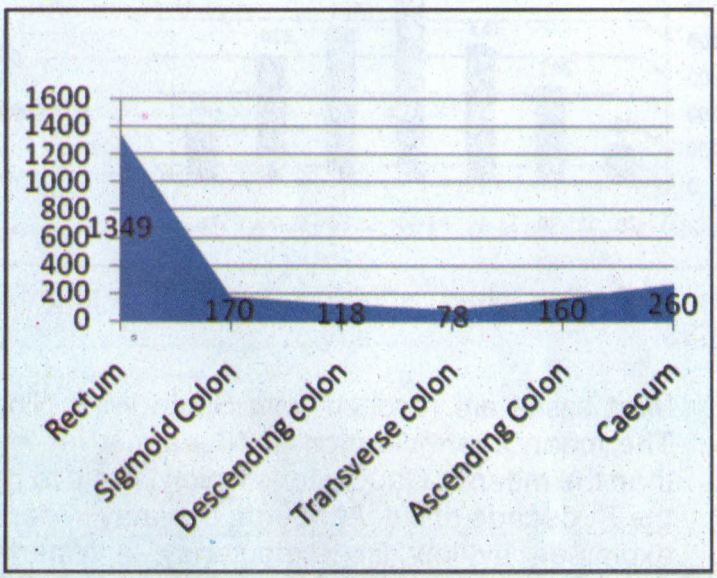


Figure 16: Site Distribution of Colorectal Cancer in Nigeria

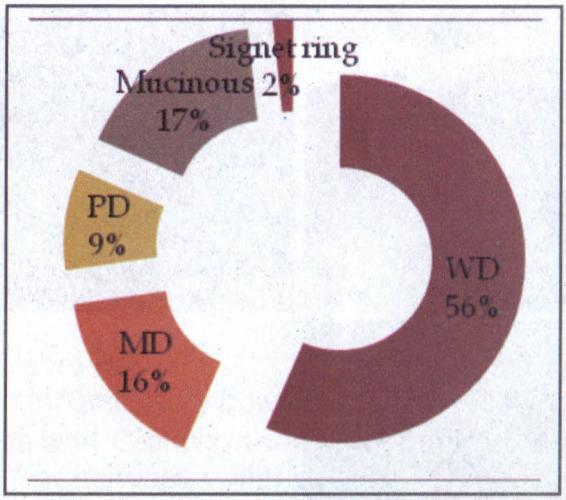


Figure 17: Histological Types of Colorectal Cancer in Nigeria (WD- Well differentiated adenocarcinoma, MD- Moderately differentiated adenocarcinoma, poorly differentiated adenocarcinoma).

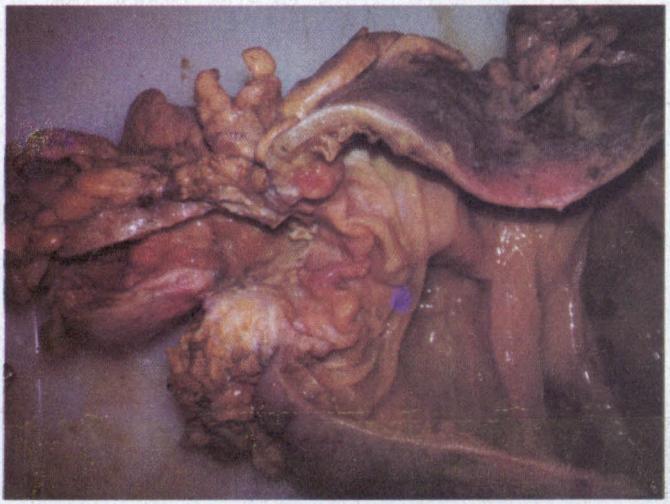


Figure 18: Gross photograph of a caecal tumour obstructing the ileocaecal junction

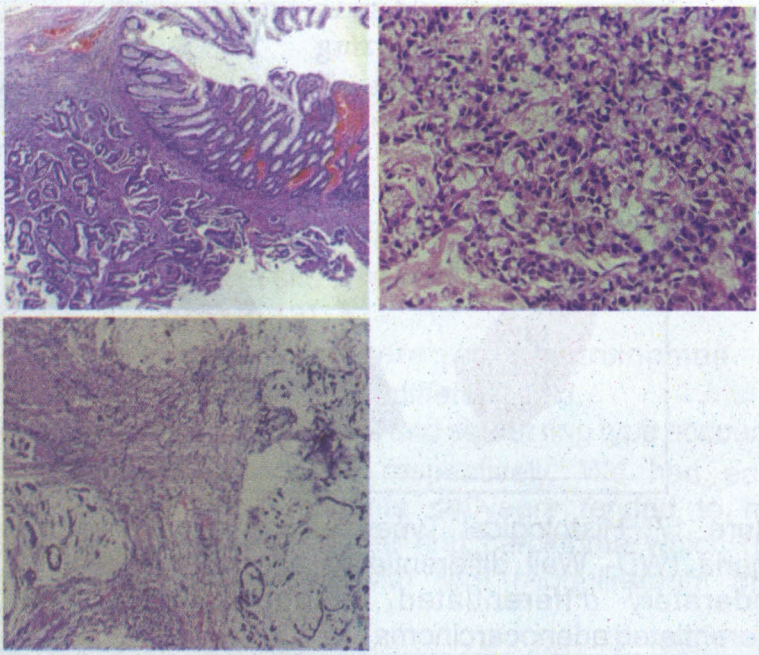


Figure 19: Photomicrographs of the major histological types of colon cancer: Well Differentiated adenocarcinoma (left), Signet Ring Carcinoma (Center) and Mucinous Carcinoma (right).

Aetiology and pathogenesis of CRC

CRC is a multi-factorial disease with aetiology varying from:

- Environmental & dietary
- host inflammatory GI disorders
- Genetic-have the greatest correlation with colon cancer

Environmental and Dietary factors include:

- High content of red meat and animal fat
- Low content of un-absorbable fiber in diet
- Low overall fruits and vegetable intake
- low intake protective micro nutrients

- Alcohol and tobacco consumption
- Obesity
- Sedentary habits

The use of NSAIDs (COX 2 inhibitors) intake of fruits and vegetables, regular physical activity, hormone replacement therapy and calcium intake have all been found to be protective against colorectal cancer.

Host GI Disorders:

- Host Inflammatory bowel diseases such as ulcerative colitis and Crohn's disease predispose to CRC and the risk increases with duration of the IBD and the extent of colonic involvement.

Genetic factors in CRC: Genetic factors play significant roles in CRC particularly the:

- Familial Adenomatous Polyposis (FAP)
- Non-polyposis coli cancer syndromes.
- Others are *MUTYH*-associated polyposis, serrated polyposis, Peutz-jeghers syndrome and Juvenile polyposis.

Familial adenomatous polyposis coli syndrome (FAP): This is characterised by presence of multiple adenomatous polyps throughout the GIT due to mutation in APC gene on chromosome 5q21. In the classical type, they are greater than 500 polyps in the GIT and the risk of developing cancer is almost 100% by age 40years while in attenuated type (about 30 polyps), cancer risk is 50%.

Hereditary non-polyposis coli cancer syndrome (HNPCC) or Lynch syndrome is an autosomal dominant disorder described by Henry Lynch. It is characterised by increased (40%) risk of colon cancer and endometrial

and ovarian cancer. It results from defective DNA mismatch repair (MMR) due to inherited mutation in one of the mismatch repair genes resulting in microsatellite instability. It is a cause of about 6% of all colon cancers and the use of aspirin is said to reduce the risk.

Table 13: Characteristics of Familial Syndromes in Colorectal Cancer

Condition	Abnormal Genes	Lifetime cancer risks	Features
Hereditary non-polyposis coli (HNPCC) syndrome	DNA mismatch repair gene MLH1, MLSH2, MSH6, PMS2	50-80%	Multiple adenomatous polyps throughout the GIT (50 - 500 polyps)
Familial adenomatous polyposis syndrome (FAP)	APC gene mutation in on chromosome 5q21.	100% by age 40yrs	No polyps, microsatellite instability

Other Genetic Disorders are:

- ***MUTYH*-associated polyposis-** (MAP) is an autosomal recessive polyposis syndrome that carries an increased risk for colorectal cancers. It is caused by bi-allelic germ-line mutations in the *MUTYH* gene. It is phenotypically similar to FAP but lacks APC mutation
- **Serrated polyposis-** It is defined by the presence of:
  - at least 5 serrated polyps proximal to the sigmoid colon with 2 or more polyps >1 cm;

- any number of serrated polyps proximal to the sigmoid colon in an individual who has a first-degree relative with serrated polyposis; or
- greater than 20 serrated polyps of any size throughout the colon.

- **Peutz-jeghers syndrome**(LKB1 mutation)
- **Juvenile polyposis**(SMAD4 mutation)

Table 14: Other Genetic Disorders in Colorectal cancer

Condition	Gene (% of detecting mutation)	Lifetime cancer risks	Other features
Peutz-Jeghers syndrome	STK11 (30-70%)	colon-39%; also breast, pancreas, stomach etc.	Mucocutaneous pigmentation, GIT harmatoma
Juvenile Polyposis	SMAD4 (20%) BMPR1A (20%)	Colon-68% UGI-21%	GI harmatoma, HHT, digital clubbing, congenital defects
Cowden syndrome	PTEN (80-90%)	Colon-9% Breast, thyroid, Endometrium, Kidney	Muco-cutaneous papules, macrocephaly, harmatomas of GIT, thyroid, breast

Clinical Presentation of Colorectal Cancer

Early in the disease, the majority of patients are a-symptomatic for several years. When the tumour becomes symptomatic, clinical presentation usually varies including abdominal pain, abdominal mass, bloody mucoid stool, change in bowel habit, weight loss,

anaemia and/or features of intestinal obstruction. Right sided tumour frequently presents with fatigue, body weakness, iron deficiency anaemia and bleeding if bulky while left sided tumour presents with occult bleeding, change in bowel habit, cramp left lower abdominal discomfort, malaena, diarrhoea and constipation.

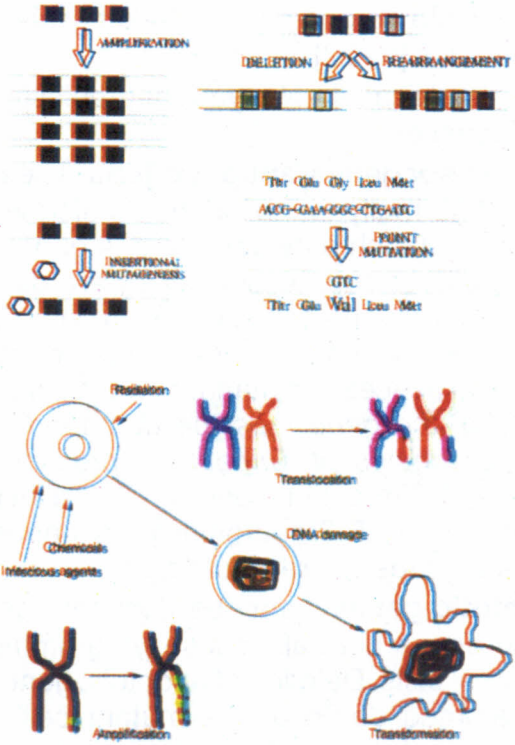
Molecular Basis of Carcinogenesis

It will be appropriate at this point before I proceed to pathogenesis of colorectal cancer to briefly describe the molecular mechanisms that underlie carcinogenesis (mechanism of cancer formation). It refers to molecular changes that form the basis of transformation of normal to malignant cell. According to Nowell's law, cancer can be defined as 'overgrowth of cells that have acquired cumulative genetic damage which confers growth advantage over normal cells'. Genetic hypothesis of carcinogenesis also states that 'a tumour mass results from clonal expansion of a single progenitor cell that has incurred genetic change called **mutation'.**

Four major classes of genes that are involved in normal cell growth and differentiation are the targets of mutation. Such mutations may be inherited or acquired through exposure to environmental agents (physical, chemical, viruses). They are classified as tumour promoter genes, tumour suppressor genes, apoptotic genes and DNA repair genes.

- **Tumour promoter/activation-** These genes are present in the body as proto-oncogenes and they normally promote cell division. They become altered through point mutation, translocation or amplification. The gene behaves in a dominant fashion i.e. *only one mutant allele of the gene need be present to cause cellular transformation. Examples are:*
- point mutation- K-ras in colorectal cancer

- Translocation-e.g. c-myc in Burkitt lymphoma [8–14] c-abl in CML [9–22]
- Gene amplification- N-myc in neuroblastoma, c-erb in breast cancer
- **Suppressor genes-antioncogens-** These genes are present normally to inhibit cell division when it is not necessary (such as when there is genetic damage). When tumour suppressor genes are deleted or; the ability to prevent cell division is lost, it results in uncontrolled or unchecked cell division. Such genes behave in a recessive manner, which implies that *the 2 alleles of the gene must be damaged to transform cells. Examples of Tumour suppressor genes are:* p53, APC (in colon cancer), Rb (Retinoblastoma gene), NF-1 NF-2(neuroblastoma genes) BRCA-1, BRCA-2 genes (in breast cancer).
- **Apoptotic genes:** (may be dominant or recessive). These genes normally cause programmed death of abnormal cells. Deletion of apoptotic gene will prevent programmed death of the mutant cell, extends its survival and thus allows it to proliferate to form malignant tumours.
- E.g.bcl–2 gene in B cell lymphoma, p53and & c-mycgenes also act similarly
- **DNA repair genes (recessive)**- These are genes that affect the ability of the body to repair non-lethal damage to other genes including the proto-oncogens, tumour suppressor genes and apoptotic genes. Inability to repair results in mutations in the genome and then neoplastic transformation. Both alleles must be lost to induce genomic instability; they act as recessive genes similar to suppressor genes.



Figures 20: Showing Various Genetic abnormalities of Tumour Promoter Genes

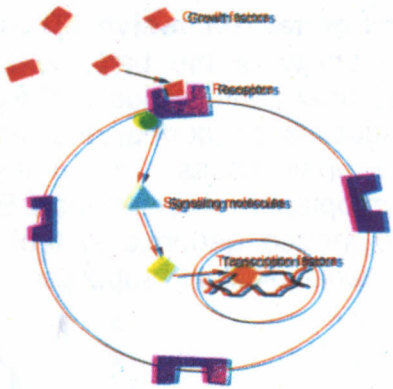


Figure 21: Showing Normal Signal Transduction in cell Division

The changes that occur in these genes make them malfunction. The abnormal genes induce production of proteins that mimic normal pathway of cellular transduction (See Figure above) to promote abnormal mitosis (cell division). Some of them function as cell membrane growth factor receptors, some as second messengers in the cytoplasm of cells and some as activator of nuclear regulatory factors that initiate DNA transcription. Thus, a single cell whose gene is altered produces factors that promote cell division until a large mass of tumour is produced. As the tumour grows, it is prone to more mutations that confer on it metastatic potential (ability to spread through blood vessels, lymphatic's and through body cavities to other parts of the body).

Pathogenesis and Molecular Genetics of Colorectal Cancer

CRC can either be sporadic or inherited although the former accounts for over 95%.Due to its heterogeneous nature, CRC is classified based on location, histology, aetiological factors and molecular mechanisms of tumorigenesis. It is now known that proximal and distal CRC involve different genetic mechanisms. Proximal cancer is that involving the right side of the colon (caecum, ascending colon and transverse colon while the distal cancer involves the left side including descending colon, sigmoid colon and rectum). Based on the genetic abnormality, CRC can be classified into 3 major types:

1. Chromosomal instability pathway (CIN). The cancers that follow this pathway account for 60-70%. They are associated with gross chromosomal abnormalities characterised by karyotypic abnormalities and chromosomal gains and losses. It is the underlying abnormality in inherited cancers associated with FAP syndrome and is equally present in 80% of sporadic cancers.

The tumour almost always harbours APC mutation and frequently K-ras and p53 mutation. Its presence is usually preceded by polyps.

2. Microsatellite instability pathway (MSI). Microsatellites are repetitive small DNA sequences scattered in the genome and are fixed in number for an individual. They are located in the coding or promoter region of genes involved in regulation of cell growth and are prone to errors during DNA replication. MS instability are replication errors resulting from inactivation of DNA mismatch repair genes (involved in genetic 'proofreading') either by mutation within hMLH1, hMSH2, hMSH6, hPMS1 or hPMS2 or more frequently by hypermethylation of the hMLH1 gene promoter at the adenoma-carcinoma interface. All cancers associated with non-polyposis coli syndrome and about 15% of sporadic cancer show microsatellite instability. MSI cancers are commonly located in the right side of the colon (proximal colon); they tend to be mucinous or poorly differentiated and occur in younger age. Usually there is no preceding polyp. This abnormality may be inherited or sporadic.
   - Inherited MSI cancer: Germ-line mutation occurs in any of the 5 genes mentioned above but 95% of mutations occur in hMLH1 or hMSH2. There is no associated B-RAF mutation.
   - Acquired/Sporadic MSI Cancer: There is hypermethylation of CpG island which occurs within the promoter region of hMLH1 gene in >80% of sporadic CRC but unlike the inherited type, associated B-RAF mutation occurs, rarely KRAS. These patients have poorly differentiated tumours.

3. Epigenetic instability-CpG island methylator pathway (CIMP).

Proximal colon cancer results from loss of function of MMR genes and follows Microsatellite Instability(MSI) ('mutator')pathways while distal cancer follows mutation in APC gene chromosomal instability pathway(CIN)-'suppressor. The genetic abnormality in proximal cancer is similar to what has been described in Lynch syndrome while that of distal cancer follows the pathogenesis of Familial Adenomatous Polyposis (FAP) Coli Cancer. Both MSI and CIN pathways CRC involve genetic abnormalities that result in loss of function of tumour suppressor genes and/or gain of function of oncogenes as highlighted above. Some of these genes are:

- Oncogenes: β-catenin, K-ras
- Tumour suppressor genes: Loss of APC gene on chromosome 5q21 as in FAP syndrome, deletion of SMAD genes (SMAD2, SMAD4) located on chromosome 18q21. Others are: Bax gene, p53 gene and TGF-βRII.
- DNA Repair genes: Mismatch repair gene (in HNPCC pathway)-
  - hMLH1 (3p21), hMSH2 (2p22), hMSH6, hPMS1, hPMS2; hMLH1 & hMSH2 are the most common.

From the above, it is obvious that CRC is a genetically heterogeneous disease; being the result of multiple genetic/epigenetic mutations involving several genes that regulate cell proliferation or repair of DNA damages. The mechanisms that underlie development of CRC have thus been described as a multi-hit, multi-stage phenomenon in which several mutations (alterations or changes) occur in multiple genes following exposure to multiple hits of environmental and dietary risk factors. These mutations occur at different stages and result in

increasing phenotypic abnormality from normal hyperproliferative epithelium, to small adenoma, large adenoma and then finally invasive cancer (see figure 17below).

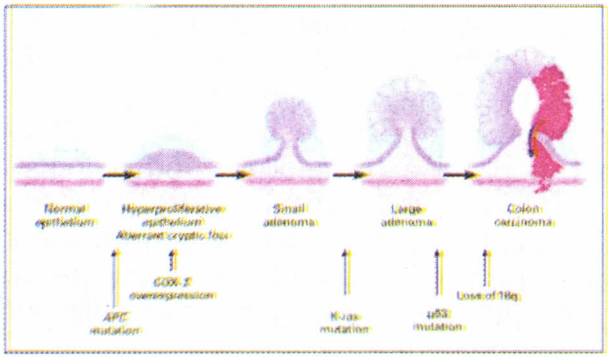


Figure 22: Adenoma-carcinoma Sequence in Colorectal cancer (Image Adapted from AJG, www.nature.com)

Molecular Genetics of CRC: What type of Colorectal Cancer do we have in Nigeria?

Familial adenomatous polyposis is rare; the systematic review of Nigerian literature over 53yrs on CRC that we carried out showed no case at all; solitary adenomatous polyps were reported in only 2% of the 2497 cases reviewed. Also, infective conditions which have been suggested in some studies are not commonly associated with CRC in Nigeria; schistosomiasiswas recorded in 12 (0.5%) and amoebiasis in 7 (0.3%) cases.

The shift from high fibre to refined diet rich in fat and animal protein (which is particularly commonly practiced by young Nigerians) has been suggested and may be co-factors in the aetiopathogenesis of CRC in Nigerians. In one study, African diet was shown to be deficient in protective antioxidants such as Vitamins C, E, A and calcium while another study by K'eefe et al has indicated

that interactions between the dietary and internal bacterial environments constitute important risk factors for CRC in Africans'.

Although, genetic study on CRC cases from Africa is scanty, a study on African-Americans in South Africa has demonstrated higher incidence of microsatellite instability (MSI-H) tumours (Ashktorab H).

Immunophenotyping of Colorectal Cancer in Lagos

In order to unravel the possible pathogenesis of CRC in Nigerians, my team carried out an immunohistochemical study to characterise some of the molecular genetics that underlie development of CRC in Nigeria (Abdulkareem et al 2014). I thank the Vice Chancellor and the University who gave us grant through the Central Research Committee of the University of Lagos. We were able to set up an immunohistochemistry laboratory in the department and we also organized an international training workshop that was co-sponsored by the International Union Against Cancer(UICC) in which experts from the United kingdom were invited to train both histopathologists and histoscientists from several parts of Nigeria.

The study was prospective with a total of 125 cases of colorectal cancer recruited between 2008 and 2009 from various hospitals and laboratories in Lagos. Immunohistochemistry was carried out on the paraffin blocks of the tumour sample using antibodies testing the two major genetic pathways of pathogenesis: Microsatellite and APC genes.

Result:

18.75% of the cases showed absence of MSI antigen and thus may have microsatellite instability.

- This figure is comparable to the finding of Duduyemi et al who reported MSI in 23% of 26 patients; 3 of whom were less than 40years. Also, a case report on colorectal cancer cases from Ibadan, Nigeria by Adebamowo et al demonstrated MSI in two of five patients with germ-line mutation in MSH2 gene.It is known that 15% of sporadic cancers show microsatellite instability.

Table16: Immunophenotyping of Colorectal cancer in Lagos (2008-2009)

Degree of Positivity	CK7	CK20	Beta Catenin	MSH2
Negative	5(14%)	22(27.2%)	4(4.5%)	15(18.75%)
Mildly positive	14(40%)	29(35.8%)	10(11.4%)	19(23.75%)
Moderate positivity	3(8.6%)	6(17.1%)	2(2.3%)	4(5%)
Strongly positive	13(37.1%)	24(29.6%)	72(81.8%)	42(52.5%)
Total	35	81	88	80

We also carried out studies on the beta catenin status of colorectal cancer. This gene is a surrogate marker for APC gene defect. APC gene defect as highlighted earlier is the basis of familial polyposis cancers and also frequently mutated in majority (>90%) of sporadic CRC. Our study showed 84 of 88 cases tested by immunohistochemistry (95.4%) was positive for beta catenin. Thus, as studies from other centres have shown, our study confirms that the pathogenesis of majority of colorectal cancer in Nigeria is related to chromosomal instability pathway that is linked with APC gene abnormality.

Conclusion and Message:

- It is therefore clear that both pathogenetic mechanisms of chromosomal instability linked to APC gene defect as well as microsatellite instability

gene pathway play significant roles in Nigerian colorectal cancer.

- Majority of these however do not appear to be germ-line mutation; they are epigenetic or sporadic. We had also earlier shown in our study that majority of the poorly differentiated tumours are right sided and found in a younger age group. The next phase of our research which is on-going is to find out the proportion of our CRC that are inherited (harbour germ-line mutations.)

As in the table above, the study also determined the cytokeratin expression pattern of CRC. These are antigens that are expressed by epithelial tumours of the GIT and are useful in confirming diagnosis especially in metastatic spread. While Cytokeratin 7(CK7) is commonly expressed by upper GI tumours, CK20 is more commonly expressed by lower GIT, majority of which is colorectal tumour. Of 81 cases analysed, 59 (73%) showed positive reaction to CK20. This also confirms the fact that majority of colorectal cancer is Cytokeratin 20 positive. However, only 35 were successfully processed for CK7 of which 30 were positive (85%) while 5 were negative. This is in sharp contrast with the knowledge that lower gastrointestinal tumours show poor reaction to CK7, it is known to be expressed by upper GIT tumours such as stomach, pancreas etc. This is being further investigated.

In another study, we have utilised these antibodies in combination with other antibodies such as CA-125, TTF-1, ER etc. in differential diagnosis of omental and liver metastatic tumours diagnosed from our hospital (Abdulkareem &Rotimi 2008)[35].

Role of K-RAS and B-RAF Genes in CRC

As a continuation of research into the genetics of colorectal cancer in Nigeria, we carried out a genetic study to determine the *KRAS* and BRAF mutation statuses of Nigerian colorectal cancers (Abdulkareem et al 2012)[36] . This was the first of its kind in Nigeria.

KRAS proto-oncogene codes for K-ras G-protein which is located downstream of Epidermal Growth Factor Receptor; a transmembrane receptor (EGFR), an essential component of EGFR signalling cascade. When a normal cell is stimulated through ligand binding to EGF receptor, KRAS becomes activated (by phosphorylation). This then recruits RAF and stimulates the RAS/mitogen-activated protein kinase (MAP-K) signalling pathway. This results in transmission of growth-promoting signals to the nucleus for cell division to occur. (Figure 21)

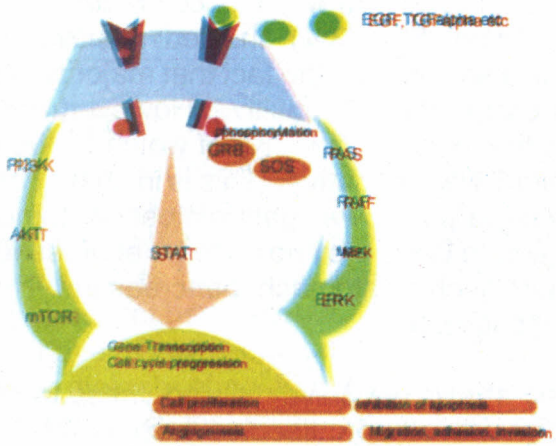


Figure 23: RAS/Mitogen-Activated Protein Kinase (MAP-K) Signalling Pathway

EGFR is over-expressed in CRC and anti-EGFR monoclonal antibody in the form of a drug (cetuximab or panitumumab) is used in treatment of advanced

metastatic CRC. It is known that in the presence of a *KRAS* mutation particularly in exon 2, the inhibition of this pathway by EGFR inhibitors becomes ineffective. The goal in treatment and management of advanced CRC is that a patient is prescribed the optimal treatment regimen for his particular tumour; so-called personalised medicine (Richman et al 2010)[37].

Activation of *KRAS* oncogene, codons 12, 13 or 16 has been associated with colorectal carcinogenesis and mutation has been recorded in 30-60% of cases". Also, BRAF, located downstream of KRAS in the same pathway can also be activated by mutation in codon 600.Mutation in either KRAS or BRAF has also been associated with poor prognosis. However, no study has been carried on these genes in CRC has been reported from Nigeria. This was thus the first of its kind in Nigeria.

Mutation analysis was carried out by pyrosequencing after DNA extraction from 200 cases using archival paraffin-embedded blocks of colorectal carcinoma tissues from various parts of Lagos. This was carried out in collaboration with colleagues at the Leeds Institute of Molecular Medicine, St. James's University Hospital, Leeds UK. The *KRAS* codons 12, 13 and 61 and *BRAF* codon 600 were assessed and mutation rates and the spectra were determined.

Results: *KRAS* mutation in codons 12 and 13 was demonstrated in 23 of 112 cases (21%); none in codon 61 while *BRAF* mutation in codon 600 was demonstrated in 5%. All the BRAF and 85.7% of KRAS mutations occurred in well differentiated tumours and 71.1% of the mutations occurred in right sided tumours. Only one of the poorly differentiated tumours demonstrated BRAF but no KRAS mutation.

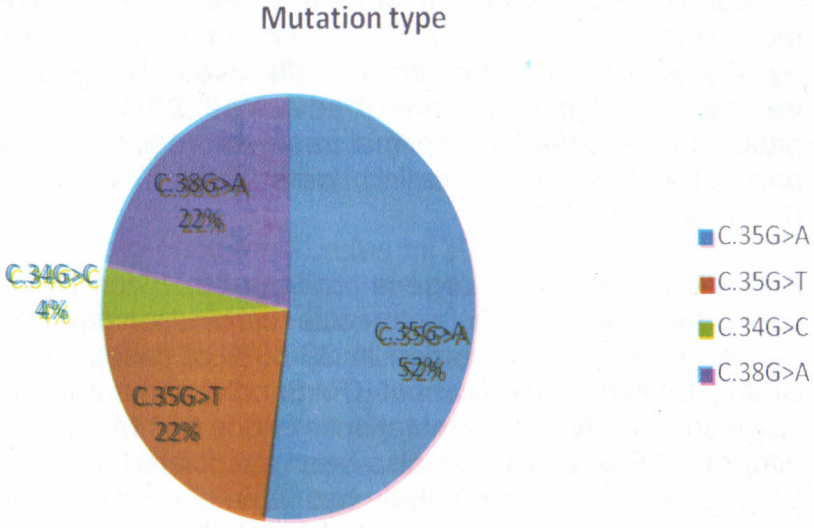


Figure 24: Types of KRAS Mutation Recorded in Nigerian Colorectal cancers

Our result shown in Table 17 and Figure 21, when compared with FOCUS trial (UK) population, was significantly lower in *KRAS* mutation frequencies ($p<0.0001$) but have similar mutation spectra (Richman et al 2009).[41]

Table 17: KRAS and BRAF Mutation Frequencies; Comparison with FOCUS TRIAL, UK.

	NIGERIA	FOCUS TRIAL, UK	P VALUE
KRAS codons 12 & 13 WT	89/122(79.5%)	422/711(59.4%)	P<0.0001
KRAS codons 12 & 13 mutant	23/112(20.5%)	288/711(40.5%)	
KRAS codon 61 WT	112/112(100%)	684/711(96.2%)	P=0.060
KRAS codon 61 mutant	0	23/711(3.2%)	
BRAF codon 600 WT	107/112(95.5%)	654/711(92%)	P=0.246
BRAF codon 600 mutant	5/112(4.5%)	56/711(7.9%)	

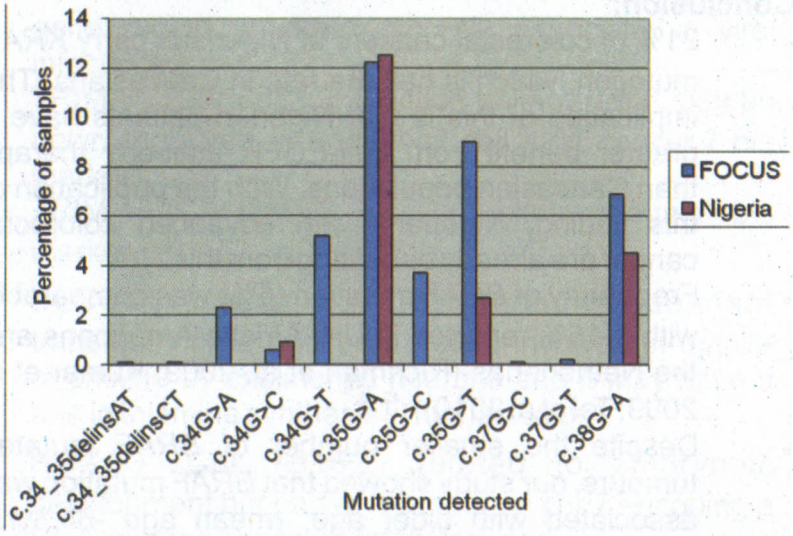


Figure 25: Comparison of mutation spectra between 'FOCUS' and Nigeria

Table 18: Characteristics of CRC with respect to KRAS and BRAF Mutations

Mutation type	M:F	Average Age	Ratio of WD/PD tumour	LT/RT sided tumour
All samples	1.5:1	52.8yrs	5.5:1	6.5:1
No mutation	1.5:1	52.5yrs	10.7:1	8.6:1
KRAS mutation	1.9:1	55.7yrs	22:1	4.3:1
BRAF mutation	1:2	62.3yrs	2:1	

Conclusion:

- 21% of colorectal cancers of Nigerians carry *KRAS* mutation, which is half the rate in Caucasians. The implication of this is that Nigerian patients have a greater benefit from anti-EGFR antibody therapy than Caucasian populations. With the publication of this finding, Nigerians with advanced colorectal cancer are already benefiting from this.
- Frequency of *BRAF* mutation (5%) was comparable with 8-15% reported in UK, African-Americans and the Netherlands (Richman et al, 2009; Kumar et al 2009, Tol et al 2010)[41,42,43].
- Despite the smaller number of *BRAF* mutated tumours, our study showed that *BRAF* mutation was associated with older age, (mean age -64.3yrs) when compared with samples without mutation (mean age-52.9yrs) but no significant association was demonstrated with gender, site or tumour

grade. Previous studies had reported that *BRAF* mutation is strongly associated with right sided tumour, higher tumour grade, absence of peri-tumoural lymphocytic inflammation and microsatellite instability (Zlobec et al 2010)[44].

On Going Study On Epigenetic Mutations in Colorectal Cancer: Interesting Finding!

We have an on-going genetic study in collaboration with the University of Birminghamin which we are comparing Nigerian cohort of colorectal cancers with those of Caucasians. This has shown that 7 genes are differentially expressed in the Nigerian cohort of colorectal cancers. These are:

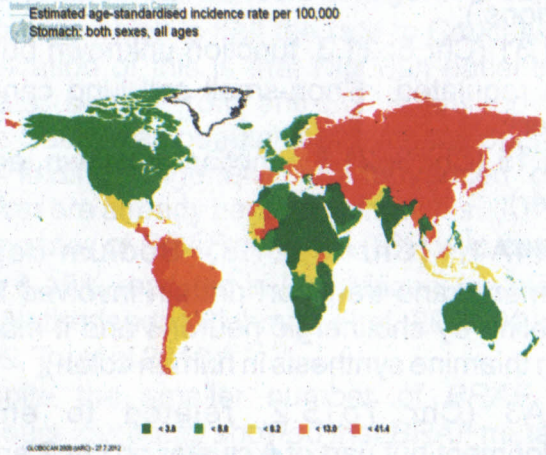
- SGCE (codes for sarcoglypan, Chr 7q21.3 which binds EGF receptor and may affect the way Cetuximab and panitumumab work);
- CD81 (Chr 11p15.5, located in the tumour suppressor gene region. Immunologic role especially in viral infections.);
- TRIM 31 (Chr 6p21.3, function unknown but may be down regulated in non-small cell lung cancer.? bio marker);
- TRIM 15 (Chr 6p21.3, function unknown, again? bio marker);
- SLC44A4, (Chr 6p21.3, Sodium-dependent transmembrane transport protein involved in uptake of choline by cholinergic neurons and it may have a role in thiamine synthesis in human colon);
- HOXA3 (Chr 7p15.2, related to embryonic development but part of A cluster on chr 7 encoding a DNA-binding transcription factor); and
- HNF4A (Chr 20q13.12 the protein encoded controls expression of several genes. The gene also plays a developmental role in the liver, kidney and intestines

may be a marker in discriminating between primary and metastatic gastric and breast cancer.

These are some interesting genes and their significance is being further investigated.

Cancer of the Stomach

Gastric cancer is one of the most common cancers and the second most common cause of cancer deaths worldwide (Parkin et al 2001)[45]. The incidence varies worldwide and this has been associated with the variable prevalence of *H. pylori* infection which was classified in 1994 by the International agency for research on cancer (IARC) as a definite (class1) carcinogen for stomach cancer (IARC 1994)[46]. According to the Global Cancer report, the incidence of gastric cancer in the sub-region is low with estimated age standardised rate of 11.4/100,000 for both sexes compared to >63/100,000 in East Asia. (GLOBOCAN-2008)[47]- Figure 26 below.



The most common histologic type is adenocarcinoma, accounting for 90% of cases in the study we carried out among patients diagnosed in Lagos and the intestinal type was the predominant histologic type (Abdulkareem

et al 2010)[48]. Majority of tumours are located in the gastric antrum and patients presented at advanced stage with attendant poor prognosis. Sarcomas, non-Hodgkin's lymphoma and carcinoid tumour were also recorded (Figure 25).

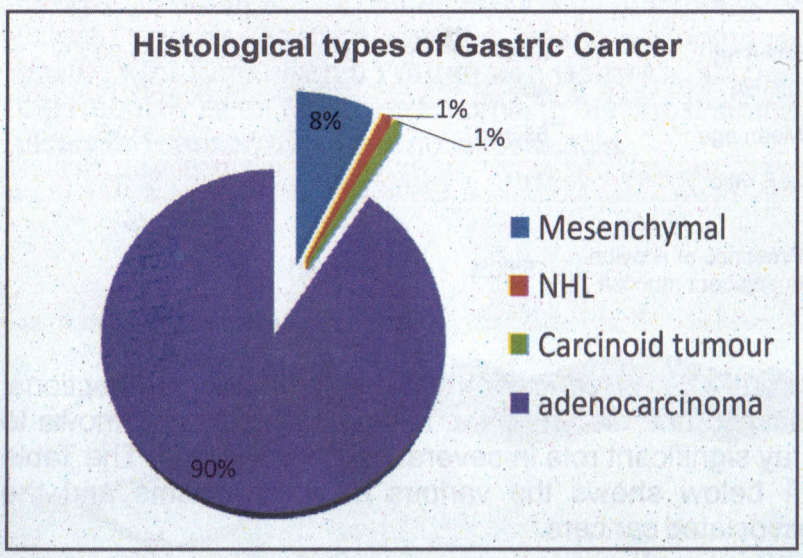


Figure 27: Showing that adenocarcinoma is the most common malignant gastric tumour (90%)

***Helicobacter pylori* infections and gastric cancer**

The relative frequency ratios of gastric cancer reported in Nigerian studies range between 1.3 and 3.6% (Abdulkareem et al 2010, Mandong et al 2008, Okobia et al 2005)[48,49,50]. Table 20 compares the clinicopathological parameters recorded in three separate studies from different parts of Nigeria[48,49,51]. The peak age was in the 6th decade and male to female ratio was 2:1.

Table 20: Characteristics of Gastric Carcinoma in Three Separate Studies from Nigeria

	Abdulkareem et al Lagos; 2010[48]	Oluwasola &Ogunbiyi Ibadan; 2003[51]	Mandong et al Jos; 2010[49]
Histologic Type			
Intestinal	60%	56%	51.20%
Diffuse	40%	22%	34.10%
Mean age	55yrs		51yrs
M:F ratio	2:01	2:01	2.4:1
Presence of H.pylori in adjacent mucosa	15.50%	17.80%	-

About 37% of cancer cases are attributed to infections, tobacco and diet in Africa. Micro-organisms are known to play significant role in several cancers in Africa. The Table 21 below shows the various micro-organisms and the associated cancers.

Table 21: List of Micro-organisms and Associated Cancer

Micro-organism	Associated Cancer
Bacterial organisms • H. pylori	Gastric adenocarcinoma MALToma
Viruses • Hepatitis B & C viruses • Human Papilloma Virus • Epstein Barr virus • HIV	Liver cancer(hepatocellular carcinoma) Carcinoma of the cervix Burkitt's lymphoma, Nasopharyngeal carcinoma High grade B cell Lymphoma
Parasite • Schistosomahaematobium	Squamous cell carcinoma of the urinary bladder

H.pyloriwas discovered in 1983. It is a spiral, microaerophilic, gram negative bacterium that spreads between persons by oral-oral and faeco-oral routes. Human beings are the only known reservoir. It is one of the first bacterial genomes to be completely sequenced. Studies have shown the organism to be associated with several gastroduodenal diseases such as gastroduodenal ulcers, chronic gastritis, gastric adenocarcinoma and gastric MALToma. Robin Warren and Barry Marshall won the Nobel Prize for Medicine for proving that most stomach ulcers are caused by a germ not excess acid.

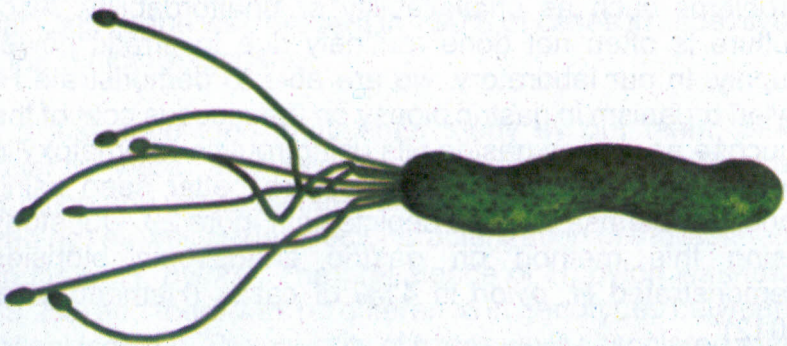


Figure 28: showing Micrographs of Helicobacter pylori organism

There is strong evidence showing causal relationship between H.pylori and gastric cancer (GC). In Africa and some Asian countries however, despite the high prevalence of H.pylori (70-90%), incidence of GC is low. This is the so-called 'African' and 'Asian' enigmas. This has been explained by several factors including host genetics and immune response mounted against the organism, different oncogenic potential of the specific strains of H.pylori as well as environmental factors.

In developing countries, infection occurs in childhood and increases with age while in developed countries, infection occurs in older age. Invasive and non-invasive methods are used in diagnosis of H pylori infection. Invasive methods most often require endoscopy which include Campylobacter-like organism (CLO) tests, culture and histology, direct gram stain and Polymerase Chain Reaction (PCR) based tests. The non-invasive tests do not require endoscopy and include: serology, Hpylori stool antigen test (HpSA) and Urea breath test (UBT).

In Nigeria, invasive methods are fraught with several problems such as unavailability or unaffordability. Also, culture is often not done routinely due to erratic power supply. In our laboratory, we are able to demonstrate H. pylori organism in gastric biopsy on the mucous coat of the mucosa as well as gastric pits using routine haematoxylin and eosin stain but usually they are better seen using modified Giemsa stain as depicted in Figure 29. Our study using this method on gastric endoscopic biopsies demonstrated *H. pylori* in 41% of cases (Hameed et al 2012)[52].

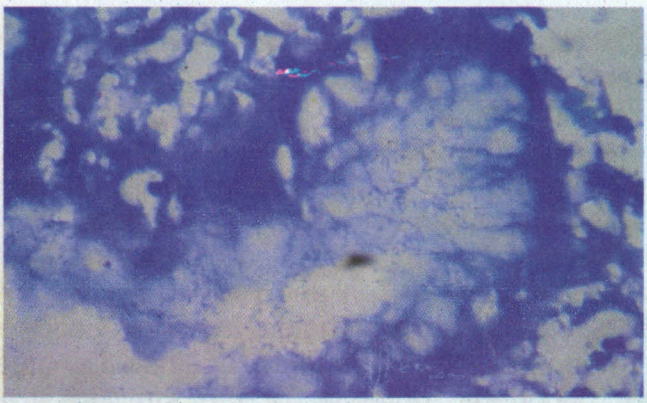


Figure 29: showing Photomicrograph of gastric mucosal biopsy demonstrating H.pylori in mucous layer (Modified Giemsa Stain X40)

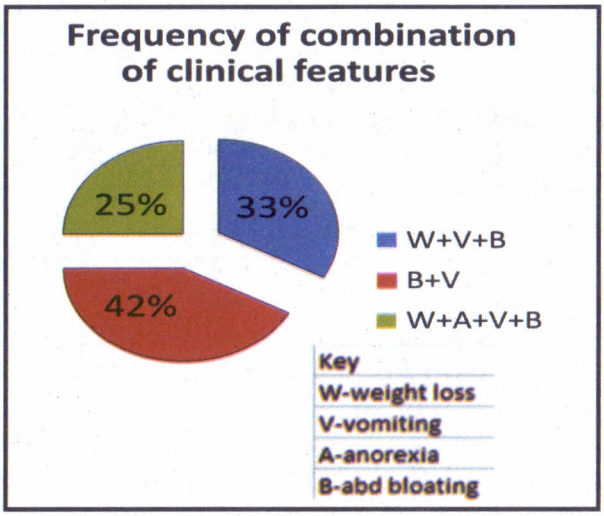
All the other diagnostic methods have been studied in collaboration with our team at the National Institute for Medical Research (NIMR, Yaba). The team compared the use of stool PCR with Urea Breath Test (UBT) (Smith et al 2012)[53]. Out of 97 stool samples analysed, 38 (39.2%) were positive for Helicobacter spp. and 20 (20.6%) positive for H. pylori by PCR, while 47 (48.5%) were positive for H. pylori by UBT. It was suggested that the method may be useful for detecting H. pylori from stool amongst children especially where endoscopy is not accessible/affordable. Smith et al (2002)[54] have also demonstrated the virulent factors (VacA s1/m2, iceA1 and Cag A+) in Nigerian patients. They found that CagA gene was present in >90% of cases irrespective of the clinical diagnosis.

In a just concluded multicenter study by our team, 577 patients were analysed for the antibiotic resistance situation and the associated disease outcome (histological grading) as well as detailed characterization of the isolated strains of *H. pylori*[55]. The prevalence of H. pylori was low (39.2%) and there was no difference in genotypes between patient isolates. The majority of cases were associated with mild pathology (mainly inflammation), despite the presence of the major virulence factors of these bacteria, the cag-PAI and the s1/m1 vacA. The study indicated that Nigerian patients are apparently being protected from more serious pathology from yet to be identified mechanism thus further strengthening the so-called 'African enigma'. The majority of patients had a KDKGPE motif in front of the first EPIYA-A regions of cagA; this needs to be further investigated as well as the role of high salt diet and immune response to H. pylori infection by Nigerians.

Majority of the cases of gastric cancer present with the so-called 'alarm symptoms and signs' such as dysphagia,

unexplained weight loss, symptom onset after age 45years, persistent vomiting, iron deficiency anaemia, upper GI bleeding and epigastric mass while only a minority of patients present with uncomplicated dyspepsia (dyspepsia without alarm symptoms/signs). As shown in figure 25, about 81% of the 105 patients we studied were above the age threshold of 45years and all patients with clinical data had one or more alarm features; the most recurring symptoms being abdominal fullness, recurrent vomiting, anorexia and weight loss (Abdulkareem et al 2010)[48].

Upper gastrointestinal endoscopy with biopsy of suspected lesions is the mainstay of definitive diagnosis. This facility is expensive and only available in few centres. For cost effectiveness therefore, endoscopy is reserved for patients with alarm features, H. pylori-positive individuals who fail test-and-treat, and those with an inadequate response to empiric anti-secretory therapy (Ebell et al 1997)[56].



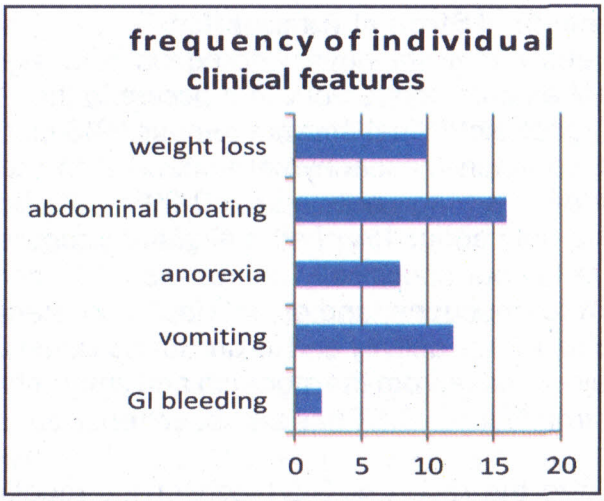


Figure 30: Alarm Symptoms & Signs in Gastric cancers Diagnosed in Lagos

Conclusion and Message

- The prevalence of H. pylori in West Africa is high and infection occurs early in childhood but gastric cancer incidence is low (so-called "African enigma");
- Invasive and non-invasive methods are used in diagnosis of H pylori infection but invasive methods are fraught with several problems such as unavailability or unaffordability. Also culture is often not done routinely due to erratic power supply;
- Majority of our patients are above the threshold of 45years and manifest with alarm features which should raise a suspicion, particularly in our setting with poor diagnostic endoscopic facilities; and
- Studies have also suggested that diets rich in anti-oxidants such as fresh fruits and vegetables decrease risk of GC while high salt diet increases the higher expression of CagA. These need to be further investigated.

Gastrointestinal Stromal Tumour (GIST)

Another entity that we have worked on is a significant though not as common tumour that occurs in the GIT; the so-called gastrointestinal stromal tumour (GIST). GIST is the most common mesenchymal tumour of the GIT with frequencies varying between 60-80%. It however represents only about 1% of all malignant tumours of the GIT[57]. The tumour specifically expresses c-KIT gene (CD 117); a proto-oncogene, and growth factor for stem cell. It has tyrosine kinase activity and its product is called CD117. While majority arise from the stomach and small intestines, extra gastrointestinal GIST has also been reported[58].

According to the report of GIST consensus meeting, the histological criteria diagnostic of GIST are:

- Standard histological examination with a central review by an expert in sarcoma for equivocal cases;
- Risk assessment profile based on tumour size, mitotic index and location;
- Immunohistochemistry (IHC) using a panel of 5 antibodies-CD117, CD34, S100, SMA, Desmin;
- Molecular analysis in suspected cases that are CD117 negative.

Through the sponsorship of UICC (as a UICC ICRETT fellow), we carried out for the first time in Nigeria a study to demonstrate the immunophenotypic characteristics of all the cases of gastrointestinal mesenchymal tumour (GMT)diagnosed in Lagos over a period of 12 years. The cases were characterized using 5 antibodies: CD117, CD34, SMA, S100 and Desmin antibodies at the research laboratory of The Leeds General Infirmary, United Kingdom following standard procedure (Abdulkareem et al 2009)[59].

Results: GISTs accounted for 41%, mean age of 45.4years with a Male to Female ratio of 1.6:1; majority (54%) was located in the stomach and only 30.7% were suspected before immunohistochemistry. The differential diagnoses confirmed by the study are shown in Figure 29. In Table 22, characteristics of GIST that has been reported from Nigeria in four separate studies are highlighted[57,60,61,62].

Conclusion and Message from the study

- Our study showed that provision of facilities for immunohistochemistry in developing countries is essential for improving diagnostic accuracy.
- The availability of effective drug has also made it imperative to make specific immunohistochemical diagnosis in order to differentiate it from other entities which have similar morphological characteristics on light microscopy.
- The major challenge is that this facility is not available/ accessible in all centers in Nigeria (only about 3 centers regularly carry out this service in Nigeria).
- The importance of 'diligent microscopy' and 'precise clinical data' cannot be over-emphasised in spite of the immuno sophistication.

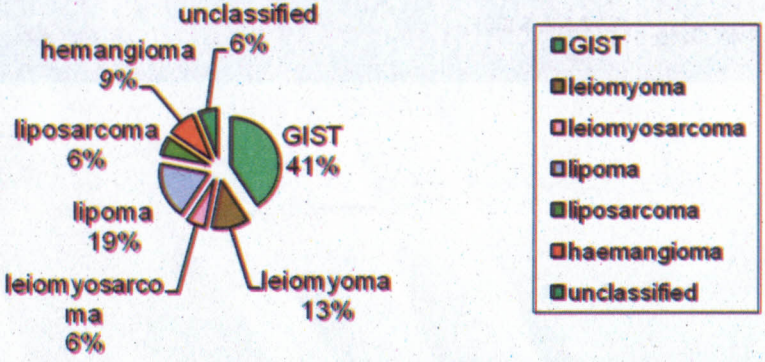


Figure 31- Immunophenotypic Categorisation of Gastrointestinal Mesenchymal Tumours in Lagos, Nigeria

Table 22: Characteristics of GISTs reported in 4 separate studies from Nigeria

	Abdulkareem et al(59)	Oludara et al(60)	Durosinmi et al (61)	Ogun et al (62)
Publication date	2009	2013	2013	2014 (In print)
Sample size	13 /32	4	27	24 /46
Mean age	46.5yrs	59-66yrs	52-median	55.1yrs
M:F	1.6:1	1:04	1.7:1	01:01.2
Commonest Site	Stomach-54% Large bowel-3 Small bowel-1	Stomach-4	Stomach-17/20	Stomach – 9 Large bowel-6
Histological type	Spindle-46% Mixed-31% Epitheliod-23%		?	Spindle-79%
SMA, S100	SMA+-3, S100+ -1			SMA+-4

Liver Diseases

Chronic liver disease 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 LUTH (Lesi et al, 2004)[63]. Due to its dual blood supply and diverse metabolic function, the liver is the most vulnerable organ in the body. Several studies from Nigeria have shown that the common forms of liver diseases are chronic hepatitis, liver cirrhosis and hepatocellular carcinoma. Abdulkareem et al (2006) recorded 39.7%, 26.4% and 17.7% for hepatocellular carcinoma, inflammatory disorders and liver cirrhosis respectively[64].

In another study, we reviewed hepatic neoplasms in Lagos and found that hepatocellular carcinoma was the commonest tumour with male to female ratio of 2.6:1 and peak age incidence in the 3rd decade of life[65]. Reports from Ile Ife and Ilorin also showed hepatocellular carcinoma to be the commonest liver diseases[66,67]. The peak age incidence for our cases which is 41-50yrs is one decade earlier than that of chronic hepatitis which suggests the existence of a continuum between these diseases. About 30% of our cases were post-cirrhotic.

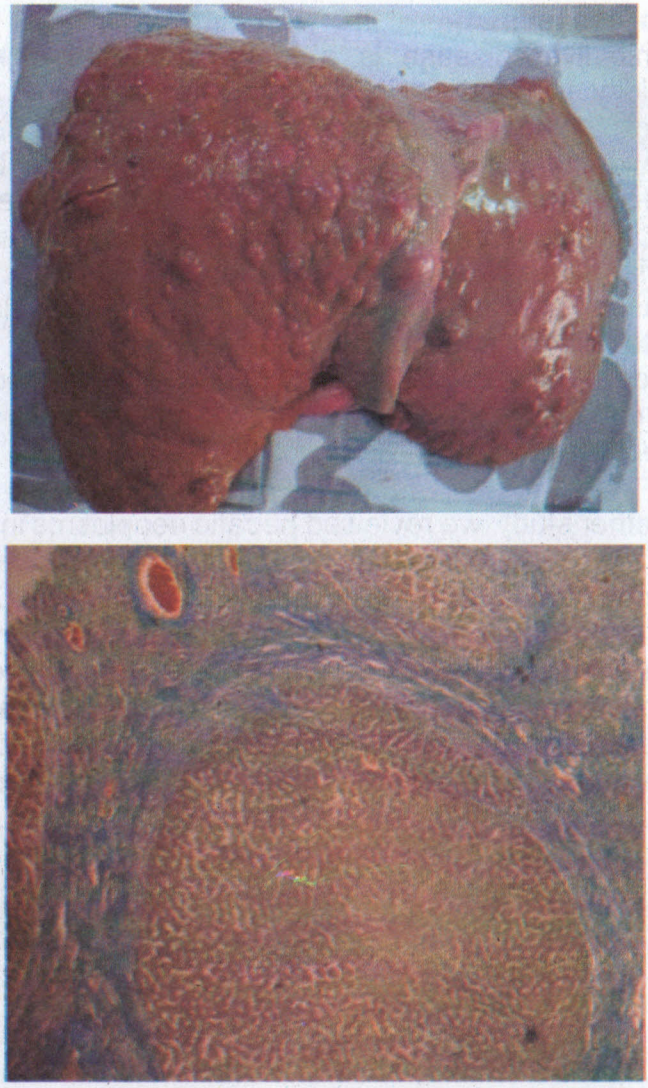


Figure 32: Photograph (gross-left, microscopy-right) of a cirrhotic liver with diffusely macro and micronodular surfaces in a 23 year old female who was diagnosed Hepatitis B infection in childhood

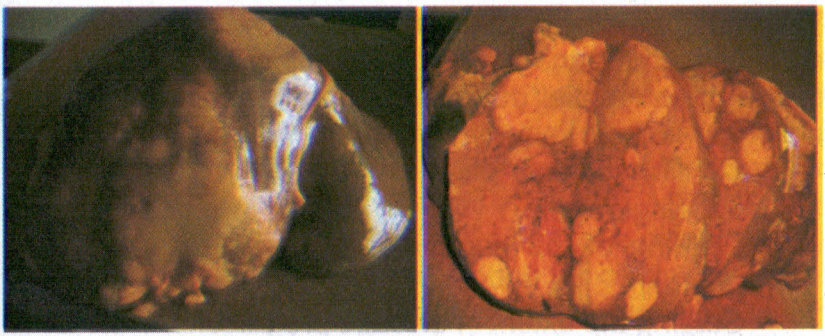


Figure 33: Gross photograph primary hepatocellular carcinoma (left) and cut surface of another liver with multiple metastatic tumour nodules, seen in a patient with colon cancer.

Of all the injuries that cause liver diseases, infective agents; particularly hepatotropic viruses account for the bulk of liver disorders in the tropics. Chronic hepatitis B and C virus infections are responsible for most cases of hepatocellular carcinoma worldwide with 57% of cirrhosis and 78% of hepatocellular carcinoma (HCC) attributable to Hepatitis B virus and Hepatitis C virus globally(Perz et al, 2006)[68].In sub-saharan Africa, hepatitis B virus is the major culprit and in Nigeria; thesero-prevalence of HBsAgis estimated to range from 10-40%(Forbi et al)[69] while Hepatitis C virus is less prevalent with figures of 4.8-5% reported in most Nigerian studies[70,71,72]. It is believed that majority of HBV infections in Nigeria is acquired in childhood by vertical transmission or personal contact with subsequent development of chronic liver disease.

The histopathology laboratory plays a pivotal role in diagnosis and management of chronic viral hepatitis and this is the essential duty of the Liver pathologist[73]. Liver biopsy is valuable in:

- Confirmation of diagnosis and to ascertain the aetiologic agent
- Grading of the necrosis and inflammatory activity present
- Staging the extent of disease progression in terms of fibrosis
- Evaluation of the effectiveness of antiviral, anti-inflammatory and or anti-fibrotic treatment
- Determine the presence or absence of premalignant changes or other co-morbidities.

Histological features of chronic viral hepatitis include: hepatocyte necrosis, mononuclear portal inflammation and portal fibrosis. The old classification of chronic hepatitis was based mainly on liver biopsy but with advancement in knowledge about the aetiologic, pathogenetic and clinicopathologic features of this syndrome, new scheme of classification involves: determination of the aetiological agents, assessment of the severity of necro-inflammatory activity (grade) and degree of fibrosis (stage). While aetiology requires the use of clinical, serological and histological parameters, the grade and stage of the disease can only be determined histologically by a liver pathologist; this I have been carrying out to the best of my ability.

Challenges of GI Pathology Practice in Nigeriaand My Contribution to Training of Specialists

A specialist gastrointestinal pathologist is defined as someone who has received at least a year of training in a section of a pathology laboratory where only tissue from

the alimentary tract and liver were examined, who has spent time in a clinical gastroenterology unit and who has restricted his or her practice to such specimens (Gent & Lash, 2008).[74] Unlike in the past, several centres in Nigeria now have endoscopic facilities resulting in increased number of GI specimens. Several diseases of the GI and liver require specialised skill for diagnosis, classification, staging and grading such as is done for chronic hepatitis and chronic gastritis among others; the precision to which this is done determines the treatment to be instituted and consequently the prognosis for the patient. Not all pathologists have this interest and the special skill. New conditions are discovered and old ones are revisited and reclassified, therefore an intimate alliance between clinicians, basic scientists, and pathologists is thus indispensable and as such every gastroenterologist deserves a GI pathologist (Gent & Lash, 2008).

There are however several challenges facing the practice of GI pathology in Nigeria[75]:

- There is general shortage of pathologists (Tables 23 and 24 below) and shortage of pathologists with interest in GI and Liver.
- There is brain drain due to poor remuneration
- Lack of specialty training in the fellowship programmes of both National and West African colleges
- Poor clinician-pathologist networking or teamwork
- Inadequate or unavailability of endoscopic facilities
- inadequate exposure of technical staff to processing of small endoscopic samples
- Inadequate specialised histochemical techniques/ tests

In Africa, there is extreme shortage of medical practitioners and pathologists in particular with rates of pathologists per million population ranging between 0.8 to 1.3 compared to 14-40 in North America and Europe.[76,77,78] In Nigeria for example, only 6% of 3056 practicing specialist physicians are pathologists. According to the data from the Medical and Dental Council of Nigeria, only 182 of 380 are practicing in Nigeria, the remaining 52% are lost to brain drain!

Table 23: Regional Analysis of number of pathologists per million populations compared with America & Europe[76-78]

Country	No of Pathologists for population	Rate per million
North America & Europe		14-40
Tanzania	15 for 38 million	0.4
Nigeria	182 for 170 million	1.1
Uganda	18 for 28 million	0.6
Sudan	51 for 40 million population	1.3

Table 24: Summary of Histopathology Laboratory Services in Nigeria

	Number of Pathologists*	Ratio/ population	No of Service centres	No of Training centres	Specialized service (immunohistochemistry)
South-West	51(30)	1/million	19	4	3
South – South	34(20)	0.9/million	7	4	1
South-East	22(12)	0.7/million	4	2	0
North-East	11(5)	0.2/million	6	2	0
North-Central	35(15)	0.7/million	11	2	1
North-West	21 (6)	0.1/million	2	0	1

(Estimated number of Anatomic pathologist in bracket)

In practice, most GI and liver samples are small sized and therefore requires careful handling in order to make any meaningful histopathology diagnosis that will be beneficial to patient management. Inadequate/improper sample fixation may result in autolysis making diagnosis difficult or impossible. Also, inadequate clinical information and lack of information on endoscopic findings make clinicopathologic correlation and interpretation difficult for the GI pathologist. The endoscopist must provide the pathologist with information about the patient, including results of the gross examination, biopsy location, relevant clinical history, bowel preparation and current medications while the pathologist must provide a reproducible and useful report that answers the clinical questions posed by the endoscopist (Lewin et al 1995). This consultation between the gastroenterologist and pathologist provides the framework for proper patient care.

Suggestions to Address the Challenges

- Subspecialty training in the fellowship programmes of pathology colleges;
- Resuscitation of one year abroad training during residency, sponsorship for short overseas fellowship, observer ship programmes, short courses and clinical/laboratory attachment;
- Improved working standard/remuneration to prevent brain drain;
- Improved infrastructure and implementation of Quality Management Systems in the laboratory.
- Training and re-training of pathologists and histoscientists on specialised techniques
- All personnel should be trained on proper specimen handling and adherence to standard operating procedures(SOPs);

- Use of telepathology either static (sharing of macro and microscopic photographs offline without interaction between operators) or dynamic can be used for expert consultation and training; and
- Improved pathologists –gastroenterologists' interaction by team work; slide seminars and clinicopathological sessions/conferences.

As an individual and as a member of the Society for Gastroenterology and Hepatology in Nigeria (SOGHIN), Association of Pathologists of Nigeria (ASSOPON) and West African Division of International Academy of Pathology (WADIAP), I have contributed to improved practice of this specialty of pathology in the following ways:

1. Training of specialists– I have taught pathology to over 3000 medical and dental students who are now practicing doctors all over the world. I have trained at least 30 specialist consultant pathologists (5 of whom are in professorial cadre) and at least quarter of the less than 10 pathologists with interest in GI in Nigeria. Many of my residents have benefited from short courses, workshops, laboratory attachments abroad.
2. I have organised several workshops to train both pathologists and laboratory scientists in this area sponsored by the British Society of Gastroenterology and UICC at different times in collaboration with foreign faculties.
3. I have served as resource person at the scientific workshops organised by SOGHIN, WADIAP and ASSOPON to train pathologists.

4. I have contributed to producing minimum dataset for reporting colorectal and gastric cancer in Nigeria and have been a strong advocate of strict compliance with optimal patient management (Obaseki et al, 2013)[79].
5. Currently in my department, we regularly use telepathology to train residents in collaboration with colleagues in the UK.
6. In the past 3 years, I have organised update courses for resident on behalf of the Faculty of pathology.
7. I have also served as chief examiner on several occasions for the Anatomic Pathology specialty at the National Postgraduate Medical College of Pathology examinations.

RECOMMENDATIONS

- The Vice Chancellor sir, because pathology is actually not a basic science, it is only a link between basic science and clinical science; I recommend that a separate faculty of **Laboratory Medicine** be created **in the College of Medicine of the University of Lagos** to 'house' all the pathology departments. This will allow for more synergy and better productivity.
- Major causes of death in Nigeria are preventable: non communicable diseases such as hypertension, diabetes mellitus, cancer and infections. I recommend regular medical check up to monitor blood pressure and blood sugar. Individuals diagnosed of these diseases should understand that treatment is for life and thus, should be encouraged to comply with treatment to prevent complications.
- Specific infections such as malaria and tuberculosis should no longer kill Nigerians in the 21st century because there are specific treatments for them. There should be improved public awareness on the symptoms so as to present for early diagnosis and prompt treatment. Also, tuberculosis should be considered by doctors in differential diagnosis of infertility and breast cancer.
- Childhood mortality should be reduced by improved antenatal care, perinatal care, good nutrition, environmental hygiene as well as immunization against childhood diseases.
- Acute appendicitis may mimic other causes of acute abdomen and especially in childhood; high index of suspicion is therefore advocated particularly in children who are more vulnerable to rupture. In addition, due to the possibility of presence of unexpected unusual pathologies in appendix, all appendices removed at surgery must be subjected to pathological assessment.

- Colorectal cancer incidence is rising and the molecular genetics differ in Nigerians. In particular is our finding of lower rate of KRAS mutation (1st of its kind in Nigeria) which predicts better response to treatment with Cetuzimab in advanced colorectal cancer cases.
- Infections, diet and environmental factors are major risks for GIT and liver cancers.
- Lifestyle modification to avoid contact with risk factors such as alcohol and tobacco, good diet low in red meat and animal fat but rich in fruits and fresh vegetables, regular physical exercise, prompt treatment of *H.pylori* infection and vaccination against and prompt appropriate treatment of Hepatitis B virus infection will reduce the risk of most GIT and liver cancers
- Most of the cancers may show be a-symptomatic at the early stage, however, change in bowel habit and dyspepsia in persons >45years should raise suspicion.
- Screening for early detection and diagnosis should therefore be encouraged such as faecal occult stool test, colonoscopy or upper GI endoscopy to detect GIT cancer, screening for hepatitis B surface antigen and liver ultrasound scan in patients with chronic liver disease for early detection of liver cancer.
- Pathology has gone beyond mere diagnosis; withadvancement in technologies, histopathology now plays essential role in management and prognostication of diseases. Particularly with personalised medicine, pathology has important role in the definition of molecular prognostic or predictive parameters used for targeted cancer therapy. The government should provide these modern facilities so that Nigerians will stop travelling abroad for medical treatment.

- Pathologists and other health professionals should be motivated and encouraged and government should be fair in dealing with these professionals so as to reduce the rate of brain drain.
- Finally, Mr. Vice Chancellor Sir, ladies and gentlemen, you will agree with me that Pathology has more to do than 'just the dead' and where he or she deals with the dead, it is the 'Living such as you and I that benefit'.
- May I then seek your permission to hereby pronounce that the public should stop calling pathologists 'doctors of the dead'.

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The Vice Chancellor and members of the University Management, I thank you for allowing me to deliver my inaugural lecture today. The VC must have forgotten that he coached me just before my professorial interview on our way from an assignment at Ede, Oyo State in 2008. His counsel that day gave me more confidence and less anxiety. May Allah reward you in abundance. My Provost, Folashade Ogunsola and the 1st female Provost in Africa; a friend and colleague, a mentor, thank you. My Dean, Prof. Olufunmilayo Adeyemi, my former Dean and brother in Islam, Prof. Sunday Omilabu; Dean dental, Prof G.T. Arotiba who is also my neighbour, Dean Clinical, Prof Afolabi Lesi, I sincerely appreciate you all. My former VC and Provost, Prof Tolu Odugbemi and Prof Olalekan Abudu, my former provost has not ceased to follow my progress, I am grateful. Prof Ogunlesi, former DVC academics, who encouraged me during the defense for CRC research grant and finally approved the grant for us.

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My esteemed audience of today, gentlemen of the Press, ladies and gentlemen, I thank you for making time out to come and listen to me and I thank you for your attention.

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REFERENCES

1. World Health Organisation. Malaria. Fact sheet N°94 Updated March 2014.http://www.who.int/mediacentre/factsheets/fs094/en/
2. Elesha, S.O., **Adepoju F.B.,** Banjo, A.A.F. Rising Incidence Of Cerebral Malaria In Lagos Metropolis-A Post Mortem Study, *East African Medical Journal 1993, 70 (5)*, 302-306.
3. Leaver, R.J., de Baetselier H, Bagshawe A, and Watters, D.A. Cerebral malaria: what is unarousable coma? Lancet. 1990 Jan 6; 335 (8680):44-5.
4. **Abdulkareem, F.B.,** Elesha, S.O., Banjo, A.A.F.: Prospective Autopsy Study of Childhood Mortality In Lagos, Nigeria (1993-1994), Nig. Qt J Hosp Med. April/June 1996, 6(2) 88-95.
5. Colditz G.A., Brewer T.F., Berkey C.S., Wilson M.E., Burdick E, Fineberg H.V., and Mosteller F. Efficacy of BCG Vaccine in the Prevention of Tuberculosis-Meta-analysis of the Published *Literature JAMA. 1994; 271(9)*:698-702.
6. **Abdulkareem F.B.,** Elesha S.O, and Banjo A.A.F: Tuberculosis Revisited-A Review Of Surgical And Autopsy Specimens. Nig. Qt J Hosp Med. April-June, 2000, 10 (2): 126-128
7. Ajuluchukwu, J.N.A., **Abdulkareem, F.B., Achusi,** I.B., Mbakwem, A.C., and Lawal, T.A. Clinical and autopsy parameters of acute medical deaths in an emergency facility in South West- Nigeria. *J Clin Sci. 2013, 10(1)*:21-26.
8. Kim Solez, M.D., Lorraine, C. Racusen, M.D., **Fatima Abdulkareem,** M.D., and EavaKemeny, M.D., Ph.D., Eava Von. Adhesion Molecules and

9 Trypkov, K., **Abdulkareem, F.B.,** Jim, K., and Solez, K: Recurrence Of Anti-GBM Antibody Disease 12 Years after Transplantation associated with de novo IgA Nephropathy, Clinical Nephrology, 1998, 49 (1): 1-5.

10 Elesha, S.O., **Abdulkareem, F.B.** Childhood Renal Neoplasms In Lagos, Nigeria –A 28 Year Review, Nig. Qt. J. Hosp. Med., 1999; 9 (1): 4-7.

11 Akinsulie, A.O., Temiye, E.O., Odelola M.A., Bode C.O, and **Abdulkareeem F.B**. Wilm'stumour-a 5year review of cases seen in LUTH. J ClinSci, 2005, 5(1):27-29.

12 **Abdulkareem, F.B.** and Awelimobor,D.I. Surgical pathology of the appendix. Nig. Med Pract, March 2009, 55(3): 32-36.

13 Marudanayagam, R., Williams, T.G., and Rees, I.B. Review of the pathological results of 2660 appendicectomy specimens. J. Gastroenterol, 2006. 41:745-749.

14 Jones, E.A., Phillips, W.A., Jarvis, R.J., and Sargen, K. The value of routine histopathological examination of appendicectomy specimens. BMC Surgery, 2007. 7:17.

15 Moore, M. Cancer Registry literature update (2006-2008). Asian Pac J Cancer Prev. 2008 Apr-Jun; 9(2):165-82.

16 **Abdulkareem, F.B.,** Faduyile, F.A., Daramola A.O., Rotimi O, Banjo A.A.F, Elesha, S.O., Anunobi, C.C., Akinde, O.R. and Abudu, E.K. Pattern of malignant gastrointestinal tumours in Lagos &Sagamu, SW, Nigeria- Histopathological review of 713 cases. *West African Med J,* May 2009 .28(.3): 173-176.

17 Edington GM, Maclean CMU. A cancer rate survey in Ibadan, Western Nigeria, 1960-63.*Brit. J Cancer.1965, 19*:471-481.

18 A Mulligan TO. The pattern of malignant disease in Ilesha Western Nigeria.British J Cancer. March 1970; 25(1):1-10.

19 Cancer in Africa: Epidemiology and Prevention Edited by Parkin D. M. *et al* IARC 2003; 87-97.

20 Williams, A.O., Edington, G.M. Malignant disease of the colon, rectum and anal canal in Ibadan, Western Nigeria. Dis. Colon Rectum, 1967, 10:301-308.

21 Okobia, M.N., Aligbe, J.U. Pattern of Malignant diseases from the University of Benin Teaching Hospital. Trop Doct., 2005, 35:91-92.

22 Abdul, A.I., Aziz, H. Al Saigh, Mohamed, M. Allam, Khalid A. Khan, and Zakaria, M. Al Hawsawi. Pattern of Cancer in Madina Al-Munawara Region. *Ann Saudi Med 1995;15(4):350-3.*

23 **Abdulkareem, F.B.,** Abudu, E.K., Awolola, N.A., Elesha, S.O., Rotimi, O., Akinde, O.R., Atoyebi, A.O., Adesanya, A.A., Daramola, A.O., Banjo, A.A.F., and Anunobi, C.C. Colorectal carcinoma in Lagos and Sagamu, Southwest Nigeria: A histopathological review. World J Gastroenterol Sept 2008; 14(42): 6531-6535.

24 Onyekwer, C.A., Ogbera, A.O., **Abdulkareem, F.B.,** and Ashindoitang, J. Colorectal Carcinoma Screening in Lagos, Nigeria, Are We Doing it Right? Gastroenterology Research, 2009; 2:38-42.

25 Irabor, D, Adedeji, O.A. Colorectal cancer in Nigeria: 40 years on, a review. *Euro J Cancer Care. 2009. 18:110*-115.

26 Rotimi, O. and **Abdulkareem, F.B.** 53 years of reporting colorectal cancer in Nigeria-a Systematic review of Nigerian literature. *Niger Postgrad Med J, 2014, 21*(1):68-73.

27 Dimou, A., Syrigos, K.N., and Saif, M.W. Disparities in colorectal cancer in African-Americans vs Whites:

27. Dimou, A., Syrigos, K.N., and Saif, M.W. Disparities in colorectal cancer in African-Americans vs Whites: before and after diagnosis. *World J Gastroenterol, 2009. 14*; 15:3734-3743.

28. Moore, P.A., Dilawari, R.A., Fidler, W.J. Adenocarcinoma of the colon and rectum in patients less than 40 years of age, American Surgeon. 1984. 50:10-14.

29. O'Keefe, S.J.D., Kidd, M., Espitalier-Noel, G.,and Owira, P. Rarity of colon cancer in Africans is associated with low animal product consumption not fibre. Am J Gastroenterol.1999; 94:1373–80.

30. O'Keefe, S.J., Chung, D., Mahmoud, N., Sepulveda, A.R., Manafe, M, and Arch J et al. Why do African Americans get more colon cancer than Native Africans? J. Nutr. 2007.137:175S-182S.

31. Ashktorab, H, Smoot, D.T., Carethers, J.M., Rahmanian, M, Kittles, R, et al. High incidence of microsatellite instability in colorectal cancer from African Americans. Clin Cancer Res. 2003.9:1112-1117.

32. **Abdulkareem, F.B.**, Rotimi, O, Elesha, S.O., Atoyebi, O.A., Adesanya, A.A., C.E. Atimomo, Oladipo, O.O., Onyekwere, C.A., Anomneze, E.E., and Ojukwu, John. Immunophenotypic Profiles of Colorectal Carcinoma in Lagos, South West Nigeria. A project report submitted to the University of Lagos central research Grant, CRC grant (537/66).

33. Duduyemi, B.M., Akang, E.E.U., Adegboyega, P.A., and Thomas, J.O. Significance of DNA Mismatch Repair Genes and Microsatellite Instability in Colorectal Carcinoma in Ibadan, Nigeria. *American Journal of Medical and Biological Research*, *1*(4), 145-148.

34. Adebamowo, C.A., Adeyi, O., Pyatt, R. Prior TW, Chadwick, R.B. et al. Case report on hereditary non-

35 **Abdulkareem, F.B.,** Rotimi, O. Immunophenotyping of Omental and Liver Metastatic Tumours in Lagos, Nigeria. *Nig. Qt J Hosp Med, 2008; 18(4):* 198-201.

36 **Abdulkareem, .FB.,** Sanni, L.A., Richman, S.D., Chambers, P., Hemmings, G., Grabsch, H., Quirke, P., Elesha, S.O., Banjo, A.F., Atoyebi, O.A., Adesanya, A.A., Onyekwere, C.A., Ojukwu, J, Anomneze, E.E.,and Rotimi, O. KRAS and BRAF Mutations in Nigerian Colorectal Cancers.West *Afr J Med. 2012 Jul-Aug;31(3)*:198-203.

37 Richman, S.D., Hutchins, G.A., Seymour, M.T., and Quirke, P. What can the molecular pathologist offer for optimal decision making? Ann Oncol 2010; 21(Supplement 7): vii123–vii129.

38 Saridaki, Z, Georgoulias, V, Souglaskos, J. Mechanisms of resistance to anti-EGFR monoclonal antibody treatment in metastatic colorectal cancer. *World J Gastroenterol 2010.16*: 1177-1187.

39 Brink, M, de Goeij, A.F., Weijenberg, M.P., Roemen, G.M., Lentjes, M.H., and Pachen, M.M, et al. K-ras oncogene mutations in sporadic colorectal cancer in The Netherlands Cohort Study. Carcinogenesis 2003. 24:703-710.

40 Karapetis, C.S., Khambata-Ford, S, Jonker DJ, O'Callaghan C.J., Tu D, Tebbutt, N.C, et al. K-ras Mutations and Benefit from Cetuximab in Advanced Colorectal Cancer. *New Engl J Med 2008.359*:1757-1765.

41 Richman, S.D., Seymour, M.T., Chambers, P, Elliott, F, Daly CL, Meade, A.M, et al. KRAS and BRAF Mutations in Advanced Colorectal Cancer are associated with poor prognosis but do not preclude benefit from Oxaliplatin or Irinotecan: Results from the MRC FOCUS Trial. *J ClinOncol 2009.27*:5931-5937.

42 Kumar, K, Brim, H, Giardiello, F, Smoot, D.T, Nouraie, M, Lee EL, et al. Distinct *BRAF* (V600E) and *KRAS* mutations in high microsatellite instability sporadic colorectal cancer in African Americans. Clin Cancer Res 2009.15:1155-61.

43 Tol J, Dijkstra, J.R., Klomp, M, Teerenstra, S, Dommerholt, M, Vink-BörgerME, et al. Markers for EGFR pathway activation as predictor of outcome in metastatic colorectal cancer patients treated with or without cetuximab. *Eur J Cancer 2010.46*:1997-2009.

44 Zlobec, I, Bihl, M.P., Schwarb, H, Terracciano, L, LugliA. Clinicopathological and protein characterisation of BRAF- and K-RAS-mutated colorectal cancer and implications for prognosis. *Int J Cancer 2010.127*:367-80.

45 Parkin, D.M., Bray, F.I., Devesa, S.S. Cancer burden in the year 2000- the global picture. *Eur J Cancer 2001.S4*-S66.

46 IARC monographs on evaluation of carcinogenic risks to humans. Schistosomiasis, liver flukes and H.pylori.Lyon, IARC 1994; 61:177-241.

47 Gastric Cancer incidence and mortality in Nigeria http://globocan.iarc.fr/factsheet.asp accessed 27th July 2012.

48 **Abdulkareem, F.B.,** Onyekwere, C.C., Awolola, N.A., Ajekigbe, A.T. Clinicopathological study of malignant gastric tumours in Lagos. Nigerian Quarterly Journal of Hospital Medicine, 2010; 20(2): 49-54.

49 Mandong, B.M., Manasseh, A.N., Tanko, M.N., et al. Epidemiology of gastric cancer in Jos University Teaching Hospital Jos a 20 year review of cases. *Niger J Med. 2010* Oct-Dec; 19(4):451-4.

50 Okobia, M.N., Aligbe, J.U. Pattern of malignant diseases at the University of Benin Teaching Hospital. Trop. Doct. Apr 2005 35(2): 91-92.

51 Oluwasola, A.O., and Ogunbiyi, J.O. H.pylori-associated gastritis and gastric cancer in Nigeria. India J Gastroenterol 2003 Nov-Dec; 22(6):212-4.

52 Hameed, L, Onyekwere, C.A., Otegbayo, J.A., **Abdulkareem, F.B**. A clinicopathological study of dyspeptic subjects in Lagos, Nigeria. Gastroenterology Insights.2012, 4: e11, 39-42.

53 Smith, S.I., Lesi, O.A., Odeigah, P, **Abdulkareem, F.B.**, Onyekwere, C.A., Agomo, C.A., Contreras M. Application of stool-PCR for the diagnosis of Helicobacter pylori from stool in Nigeria; a pilot study. Springer Plus, 2012, 1:78.

54 Smith, S.I., Kirsch, C, Oyedeji, K.S., Arigbabu, A.O., Coker, A.O., Bayerdöffer, E, Miehlke, S. Prevalence of Helicobacter pylori vacA, cagA and iceA genotypes in Nigerian patients with duodenal ulcer disease. *J Med Microbiol, 2002 Oct*; 51(10):851-4.

55 Ute Breithaupt, MuinahFowora, AbiodunSeriki, Eva Loell, Susanna Mueller, Margaret Ugo-Ijeh, Charles Onyekwere, Olufunmilayo Lesi, Jesse Otegbayo, Adegboyega Akere, Dennis Ndububa, Olusegun Adekanle, Ebere Anomneze, **Fatimah Abdulkareem,** Isaac Adeleye, Alexander Crispin, Wolfgang Fischer, Stella Smith, and Rainer Haas. "Helicobacter pylori infection in Nigeria is associated with low prevalence, divergent antibiotic resistance patterns, and mild pathology" submitted to JCM November 2014.

56 Ebell, M.H., Warbasse, L, Brenner, C. Evaluation of the dyspeptic patient: a cost-utility study. *J FamPract 1997. 44*:545-555.

57 Sugar, I, Forgacs, B, Istvan, G, et al: Gastrointestinal stromal tumours (GIST). Hepatogastroenterology 2005 Mar-Apr; 52(62): 409-13.

58 Lam, M.M., Corless, C.L., Goldblum, J.R., Heinrich, M.C., Downs-Kelly, E, Rubin, B.P. Extra-intestinal Stromal Tumours presenting as vulvovaginal/rectovaginal septal masses: a diagnostic pitfall. *Int J GynaecPathol, 2006 Jul; 25*(3): 288-292.

59 **Abdulkareem, F.B.,** Rotimi, O, Elesha, S.O., Banjo, A.A.F. Immunophenotyping of Gastrointestinal Mesenchymal Tumour in Lagos. *West Afr J Med. 2009 Nov-Dec; 28*(6):358-62.

60 Oludara, M.A., Onyekwere, C.A., Ibrahim, N.A., Popoola, A., Omodele, *F.O* .Gastrointestinal stromal tumours: a review of cases seen at a university hospital over an eight year period. Nig. *J. of GastroenterolHepatol 2013, Vol 5*, No 1

61 Durosinmi, M.A., Salawu, L, Lawal, O.O., Ojo, O.S, Alatishe, I.O. et al. Imatinib (Glivec) and gastrointestinal stromal tumours in Nigerians. *Afr. J.Med.med. Sci. 2013: 42*

62 Ogun, G.O. Mesenchymal tumours of the GIT: the importance and use of immunohistochemistry in characterizing specific tumour entities. Tropical Gastroenterol 2014(in print).

63 Lesi, O. A, Kehinde, M.O., Anomneze, E.E. Chronic Liver diseases in Lagos: aclinicopathological study. *Nig Postgrad Med J 2004; 11(*2):91-96.

64 **Abdulkareem, F.B.,** Banjo, A.A.F, Elesha, S.O., Daramola, A.O. Histopathological Study of liver diseases at the LUTH, Nigeria (1989-2000).*Nig Postgrad Med J, March 2006, 12*(1), 41-46.

65 **Abdulkareem F.B.**, Banjo, A.A.F., Elesha, S.O. Hepatic Neoplasms in Lagos, a 10year

Histopathologic Review of Surgical Biopsies. Nig. Postgrad, Med J. Sept. 1999 6 (3): 126-129.

66 Ojo, O.S., Olude, I.O., Odesanmi, W.O. The pathological basis of chronic liver diseases in a tropical population; a biopsy study. *Orient J. Med, 1990, 2*(4):190-193.

67 Adeniji, K.A., Anjorin, A.S. The pattern of malignant tumours of the liver in a tertiary health institution in Nigeria. *Afr J Med Med Sci. 2004 Mar; 33*(1):27-30.

68 Perz, J.F., Armstrong, G.L., Farrington, L.A., Hutin, Y.J.F., Bell, B.P. The contributions of hepatitis B virus and hepatitis C virus infections to cirrhosis and primary liver cancer worldwide Bottom of Form. J Hepatol, 2006; 45(4):529-538.

69 Forbi, J.C., Vaughan, G, Purdy, M.A., Campo, D.S., Xia GI et al. Epidermic history and evolutionary dynamics of Hepatitis B virus infection in two remote communities in rural Nigeria. PLoS ONE 5(7):e11615. Doi:10.1371/journal.pone.0011615.

70 Ojo, O.S., Thursz, M, Thomas, H.C., Ndububa, D.A., Adeodu, O.O., Rotimi, O. et al. Hepatitis B virus markers, hepatitis D virus antigens and hepatitis C virus antibodies in Nigerian patients with chronic liver disease. *East Afr. Med J. 1995 72*(11):719-721.

71 Jeremiah, Z.A., Koate, B, Buseri, F, Emelike, F. Prevalence of antibodies to hepatitis C virus in apparently healthy Port Harcourt blood donors and association with blood groups and other risk indicators. Blood Transfusion 2008; 6:150-155.

72 Kawo, A.H., Bala, J.A., Dabai, Y.U. Seroprevalence study of hepatitis C virus infection among blood donors attending selected blood banks in some attending selected blood banks in some local government areas in Kano Nigeria. Journal of Public Health and Epidemiology 2012, 4(6):178-183.

73 Omolade Adegoke, Fred John Obiajulu, **Fatimah Abdulkareem,** Olusegun Ojo. The Clinical Laboratory and the Diagnosis and Management of Chronic Viral Hepatitis. Annals of Tropical pathology, 2012, 3(2):85-91.

74 Genta, R.M., Lash, R.H. Every gastroenterologist deserves a gastrointestinal pathologist. Dig Liver Dis. 2008 Aug; 40(8):627-31.

75 Fred John Obiajulu, Omolade Adegoke, **Fatimah Abdulkareem,** Olusegun Ojo. The Challenges facing laboratory diagnosis of Chronic Viral hepatitis in Nigeria. *Nigerian Journal of Gastroenterology and Hepatology Vol. 4 No.* 1 June, 2012 5-8.

76 Awadelkarim, K.D., Muhammedani, A.A., Barberis, M. Role of pathology in sub-Saharan Africa: An example from Sudan. Pathology & laboratory Med International, 2010; 2: 49-57.

77 Peter, F. Rambau. Pathology Practice in a Resource-Poor Setting: Mwanza, Tanzania. Archives of Pathology & Laboratory Medicine: February 2011, Vol. 135, No. 2, pp. 191-193.

78 Benediktsson, H, Whitelaw, J, Roy, I. Pathology services in developing countries-A challenge. Arch Pathol Lab Med, 2007, 131:1636-1639.

79 Obaseki, D.E., **Fatimah Abdulkareem**, O Rotimi, J.O. Ogunbiyi, S.O Oluwasola, O.S Ojo, B.M Duduyemi, U.O Igbokwe. Minimum pathology reporting standard for gastro-intestinal cancers in Nigeria: A draft proposal. *Nig. J GastroenterolHepatology. 2013, 5*(1): 21-28

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