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SURGICAL DIATHERMY: MECHANISMS, USES, RISKS AND RISK REDUCTION

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Abstract

Surgical diathermy is an electrosurgical device that enables precise dissection with minimal bleeding. It uses high-frequency alternating electrical current to cut, coagulate, and vaporize tissue. It reduces surgery time and reduces possibility of blood transfusion. Risks involved in the use of surgical diathermy include burns, nerve injury, infection, post-operative pain and inhalation of hazardous surgical smoke containing cells, viruses and potentially carcinogenic chemicals. Surgical diathermy also causes electromagnetic interference with implantable cardiac devices such as with pacemakers and defibrillators. It is important to take all measures to minimize risks to the patient, the surgical team and other theatre staff. This review discusses the basic mechanisms of diathermy function, its uses, risks and basic measures to minimize complications.

Keywords: Diathermy, electrosurgery, uses, mechanisms, risks

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Introduction

Electrosurgical devices have revolutionized surgery in recent times. Surgical diathermy enables precise tissue dissection with minimal bleeding. It reduces surgery time, blood loss and the consequences, and reduces possibility of blood transfusion. It uses high-frequency alternating electrical current to cut, coagulate, and vaporize tissue, enabling precise dissection with minimal bleeding by generating localized heat that destroys cells.¹ Current passes through the body, often via an active electrode, creating high current density at the diathermy tip to heat the tissue. Cutting occurs by vaporization at $\sim 100^{\circ}\text{C}$ and coagulation by dehydration at $60\text{--}99^{\circ}\text{C}$.² The passage of current through the body is via electrolytic solutions in the tissues and bloodstream. The source voltage is created by the diathermy generator which converts mains 50 Hz current into a high-frequency current of 0.2–3 MHz. At these radiofrequencies there is minimal risk of muscle or nerve stimulation. Instead, electrical energy is converted to heat as the electrons overcome the impedance of the body.^{2,3} Risks involved in the use of surgical diathermy include burns, tissue damage, infection, post-operative pain and inhalation of hazardous surgical smoke (fume). Diathermy fume is a recognized occupational hazard, exposing surgery staff to smoke equivalent to about 27 to 30 cigarettes per day.



Consequences of inhaling this smoke include acute and chronic inflammatory lung conditions, exposure to pathogens such as Viruses and bacteria.^{4,5,6}

Types of Diathermy

i) Monopolar: In this mode, current flows from the diathermy device through the active electrode called the diathermy pencil tip (which has the highest current density and is where heating occurs), through the body (serving as the electrolyte), and back to the diathermy device via a dispersive electrode (the return pad). Monopolar diathermy is used more frequently due to its greater versatility. The *cutting effect* in diathermy uses a pure continuous sine wave of low-voltage, high-frequency alternating current to create high temperatures ($>100^{\circ}\text{C}$) at the electrode tip causing rapid intracellular fluid vaporization and clean cutting. *Coagulation mode* uses high-voltage, low-frequency pulsed waveforms (wave with a short ‘on’ time and a longer ‘off’ time) to achieve haemostasis by desiccating or charring tissue, rather than cutting it. It causes protein denaturation at $60\text{--}100^{\circ}\text{C}$ via contact (desiccation) or non-contact (fulguration) methods, providing deep, controlled coagulation of bleeding vessels.³

ii) Bipolar: Current flows between two closely placed active and return electrodes. A bipolar handle has a pair of forceps where one blade acts as the active electrode and the other as the return, obviating the need for a distally placed return electrode/pad. It causes less tissue destruction. Conventional bipolar diathermy only coagulates but when combined with ultrasonic energy devices it can also achieve tissue cutting.

Key Surgical Uses

i) Cutting/Dissection: Creating precise cuts in a tissue with minimal bleeding.

ii) Coagulation: Achieving haemostasis by coagulating blood vessels. Conventional diathermy is generally effective for sealing vessel smaller vessels, typically up to 2–3 mm in diameter while advanced vessel

sealing systems of combined bipolar diathermy and ultrasonic devices can seal vessels up to 7 mm in diameter.

iii) Fulguration/Desiccation: Shrinking or destroying tissue achieved by keeping the probe in contact with the tissue while applying heat insufficient for cutting. This dries out the tissue and a coagulum is formed.^{2,3}

Useful definition of terms

Lateral thermal spread: It is the unintended heat transfer to tissues adjacent to the target site; the risks increase with higher power usage, longer application time, and depends on instrument type. In electrosurgery, Monopolar diathermy causes the highest heat spread (>20mm), compared to bipolar diathermy, Harmonic scalpel (approx. 2.9mm) and LigaSure (<1mm).^{7,8}

Capacitive coupling: Accumulation of current (heat) on a metallic instrument high enough to cause burn at the site of patient contact. The metal causing the burn injury is not the primary source of heat. The heat at this secondary conductor accumulates due to current flowing through electrostatic field created between the two conductors (the diathermy tip i.e. the active electrode and a nearby conductor such as a trochar in laparoscopic surgery). Capacitive coupling can occur despite intact insulation of secondary conductor when the insulating capacity is exceeded.

Conductive coupling (Direct Coupling): Accumulation of current (heat) when an energized electrode directly (often accidentally) touches another metal instrument, transferring high-frequency current and causing unintended, often unseen, thermal injuries to tissues. It is a major risk in monopolar electrosurgery, preventable by visualizing the tip and avoiding contact with other metal objects. In addition, when an active electrode is too close to (but not touching) another metal object in direct contact with the patient, current may jump from the diathermized

tissue into the metal conductor, resulting in high heat in an unintended tissue or organs in contact with the secondary instrument. Proper spacing and insulation of instruments prevents this complication.

Active Electrode Monitoring (AEM) is a safety technology in monopolar laparoscopic diathermy that prevents stray energy injuries caused by insulation failure and capacitive coupling. It uses a shielded instrument to detect breaches and automatically shuts down the generator, enhancing patient safety during minimally invasive surgery.^{9,10,11}

Risks Considerations in Surgical Diathermy use

1) Risks to patients

Thermal injury: Risks of surgical diathermy in patients undergoing surgical procedures include *burns* due to unintended contact of the activated diathermy pencil tip to skin. Full thickness injury to the skin *called button hole skin injury* occurs when dissection is carried too close to, and perforating the skin. Thermal injury to nerves may occur when an activated pencil tip nears a normal or an anomalous nerve. Pedal-controlled diathermy machines are prone to inadvertent device activation and thermal injuries. Thermal injuries may also result from direct (conductive) coupling, capacitive coupling or lateral thermal spread (see section above). Thermal injury due to ignited local fires may occur when dissecting tissues with flammable agents such as mannitol (as used for pre-operative bowel preparation). Diathermy use on body areas still wet with alcohol-based skin preparations such as methylated spirit (ethanol) carries high risk of burns, fires, and operating room mishaps. Alcohol-based antiseptics are highly flammable, and when combined with the heat produced by electrocautery, can easily ignite, leading to severe, often full-thickness burns.¹² In laparoscopic surgery, intraperitoneal diathermy smoke may reduce visibility and increase operating time.

Return electrode burn (also called grounding pad burn) occurs when there is ineffective contact between the return diathermy pad and the skin. Bony prominences and excessively hairy or scalded skin increase the possibility of burns at the conductive pad site as the concentration of current occurs at a point of least resistance. Lack of good contact creates a high-impedance, low-resistance, or unevenly distributed contact area, causing the electric current to concentrate on a small area of skin, resulting in heat buildup and subsequent thermal injury. Patients with poor vascular supply as diabetics, smokers and those with peripheral vascular disease are susceptible to tissue burns even with standard pad placement, primarily due to impaired tissue perfusion, which reduces the body's ability to dissipate heat, leading to tissue damage.^{3, 13, 14}

Another complication of diathermy use include post-operative *wound infection* due to melting of diathermized fat tissue (a good medium for bacterial proliferation).

Wrong connections and insulation breaches may cause electrocution to patients and staff.

Diathermy can interfere with both electrocardiography (ECG) and electroencephalography (EEG) monitoring probes placed during surgery through *Electromagnetic interference (EMI)*. Of greater consequence is the interference with cardiac pacemakers and implantable defibrillators. Interference is more likely if a monopolar diathermy tip is used in the path of electric flow of such devices. The effects are unpredictable and include inappropriate pacing, damage to the device, inappropriate defibrillation, and myocardial heat damage. Bipolar diathermy is safer than monopolar in this regard, but can still cause electromagnetic interference. Modern pacemakers have a titanium shell and interference monitor to protect them.^{3, 13}

2) Risk to operating team

Surgical diathermy poses significant risks to the surgeon, his assistants, the peri-operative

nursing staff/surgical technician, anesthesia staff and other theater team members in the form of *electric shocks, burn and fires*.¹⁴ Diathermy *fume* or *surgical smoke* may contain hazardous, toxic, and, infectious agents and in some cases, mutagenic or carcinogenic compounds in the form of cells, viruses, and chemicals.¹⁵ Diathermy smoke consists of approximately 95% water vapor (steam) and 5% cellular debris/solid particles. This 5% *solid portion* contains over 150 known chemical and biological compounds. Chemical compounds in diathermy smoke include acetaldehyde, acrylonitrile, acrolein, benzene, cyclohexanone, furfural, formaldehyde, polyaromatic hydrocarbons, styrene, toluene and xylene which have been classified as carcinogens by the International Agency for Research on Cancer (IARC).^{16, 17} The biological components of surgical diathermy smoke are cellular debris including cancer cells and infectious viable materials such Human Papillomavirus (HPV) and Human Coronavirus (SARS-CoV-2). In addition, fragments of human immunodeficiency virus (HIV) and hepatitis B virus (HBV) were isolated in the inner lumen of smoke evacuation tubing following diathermy use. Bacteria isolated from surgical smoke include *Serratiamarcescens*, *Escherichia coli*, and others.^{18, 19, 20, 21}

3) Risks to other theatre staff

In addition to inhalation of diathermy smoke other operating room (OR) staff may be exposed to *electrocution* and *operating room fires* resulting from inadequate fuse fixation, improper earthing (grounding) and failure of insulation.^{2, 21}

Preventive Measures and Risk reduction strategies

(I) Diathermy Set up, Patient connection and settings

Proper connection to electrical source and avoidance of exposed wires (insulation defects) prevents electrocution and fires from

sparkling exposed wires. Energy settings on the machine should be at the minimum effective level. Risk of burn injury at the site of return pad is minimized by ensuring proper skin contact. The pad should be applied to a flat, muscular area.^{2, 20} The site, often behind the gluteal area, thigh or the calf, should not be excessively hairy, harboring large scars, bony prominences or be excessively wet. In men (especially the elderly), it should be ensured that the scrotum is not resting on a return pad to avoid burn injury.

Pad-related complication in obese patients is minimized by using larger pads or dual-dispersive return pads. Newer diathermy units have Return Electrode Monitoring (REM) for real-time assessment of the quality of contact between the return pad and the patient. Consultation with a cardiologist should be made before using diathermy on patients with implanted cardiac devices and where possible, bipolar diathermy should be used. If a monopolar diathermy is to be used, current flow near or across the cardiac implant should be avoided.²

(II) Operative use and techniques

Accidental skin burns including ‘button hole’ injury is prevented by minimizing energy delivery and careful dissection. Activation of the tip of the electrode should be done only when it is in contact with the intended tissues. Accidental activation in cases of foot-activated pedals should be avoided. In laparoscopic diathermy use, trochairs with plastic insulation prevent thermal injury to the abdominal wall.

Where available, an Active Electrode Monitoring (AEM) device should be connected to a diathermy machine. As a safety measure, when an AEM device detects stray currents it activates an auto shut-off action on the diathermy machine. Diathermy use should be avoided in body areas that are wet with alcohol-based preps. Intestinal luminal entry with diathermy should be

avoided where mannitol is used for pre-operative bowel preparation to avoid sparks and thermal injuries.^{2, 12}

(III) General safety protocols

General measures: Crucial steps in improving patient outcomes include implementation of proper safety protocols, updating the equipment, and training surgeons and other OR staff about the equipment, the nature and possibility of complications, and prevention. Diathermy cables, handpicks and insulations should be inspected periodically. Diathermy-related injuries and near-miss events should be investigated and documented.²

Smoke barriers and protective equipment. It is important to note that face shields and basic surgical masks provide only limited protection through avoidance of direct smoke inhalation. It is advisable to wear N95 masks or masks with layers of activated carbon particularly during lengthy procedures involving diathermy use.^{22, 23}

Smoke extractors: These are designed to remove diathermy smoke during electrosurgery. They are essential but often underutilized. They include the usual separate suction tube or the specialized diathermy pencil-attached suction system (also called suction-integrated pencils, Figure 1). Examples include SuperVac and PlumeSafe® - X5™.^{4, 22}

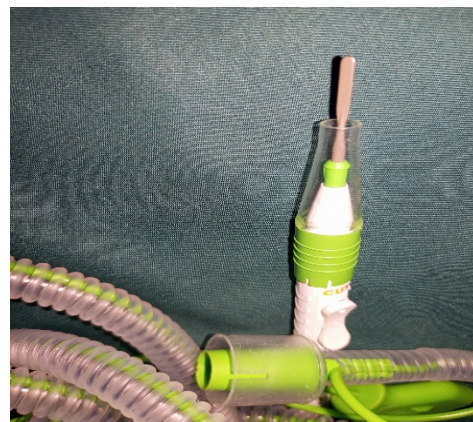


Figure 1. Diathermy pencil-attached suction system.

Smoke Evacuation: These are the wall-mounted filtration units and local exhaust ventilation (LEV) systems which reduce toxic exposure to personnel (Figure 2).



Figure 2. Wall-mounted ventilation system.

Advances in the electrosurgery equipment such as adaptive tissue feedback systems, advanced bipolar devices, Return Electrode Monitoring (REM), Active Electrode Monitoring (AEM), and impedance monitoring have provided additional safety features, contributing to patient safety. Integration of these systems into laparoscopic and robotic gadgets has improved safety and precision of surgery.²⁵

Many recent innovations utilize other energy modalities with electro-surgical principles. These include ultrasonic scalpel/dissectors (e.g., Harmonic scalpel, THUNDERBEAT® and SonoSurg), advanced bipolar electrosurgery systems (e.g., LigaSure™ and EnSeal™), laser energy systems (e.g., argon laser and CO₂ laser), Radio-frequency energy systems (e.g., StarBurst® and Cardioblate®) and argon-enhanced coagulation and vessel sealing systems.²⁶ With these innovations, more precision is achieved and thermal spread is reduced.

Artificial intelligence (AI) is revolutionizing electrosurgery by enabling real-time, adaptive energy delivery that improves precision, safety, and efficiency during surgical procedures. AI-powered, voice-controlled, robotic-integrated technologies are becoming commonplace in contemporary operating rooms. Smart

Electrosurgical Units (ESUs) uses machine learning (ML) to measure tissue impedance thereby minimizing heat damage and optimizing coagulation.²⁷

Conclusion

Surgical diathermy has changed surgical practice by enabling effective haemostasis and precise tissue dissection, resulting in shorter operating times and less bleeding. However, it also has its inherent risks and complications to patients and OR staff. Surgeons and operation room staff should be aware of the functioning of the device and strictly follow the safety guidelines to reduce its complications and ensure patient and theatre staff safety.

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PATTERN AND OUTCOME OF ADMISSIONS OF PATIENTS WITH DIABETES MELLITUS INTO RASHEED SHEKONI TEACHING HOSPITAL DUTSE, JIGAWA STATE

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Abstract

Background: Diabetes mellitus affected 537 million people worldwide in 2021, with projection indicating an increase to 643 million by 2030, and 783 million by 2045. It is estimated that over 6.7 million people aged 20–79 have died from diabetes-related causes in 2021. Despite this, data on this subject matter, remain limited in our center. **Objectives:** we determined the pattern and outcome of admissions of patients with diabetes into the medical wards of Rasheed Shekoni Teaching Hospital, Dutse, Nigeria, over a two-year period. **Methods:** a descriptive cross-sectional retrospective review of secondary data obtained from the patients' records in the records department of the hospital. The study population included all patients with diabetes mellitus who were admitted into the medical wards of this hospital within the period under review. Information on demographic, reason for admission, baseline clinical, and biochemical indices were cleaned and analysed. **Results:** one hundred and sixty-seven patients (5.9%) with diabetes mellitus were admitted over the period under review. The mean age of the patients was 51.82±17.67. Type 2 DM contributed 80.2% of the DM admission. Fifty-eight Patients (34.7%) presented with diabetic emergencies; among which Hyperosmolar Hyperglycemic State, Diabetic Ketoacidosis and hypoglycemia contributed 18.6%, 11.4% and 4.8% respectively. The overall outcome was good, with 94% discharged and 5.4% mortality. Hypertension was the predominant comorbidity identified among the patients (22.2%). **Conclusion/Recommendation** Hyperosmolar hyperglycemic state was the most common cause of mortality among admitted DM patients in Dutse. Infection is most common reason for admission of patients with DM. There is need for adequate health education to the people as well as provision of adequate health facilities for management of diabetes and diabetes related complications.

Key words: outcome, Prevalence, Type1DM, Type2DM, Dutse.

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Introduction

Diabetes mellitus affected 537 million people worldwide in 2021, and this number is projected to reach 643 million by 2030, and 783 million by 2045. In addition, 541 million people are estimated to have impaired glucose tolerance in 2021. It is also estimated that over 6.7 million people aged 20–79 have died from diabetes-related causes in 2021. More than 122.5 million are not aware of their condition¹.

Diabetes mellitus is a metabolic disorder of multiple etiology characterized by chronic hyperglycemia with disturbance of carbohydrate, fat and protein metabolism resulting from defect in insulin secretion, insulin action, or both. The effect of diabetes includes long term damage, dysfunction and failure of various organs.²

The world health organization recently classified diabetes mellitus into six main groups namely type 1 diabetes, type 2 diabetes, Hybrid forms of diabetes, unclassified diabetes, other specific types of diabetes and hyperglycemia first detected in pregnancy.³ Type 2 diabetes (previously referred to as Adult –onset or non-insulin dependent diabetes) is the most prevalent form of diabetes. It is a heterogeneous disorder most commonly associated with insulin resistance in the presence of impairment in compensatory insulin secretion.⁴

In Nigeria, the most populous country in Africa, the prevalence of T2DM is still increasing, with the country widely reported as having Africa's highest burden of diabetes.⁵ The prevalence of diabetes in Nigeria, based on the 1997 national expert committee report on non-communicable disease (NCD) was 2.2% with male: female ratio of 1.1:1.⁶ A recent systematic review and meta-analysis in 2018 by Uloko A.E et.al⁷ showed the national pooled prevalence of diabetes to be 5.77%. The pooled prevalence of diabetes in the six geopolitical zones of Nigeria was 3.0% North-West, 5.9%, North -

East, 3.8% North-Central zone, 5.5% in the South-West, 4.6% in South-East, and 9.8% in the South-South zone.⁷ In 2011, the International Diabetes Federation (IDF) estimated the prevalence of DM among Nigerian adults at 4.04%.⁸ In 2021 IDF estimated approximately 537 million adults (20-79 years) were living with diabetes; by 2045 this would rise to 783 million.¹

The American Diabetes Association (ADA) in 2010 came up with additional criteria based on HbA1c; $HbA1c \geq 6.5\%$ according to the ADA confirmed a diagnosis of type 2 diabetes mellitus. Values of $HbA1c < 6.5\%$ does not exclude the diagnosis of diabetes from other glucose tests. The WHO in 2011 adopted these criteria as proposed by ADA.⁸ The present study may serve as baseline for the pattern/spectrum of patients with diabetes mellitus admitted into RSFUTH Dutse. The findings would guide stakeholders in tackling the disease as well as preventing associated complications.

Methods

Ethics – ethical clearance with approval number RSFUTH/GEN/226/V.II dated 25th June, 2024, was obtained from the research ethics committee of RSFUTH Dutse, before commencement of the study. All the provisions of HELSINKI declaration were respected throughout this study.

Study design and population

A descriptive retrospective review of secondary data obtained from the patients' records in the records department of the hospital. The study population included patient with diabetes mellitus who were admitted into the medical wards of the Rasheed Shekoni Federal University Teaching Hospital, Dutse and have met the inclusion criteria for the study.

Study period: The review of secondary data obtainable from the records of patients admitted into the medical wards of RSFUTH, who met the inclusion criteria; from December 2022 to November 2024.

Study area

The study was conducted in Dutse, Nigeria. The site of the study was Rasheed Shekoni Federal University Teaching Hospital (RSFUTH). The hospital is a secondary facility that was established in 2009 by the Jigawa state government which was handed over to the federal government in 2022 for teaching and training.

The Hospital serves the people of Jigawa state and as a referral Centre for some local government from neighboring States like Bauchi and Kano States. The Hospital has four major clinical departments supported by well-equipped laboratories (Chemical pathology, Haematology, Microbiology and histopathology).

Sample size determination and sampling technique: The minimum sample size was determined using convenient sampling of all those who met the inclusion criteria.

Inclusion/Exclusion Criteria

The criteria for inclusion in the study was Known patients with diabetes or newly diagnosed with diabetes aged 18 years and above on admission in the medical wards of RSFUTH within the period under review.

Data collection- A pro forma was developed to extract information from the folders of the patients admitted in the medical wards of RSFUTH, Dutse. Diagnosis based on history, physical examination, and investigations done, as well as outcome of admissions were collated, documented, and analyzed.

Data analysis - The data generated were collated, checked, and analyzed using a computer based statistical programme for social sciences (SPSS) version 20.0 [SPSS

Inc]. Descriptive statistics such as frequencies and percentages were presented in the form of tables to summarize categorical variables. Chi square test was utilized to compare proportions. A confidence interval of 95% was used, and a p-value of ≤ 0.05 was considered significant.

Results – the total number of admissions into the medical wards over the period under review (December 2022 to November 2024) was 2826. Out of this, there were one hundred and sixty seven (5.9%) diagnosed with diabetes mellitus. The mean age of the patients was 51.82 ± 17.67 . More than half of the patients were females contributing 51.5%. Type 2 DM contributed 80.2% of the DM admission as shown in table 1. Sixty six (39.1%) of the patients were either diagnosed with DM < 5 years or were newly diagnosed. Fifty eight patients (34.7%) presented with diabetic emergencies; among which Hyperosmolar Hyperglycemic State, Diabetic Ketoacidosis and hypoglycemia contributed 18.6%, 11.4% and 4.8% respectively. The prevalence of diabetes mellitus among the admitted patients into the medical wards was 5.9%. Sepsis was the most common precipitant among all the patients, taking 35.3% of the admission as shown in table 2. The overall outcome was good with 94% discharged and 5.4% mortality as shown in table 3. Majority of the patients had no background comorbidities (74.5%). Hypertension was the predominant comorbidity identified among the patients (22.2%). Mortality is higher among those with short hospital stay, contributed 5 out of the 9 mortalities with p- value of 0.037 and strong correlation with coefficient of 4.87 and p –value of 0.027 as shown in table 4.

Table 1: socio- demographic characteristics of the participants

Age Group (Years)	Frequency (N)	Percentage (%)
18 – 44	48	28.7
45 – 64	80	47.9
65 and above	39	23.4
Gender Distribution		
Female	86	51.5
Male	81	48.5
Total	167	100
DM class		
Type 1 DM	33	19.8
Type 2 DM	154	80.2

Table 2 clinical characteristics of the participants

Hospital stay (days)	Frequency (N)	Percentage (%)	
1 – 4	37	22.2	
5 – 10	88	52.7	
>10	42	25.1	
Duration of DM (years)			
<5	66	39.6	
5 – 10	48	28.7	
>10	53	31.7	
Total	167	100	
Diabetic emergency			
	Frequency (N)	Percent age (%)	% among diabetic emergencies
DKA	19	11.4	32.8
HHS	31	18.6	53.4
Hypoglycemia	8	4.8	13.8
Subtotal	58	34.7	100.0
Others	109	65.3	
Total		100.0	
Precipitants/diagnosis			
	Frequency	Percentage (%)	
Sepsis			
(DMFS+UTI)	59	35.3	
CAP	6	3.6	
Heart failure	2	1.2	
ACS	3	1.8	
Stroke	9	5.4	
CKD	6	3.6	
Subtotal	85	50.9	
Others	82	49.1	
Total	167	100.0	

Others = DCLD, acute gastroenteritis, newly diagnosed DM with no identifiable precipitants.

Table 3: outcome of the admission and presence of comorbidities

Outcome	Frequency (N)	Percentage (%)
Discharge	157	94.0
Mortality	9	5.4
Referral	1	0.6
Total	167	100.0
Comorbidities		
Absent	124	74.3
HTN/HHDx	37	22.2
Dyspepsia	1	0.6
CKD	1	0.6
IHD	2	1.2
BPH	1	0.6
DCM	1	0.6
Total	167	100.0

Keys: HTN/HHDx =hypertension/hypertensive Heart Disease; CKD = chronic kidney disease; IHD = Ischaemic Heart Disease; BPH = Benign prostatic Hyperplasia; DCM = Dilated cardiomyopathy.

Table 4: Outcome characteristics

Parameter	Outcome			P –value
	Discharge	Mortality	Referral	
T1DM	31	2	0	0.87
T2DM	126	7	1	
Gender				0.49
Female	81	4	1	
Male	76	5	0	
Age				0.49
Young	46	2	0	
Middle age	76	3	1	
Elderly	35	4	0	
Duration of DM				0.44
< 5 years	63	3	0	
5 – 10 years	43	4	1	
>10 years	51	2	0	
Duration of hospitalization				0.037
1 – 4 days	31	5	1	
5 – 10 days	86	2	0	
>10 days	40	2	0	
Diabetic Emergencies				0.17
DKA	18	1		
HHS	25	6		
Hypoglycaemia	8	0		
Absent comorbidities	117	6	1	1.000
HTN/HHDx	34	3	0	
Dyspepsia	1	0	0	
CKD	1	0	0	
IHD	2	0	0	
BPH	1	0	0	
DCM	1	0	0	

Keys: HTN/HHDx =hypertension/hypertensive Heart Disease; CKD = chronic kidney disease; IHD = Ischaemic Heart Disease; BPH = Benign prostatic Hyperplasia; DCM = Dilated cardiomyopathy; T1DM=type1 Diabetes mellitus; T2DM = type2 Diabetes mellitus.

Discussion

In this study the prevalence of DM among patients admitted into the wards was 5.9%. Similar findings was reported by Omar et al⁹ from Al-Ain UAE, and Chijioke et al¹⁰ 5.1% from Ilorin south western Nigeria respectively. Lower prevalence of 1%, 2.6% and 4.4% were reported from among admitted patients to hospitals in Abu Dhabi, Saudi Arabia and south western Nigeria respectively.^{11, 12, 13} Higher prevalence of 9.6% was reported by Umoh et al¹⁴ from Calabar South Eastern Nigeria, 10.3% and 10.4% by Ogbera et al¹⁵ and Unachukwu et

al¹⁶ from Lagos and Port Harcourt respectively. Kefale et al¹⁷ also reported high prevalence of 48.3% from Ethiopia.¹⁷ The wide range of reported prevalence from within Nigeria could be due to environmental factors, socio-economic status as well as lifestyle changes..

Among the patients with DM 51.5% were females. Higher percentage of females was reported by Omar et al⁹ from Al-Ain UAE of 61.8%. However, Unadike et al¹⁸ reported that more males were admitted than females in a ratio of 1.1:1. The reason may be that males are more economically empowered

than females and hence will seek treatment earlier than their female counterparts.^{6,18}

In our study T2DM patients contributed 80.2% of the patients admitted with DM into the medical wards. Similar prevalence of T2DM of 90.2% was reported by Alsayed et al¹⁹ from Egypt. However, both findings were higher than what was reported by Omar et al⁹ of 71.7% from UAE. The finding in our study is consistent with global epidemiology of DM with T2DM contributing 85 to 95% overall.

In the current study the mortality rate was 5.9% among patients with diabetes admitted into the medical wards. Lower rate of mortality of 3.2% was reported by Beshyah et al¹¹ from Al-Ain, and no deaths were directly attributed to the metabolic derangements. A larger data set was quoted to show similar findings to the Al-Ain study. Lower mortality rate of 3.4% was also reported by Ajayi et al¹³ from south western Nigeria. The difference reflects the economic status and prevalence of diabetes. Higher mortality rate of 11.2% was reported by Kefale et al¹⁷ from Ethiopia and 23.7% by Okafor et al²⁰ South Eastern Nigeria and Lagos 22.6%.¹⁵ possible reason for the differences in our findings may include variation in access to healthcare services, early diagnosis and treatment, presence of comorbidities and difference in study population. The overall treatment outcome of the DM patients was good. This is comparable to report from previous studies of 76.4% and 74.6% from Ethiopia and south western Nigeria respectively.^{13,17}

Infection was the most common reason for admission in our study accounting for 35.3%. The finding was similar to previous report from Sudan and Ethiopia of 36% and 36.3% respectively.^{17,21} in contrast cardiovascular disease was predominant reason for admission in UAE.¹¹

In our study DKA was reported in 11.4% of the DM patients on admission. Higher prevalence of 47% was reported from Sudan by Bchir et al²² and 38.2% by Kefale et al¹⁷ from Ethiopia. HHS was the predominant

hyperglycemic emergency reported in our study. This is contrary to report by Bchir and Kefale, where DKA predominates. This may be attributed to a lack of knowledge about the acute symptoms of diabetes among the patients with diabetes on admissions in our Centre and the preference for native medicine among our people thus they present late in emergency situations.¹⁴

In this study hypoglycaemia was reported in 8 (4.8%) of DM related admissions. Most of the patients admitted with hypoglycaemia were elderly. Our finding is similar to that of Kefale et al¹⁷. In both studies patients with hypoglycaemia were elderly, 65 years and above. Patients in the older age-groups are especially vulnerable to hypoglycemia. Age-related declines in renal function and hepatic enzyme activity may interfere with the metabolism of sulfonylureas and insulin, thereby potentiating their hypoglycemic effects. The vulnerability of the elderly to severe hypoglycemia may be partially related to a progressive age-related decrease in β -adrenergic receptor function.^{17, 23} Thirty percent of the patients presented with diabetic emergency (DKA/HHS). This indicates lack of good metabolic control, leading to admission with emergency, hence the need for more education /awareness on the disease by the people. Lack of access and high cost of insulin, delays in seeking medical attention, misdiagnosis and poor diabetic care are all contributory factors to this attendant mortality.¹⁸

Hypertension was the predominant comorbidity identified among the patients admitted with diabetes mellitus. In our study, 37 (22.2%) of the patients has Hypertension. Higher prevalence of Hypertension was reported by Ajayi et al¹³ in 49.2% of the patients. Hypertension is a major cardiovascular risk factor, and the prevalence of hypertension in diabetic patients is considerably higher than in the general population.¹³

Conclusion

Hyperosmolar hyperglycemic state was the most common cause of mortality among

admitted DM patients in Dutse. Infection is most common reason for admission of patients with DM. Recommendation – adequate health education to the people as well as provision of equipped health facilities for management of diabetes and diabetes related complications.

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CLINICO-PATHOLOGICAL ANALYSIS OF CERVICAL CANCER IN MAIDUGURI, NORTH EAST NIGERIA

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Abstract

Background: Cancer of the cervix is an important health problem and one of the leading cause of morbidity and mortality amongst women worldwide. It continues to be the most common gynecological malignancy especially in developing nations despite being a preventable cancer. The aim of this study is to review the clinico-pathological features of cervical cancer and provide update on these cancers that were diagnosed in our centre.

Materials and Methods: This is a retrospective, descriptive study of all cervical cancer cases that were histologically-diagnosed over a ten-year period (2015– 2024), at the Department of Histopathology, University of Maiduguri Teaching Hospital (UMTH), Maiduguri. The records of the cancer cases were retrieved from the Histopathology request forms and Cancer Registry of the hospital. Clinico-pathological information such as demographic data, clinical features, and stages of the tumors at presentation, and histopathological types and grades were extracted. The results were analyzed using descriptive statistics and presented in tables and charts.

Results: A total of 530 gynecological malignancies were diagnosed during the study period, out of which 337 cases was cervical cancer thereby constituting 63.6% of the gynaecological cancers. The patients' ages ranged between 25 and 84 years, with a modal age group of 41–50 years and mean age of 48.5 years. The three most common clinical presentations were abnormal vaginal bleeding, abnormal vaginal discharge and lower abdominal pain; while the commonest stage at presentation was stage III. The predominant histological type was squamous cell carcinoma representing 84.8% of the cancers. Adenocarcinoma was the second most common and accounted for 13.1%, while the other less common subtypes together constituted 2.1% of the cervical cancer. Majority of the patients then were referred for chemo-radiation and thus lost to follow-ups.

Conclusion: Cervical cancer was still the most common gynecological malignancy, with most patients presenting at advanced stage. Although squamous cell carcinoma was the predominant histological type, there was relative increase in the proportion of adenocarcinoma when compared to previous studies.

Keywords: Cervical cancer, Clinico-pathological features, Maiduguri, Nigeria

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Introduction

Cervical cancer is a major health problem and is the fourth most common cancer in women worldwide.¹ Globally, it represents 7.9% of all cancer cases in women, with an estimated incidence of 662,044 and mortality of 348,709 in 2022.^{1,2} In sub-Saharan Africa where up to 80% of the cancer cases occur, cervical cancer is the second most common cancer in the female population.^{2,3,4} Furthermore, in this part of the world and other low- and middle-income countries (LMICs), cervical cancer is the most common cancer of the female genital tract.²⁻⁷ In the Sub-Saharan Africa, this higher incidence of cervical cancer is associated with concomitant high mortality affecting women at their prime age.^{2,3,7} This is a source of great concern considering the fact that cervical cancer is preventable and curable at low cost with currently available preventive methods.^{2,3,7}

In Nigeria, with 12,075 new cases and 7968 deaths due to cervical cancer, it is responsible for the highest number of incident cases and deaths in Africa, and one of the eight countries with the largest number of incident cases in the world.⁸

Several studies on cervical cancer reported similar clinico-pathological findings regarding patients' biodata, risk factors, clinical presentations, and management strategies.^{6,9-16} Cancer of the cervix uteri is mostly seen in middle-age, multiparous, un-screened women in a polygamous setting and of low socio-economic status. Additionally, significant risk factors for development of cervical cancer include smoking, long-term use of oral contraceptives and immunosuppression.^{6,9-16} Persistent infection with high-risk human papilloma virus (HPV) has been strongly and globally implicated in the development of cervical cancer.¹⁷⁻¹²⁰ As result, it has become increasingly apparent that most of the risk factors (e.g., age at first coitus, multiparity, number of partners, socioeconomic status) merely reflect the probability of HPV exposure and acquisition.²¹ Most patients

usually present at advanced stage with history of abnormal vaginal bleeding, foul-smelling vaginal discharge and lower abdominal pain.⁹⁻¹⁶ Depending on the stage of disease and availability and affordability of treatment facility, modalities of treatment include surgery, chemo-radiation, and palliation.^{2,4,16}

There are several histopathological types of carcinoma of the cervix and as result, the WHO has grouped these epithelial tumours into three major categories namely: squamous cell tumours and precursors, glandular tumours and precursors, and other epithelial tumours.²² Squamous cell carcinoma (SCC) along with its variants, is the predominant histologic type of cervical cancer seen worldwide.^{9-16,23-25} The glandular tumours are the adenocarcinomas and constitute the second most common histologic type.^{9-16,23,24} However, recent reports have indicated a rising incidence of adenocarcinoma relative to SCC, which may be attributed to an improved method of screening for early squamous lesions and better identification of glandular lesions in cervical cytology samples.^{16,22,26} The other epithelial tumours group of cervical carcinoma include adenosquamous carcinoma, adenoid cystic carcinoma, neuroendocrine tumours, e.t.c.²² Although not as strong as tumour staging in cervical cancer prognostication, grading of both squamous cell carcinomas and adenocarcinomas are similar to their histological counterparts in other parts of the body, ranging from well- (grade I) to poorly-differentiated (grade III) carcinomas, whereas adenosquamous carcinoma is regarded as grade III tumour.^{22,27}

In an earlier study in our center 19 years ago, Mayun et al.²⁸ analysed histopathological features of non-squamous cell malignancies of the cervix. In this study, the aim was to determine the clinico-pathological features of all types of carcinoma of cervix and provide update on these cancers that were diagnosed

at the University of Maiduguri Teaching Hospital, Maiduguri, Northeast Nigeria.

Materials and Methods

This is a retrospective, descriptive study conducted at the University of Maiduguri Teaching Hospital, Maiduguri over a ten-year period from January 1, 2015 to December 31, 2024. The hospital is a tertiary health institution and a center for training, research and clinical services in Borno state, Northeast Nigeria.

All records of cases of histologically-confirmed cervical cancer were retrieved from the archives of Histopathology department and Cancer Registry of the hospital. The records of cases of gynaecological malignancies as well as total cancers of all histological types during the study period were collected from the hospital Cancer Registry. Clinico-pathological information such as demographic data, chief complaints, and stages of the tumors at presentation, and histopathologic types and grades were extracted. The results were analyzed using descriptive statistics and displayed in frequency tables and charts.

Results

During the period of study, the total number of histologically-confirmed cervical cancer cases was 337. The total number of gynecological malignancies was 530, whereas those of female cancers and overall total cancer cases respectively, were 1621 and 2809. Therefore, cervical cancer accounted for 63.6% of gynecological malignancies, 20.8% of female cancers and 12.0% of total cancer cases. The age range of the patients was from 25 to 84 years, mean age was 48.5 years and the modal age group was 41–50 years as shown in table 1.

As shown in table 2, most of the patients had more than one symptom at presentation, and the three most common chief complaints were abnormal vaginal bleeding, abnormal vaginal discharge and lower abdominal pain. Other features included loss of weight, difficulty in passing urine, dyspareunia,

leakage of urine and leakage of feces. Majority of the patients presented at stage III (51.2%), followed by Stages II (23.4%), whereas stages I and IV respectively, accounted for 6.8% and 18.6%.

During the period of study and before the commencement of chemo-radiation in our center, most of the patients were referred for such modalities of treatment and thus lost to follow-up. A total of 41 cases (12.2%) were referred to the UMTH's Cancer Centre (commissioned in 2023) for chemo-radiation. Squamous cell carcinoma (SCC) was the most common histological type and constituted 84.8% (286/337) of total cervical cancer cases, with large cell non-keratinizing accounting for the majority of subtypes of SCC (226/286; 79.0%). Cases of adenocarcinoma constituted 13.1% of the carcinoma of cervix, of which the usual-type adenocarcinoma represented the predominant subtype (39/44; 88.6%). Other less common subtypes of adenocarcinoma included clear cell (2/44; 4.5%) villoglandular (2/44; 4.5%) and mucinous (1/44; 2.3%). Adenosquamous carcinoma and adenoid cystic carcinoma respectively, contributed 1.8% and 0.3% of total cervical cancer cases as depicted in table 3 and figure I.

Grade 2 (moderately-differentiated) was the most common histological grade in squamous cell carcinoma and accounted for 66.4% of the cases. Grade 1 (well-differentiated) constituted 19.9% whereas grade 3 (poorly-differentiated) represented 13.6% of the cases. For adenocarcinoma, grade 1 was the most common and constituted 52.3%, while grade 2 and grade 3 respectively, accounted for 34.1% and 13.6% of adenocarcinoma cases.

Table 1: Age distribution of patients with cervical cancer

Age group (years)	Number of cases	Percentage (%)
21-30	6	1.8
31-40	65	19.3
41-50	117	34.7
51-60	88	26.1
61-70	43	12.8
71-80	17	5.0
81-90	1	0.3
Total	337	100

Table 2: Clinical presentation of patients with cervical cancer

(This table allows multiple responses)

Clinical features	Number of cases	Percentage (%)
Abnormal vaginal bleeding	241	71.3
Abnormal vaginal discharge	168	49.7
Lower abdominal pain	80	23.7
Weight loss	55	16.3
Difficulty in passing urine	14	4.1
Dyspareunia	13	3.8
Leakage of urine	6	1.8
Leakage of feces	2	0.6

Table 3: Frequency distribution of histological types of cervical cancer

Cervical cancer	Number of cases	Percentage (%)
Squamous cell carcinoma	286	84.8
Large cell non-keratinizing	226	67.0
Large cell keratinizing	57	16.9
Basaloid/Small cell	3	0.9
Adenocarcinoma	44	13.1
Usual-type	39	11.6
Clear cell	2	0.6
Villoglandular	2	0.6
Mucinous	1	0.3
Other epithelial tumours	7	2.1
Adenosquamous carcinoma	6	1.8
Adenoid cystic carcinoma	1	0.3
Total	337	100

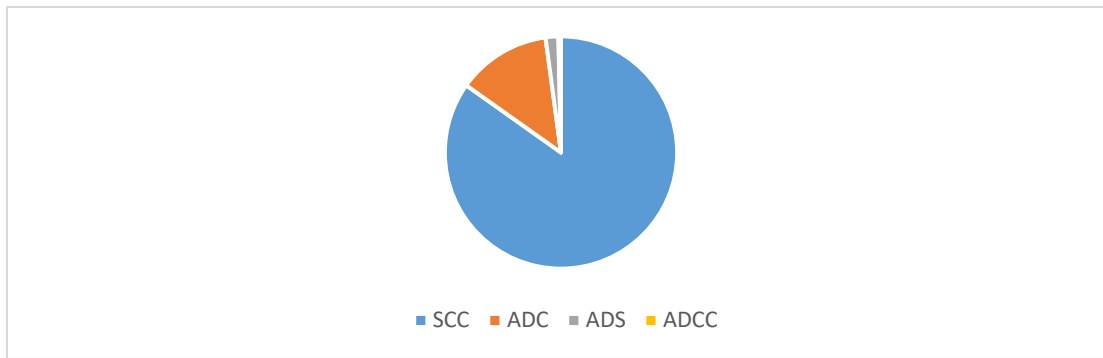


Figure I: **Histological types of cervical cancer**

Legends: **SCC**= squamous cell carcinoma; **ADC**= adenocarcinoma; **ADS**= adenosquamous carcinoma; **ADCC**= adenoid cystic carcinoma

Discussion

This study was conducted to review cervical cancer cases in Maiduguri, showing the prevalence over a 10-year period and detailing the clinico-pathological features.

Cervical cancer is the most common female genital tract cancer found in the study, a finding that aligns with findings of the studies conducted in Nigeria and other low- and middle-income countries (LMICs).^{3-5,7-16} The predominance of cervical cancer in this study and other parts of Nigeria as well as most LMICs could be attributed to the prevailing risk factors, and above all, the lack of organized population-based cervical cancer screening programme.²⁻⁷ In this study, cervical cancer accounted for 63.6% of the malignancies of female genital tract, which is lower than 70.5% observed in a previous study from the same centre.²⁹ The low prevalence in this study may not be unrelated to the availability of routine opportunistic cervical cancer screening programme in the health institution.

However, it is important to note that in recent years, the incidence and mortality of cervical cancer has been estimated to be on the decline in most regions of the world, except for few Sub-Saharan countries where it is still the leading cause of cancer mortality in women.^{16,30} This downward trend could be due to increase in the utilization of cervical cancer preventive measures and a relative surge in other gynecological malignancies and breast cancer.³⁰ To buttress the above

claim, a more recent report by Lawal Qudus O, et al.⁸ in 2023 has shown that in Nigeria, the numbers of incident cases and mortalities from cervical cancer were 12,075 and 7968, respectively compared to 14,089 new cases and 8240 deaths as reported by Bruni L, et al. in 2015.³¹

In this study, the age distribution with a mean age of 48.5 years is similar to those reported in several studies in Nigeria and other developing countries, corroborating the fact that most cases of cervical cancer occur in the middle-aged women.^{4, 6, 9-16} In majority of cases, women with cervical cancer present with more than one symptom as observed in this study; in which the three most common symptoms at presentation were abnormal vaginal bleeding, abnormal vaginal discharge and lower abdominal pain. Other uncommon chief complaints reported such as leakage of urine, leakage of feces and difficulty in passing urine are findings of advanced disease, as most women presented with stage III disease. These findings are consistent with observations by several other scholars.^{4,5,9-11,16,25,26} Depending on the stages of cervical cancer, modalities of treatment include surgery, chemo-radiation, or palliative care.^{2,16,25,26} The majority of our patients presented in advanced stages and were referred for chemo-radiation and thus lost to follow up.

Worldwide, squamous cell carcinoma is the most common histological type of cervical cancer constituting 70-80% of all cases.^{9-16,22-24,26} Adenocarcinoma is the second most common histological type and accounts for

10-15% of the cases.^{16,22,26} The other epithelial tumours of the cervix which include adenosquamous carcinoma, adenoid cystic carcinoma, neuroendocrine carcinoma, together comprise about 5% of all carcinoma cases.^{16,22,26} In this study, squamous cell carcinoma was the most common histological type and constituted 84.8% of the cases. Adenocarcinoma was the second most common (13.1%), while the other epithelial tumours together contributed 2.1% of all cases of cervical cancer. These findings are in consonance with observations in local and international studies on cervical cancer.^{9-16,22-24,26s} The major histological subtypes of squamous cell carcinoma of the cervix are large cell non-keratinizing, large cell keratinizing and basaloid/small cell carcinoma. The predominance of large cell non-keratinizing squamous cell carcinoma in our study is in keeping with most studies, but lower than a finding in a Ghanaian study which could be due to regional variation.^{9,11-16,22,26}

In this study, the non-squamous carcinoma of the uterine cervix constituted 15.2% and included adenocarcinomas (13.1%), adenosquamous carcinoma (1.8%) and adenoid cystic carcinoma (0.3%). The proportion of non-squamous carcinoma of 15.2% in this study is greater than that of Mayun et al²⁸ (12.0%) from the same centre 19 years ago. In their study, adenocarcinoma accounted for 77.9% of non-squamous cell carcinoma which is lower than 86.2% found in this study. This difference could be due to the global increase in the incidence of adenocarcinoma relative to squamous cell carcinoma attributed to an improved method of screening for early squamous lesions and better identification of glandular lesions in cervical cytology samples, as reported in more recent studies^{16,22,26}

Squamous cell carcinoma of the cervix is graded similar to those squamous cell carcinomas in other parts of the body, while adenocarcinomas are graded based on architectural features, similar to that of endometrial adenocarcinomas.^{22, 27} This

study has found out that majority (66.4%) of the cases of squamous cell carcinoma were grade 2 tumours, which is in keeping with similar observation in most reports.^{9, 16, 27, 32} In adenocarcinoma, grade 1 (well-differentiated) was the most common and constituted 52.3% of the histological tumour grading. The predominance of the grade 1 adenocarcinoma in this study could be due to the large number of usual-type adenocarcinoma- an observation also reported by Mayun et al,²⁸ although more studies are needed to confirm it. Several studies reported that adenosquamous carcinoma is a high grade and aggressive tumour with a poorer outcome than common adenocarcinomas or squamous cell carcinomas.^{16, 22, 27} It has been reported that tumour grading may convey some degree of prognostic information related to tumour sensitivity to chemotherapy or radiation therapy; in that high histologic grade was associated with decreased survival in patients with cervical carcinoma treated by radical surgery and radiation therapy.^{16, 22, 33} Of note, the utility of tumor grading and typing in prognostication of cervical cancer may be limited, because some studies have reported that when these tumour types were compared stage by stage, there was no difference in survival.^{16, 33, 34}

Conclusion

This study has also found out that cervical cancer was still the most common gynecological malignancy in our community, with majority of women presenting at advanced stages of disease. Although squamous cell carcinoma was the predominant histological type, there was relative increase in the proportion of adenocarcinoma when compared with previous studies. The menace of this preventable cancer can be curtailed by establishment of organized screening program and enrollment of such individuals in health insurance scheme.

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Conflict of Interest

The authors declare no conflict of interest

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COMPARATIVE EVALUATION OF OPHTHALMIC ARTERY DOPPLER INDICES IN PRE-ECLAMPTIC AND NORMOTENSIVE PREGNANT WOMEN IN KANO, NIGERIA**Hussaini Dede¹ Anas Ismail², Yusuf Lawal²**¹Department of Radiology, College of Medical Sciences Yobe State University, Damaturu, Nigeria²Department of Radiology, Bayero University Kano, Nigeria.**Corresponding Author:** *Hussaini Dede*, **Email:** dedehussaini@yahoo.com**Received:** 30-Mar-2026**Accepted:** 21-Apr-2026**Published:** 30-Apr-2026**Abstract**

Background: Hypertensive disorders in pregnancy are widely acknowledged as among the most severe complications, significantly impacting maternal as well as neonatal morbidity and mortality rates globally. Pre-eclampsia (PE) is the most important gestational condition associated with hypertension. Maternal ophthalmic artery Doppler velocimetry enables the identification of pregnant women with increased cerebral blood flow who are at risk of developing severe PE and eclampsia.

Objectives: To sonographically determine the ophthalmic artery Doppler velocimetric indices among patients with pre-eclampsia and compare with that of match normotensive pregnant controls.

Methods: - This cross sectional study was carried out in a tertiary health care facility in Nigeria. Eighty pre-eclamptic patients an equal number of normotensive matched pregnant controls were recruited for the study. A comprehensive history of hypertension was obtained, and an obstetric scan was conducted to assess the gestational age. The ophthalmic artery peak ratio, pulsatility index, and resistive index of both groups were obtained (and compared) using high resolution ultrasound Doppler examination.

Results: The key hemodynamic finding was a **significantly lower ophthalmic artery peak systolic velocity (PSV)** and **relatively higher end diastolic velocity (EDV)** in pre-eclamptic subjects compared to controls ($P < 0.001$). This resulted in significantly lower resistive index (RI) and pulsatility index (PI), alongside a higher peak ratio (PR) in the pre-eclamptic group- a pattern of **reduced vascular resistance and increased blood flow**.

Conclusion: Ophthalmic artery Doppler ultrasonography can be useful in distinguishing pre-eclamptic from normotensive pregnant women through characteristic low-resistance, high-flow hemodynamic profiles.

Key Words: - Doppler, Ophthalmic artery, pre-eclampsia, velocimetry

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INTRODUCTION

Hypertension is the most prevalent disorder affecting pregnancies worldwide.¹ Maternal mortality continues to pose a significant challenge on a global scale, as it is estimated that approximately 810 women lose their lives on a daily basis due to complications related to pregnancy or childbirth.¹ Classically, the American College of Obstetrics and Gynaecology (ACOG) defines pre-eclampsia as the presence of hypertension and proteinuria occurring after 20 weeks of gestation in a previously normotensive patient.^{2,3} However, a significant proportion of women develop systemic manifestations of PE such as low platelets or elevated liver enzymes before the hallmark of proteinuria is detectable resulting in delayed diagnoses.⁴ In Nigeria, about 34% of pregnant women receive no antenatal care, putting them at higher risk of maternal mortality.⁵ A recent, nationwide cross-sectional survey found that PE and eclampsia are the leading causes of maternal mortality in Nigeria and is responsible for 28.2% of maternal deaths; the other main contributors to maternal mortality are haemorrhage (24.4%) and pregnancy-related infection/sepsis (14.2%).⁵ Ranging in severity, hypertensive disorders of pregnancy include: chronic hypertension, defined as systolic blood pressure (BP) ≥ 140 mm Hg or diastolic BP ≥ 90 mm Hg that predates the onset of pregnancy; gestational hypertension, defined as hypertension diagnosed after 20 weeks of gestation without concurrent proteinuria; pre-eclampsia is classically defined as new-onset hypertension with new-onset proteinuria; and chronic hypertension with superimposed PE which is defined as chronic hypertension with new-onset proteinuria or other signs/symptoms of PE after 20 weeks or chronic proteinuria with new onset hypertension.⁶

The high morbidity and mortality associated with PE arouse interest for new methods to better identify risk in pre-eclamptic patients.⁷ The ophthalmic artery, which is the first

branch of the internal carotid artery and has embryological, anatomical and functional similarities with the intracranial vasculature, is an easily accessible vessel for Doppler assessment that provides information on the less accessible intra-cranial circulation.⁸

Uterine artery and several peripheral vessels Doppler indices have been investigated as a potential marker for the development of pre-eclampsia, among which is ophthalmic artery Doppler (OAD). Evaluating ophthalmic artery with Doppler sonography is easy using standard ultrasound equipment and is unaffected by adiposity. Furthermore, the Doppler velocimetric indices have constant reference ranges throughout trimesters of pregnancy.^{10,9}

There are few studies in Nigeria regarding the ophthalmic artery velocimetric indices in patients with pre-eclampsia. This study is aimed at evaluating the parameters of the ophthalmic artery Doppler velocimetry in patients with PE and compare them with those of normotensive pregnant controls.

Aim and objectives

Broad

To sonographically determine the ophthalmic artery Doppler velocimetric indices among patients with pre-eclampsia and compare with that of match normotensive pregnant controls.

Specific

1. To sonographically determine ophthalmic artery resistive index (RI), pulsatility index (PI) and peak ratio (PR) among patients with pre-eclampsia and their matched controls.
2. To compare resistive index, pulsatility index and peak ratio between pre-eclamptic patients and matched normotensive pregnant controls.

Materials and methods

This observational cross sectional study was carried out in Aminu Kano Teaching Hospital (AKTH). It is a tertiary care facility in Kano, Nigeria. Using a systematic random sampling technique, 80 pregnant women

being managed for pre-eclampsia at the obstetrics and gynaecology department of AKTH, and an equal number of matched normotensive pregnant women as controls were recruited into the study. The two groups were matched in terms of maternal age, gestational age and parity.

Pregnant women who were not-consenting, smokers, having multiple pregnancies, orbital pathologies and maternal conditions before pregnancy, such as diabetes mellitus, chronic hypertension, and HIV infection, were excluded from both groups.

Informed consents were obtained from the study and control groups. Data were obtained using structured data collection sheet. The maternal age, blood pressure (BP), gestational age and estimated foetal weight (by ultrasound scan) of study group were obtained. Similar information were obtained from the control group. The ophthalmic artery peak ratio (PR), pulsatility index (PI), and resistive index (RI) were obtained for both study and control groups.

Ultrasound scanning was performed using HYVission V5 Panascope digital ultrasound machine, equipped with 6.8-15MHz transducer. An acoustic coupling gel was applied on the transducer which was then placed directly and gently on the closed eyelid with the gaze directed at the ceiling.¹¹ The examiner's hand was rested on the orbital margin to minimize the applied pressure to the globe and the orbit. The insonation angle was kept below 20° with high-pass filter set to its minimum value.¹² Real time grey scale and colour Doppler scanning was then performed in longitudinal and transverse planes of both globes. The hypoechoic stripe of the optic nerve was then identified with the ophthalmic artery just medial to it.¹³ Using colour Doppler, the ophthalmic artery was further identified by its direction of flow (toward probe) and pulsatility at about 15 millimetres from the optic disc (on the medial aspect of the optic nerve). Pulsed-wave Doppler was then applied, with sample volume placed around 15mm behind optic disc, medial to optic

nerve; sample volume was about 2mm in length.¹²

The Doppler sample gate (≤ 2 mm) was placed at the centre of the detected vessel to image the spectral pattern. Pulse repetition frequency (PRF) was set at 125 kHz and adjusted as appropriate.¹¹

The spectral waveform (figure 1) as well as the velocimetric indices which include, Resistive index (RI), Pulsatility Index (PI) and peak ratio (PR) were obtained from the ultrasound machine which has the manufacturer calibrated automatic calculator for RI and PI. While the PR was calculated manually by dividing the second peak systolic velocity (P2) with the peak systolic velocity (PSV). Both ophthalmic arteries were insonated and measurement taken three times on both right and left side, and average of each of the three reading were recorded.

Data generated were analysed using IBM statistical product and service solutions (SPSS) statistics software version 22.0 New York, USA. Mean \pm standard deviation was used to summarize quantitative variables. T-test was used to compare continuous with group/categorical variables with two levels. Findings were then presented numerically, graphically and in tabular forms. A p-value of 0.05 or below was considered to be statistically significant.

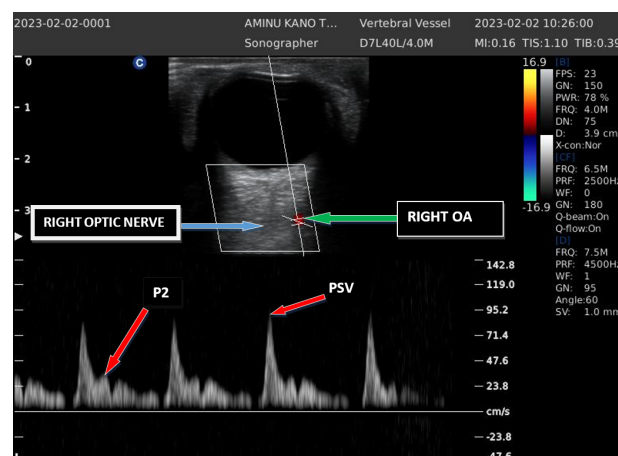


Figure 1: - Triplex transverse ultrasonogram showing the colour filled right ophthalmic artery (green arrow) and its spectral waveform (red arrows). PSV= peak

systolic velocity, P2= second peak systolic velocity, OA = ophthalmic artery.

Results

This study was conducted over a period of 8 months from December 2023 to July 2024. A total of 160 subjects were recruited into the study, comprising 80 pre-eclamptic subjects and equal number of normotensive pregnant controls.

Socio-demographics of the study subjects

The age range of pre-eclamptic subjects was 19 – 38 years with a mean age of 28 ± 3.86 years while that of the normotensive pregnant control subjects was 18 – 37 years with a mean of 27.52 ± 4.36 years. The mean age

difference between the two groups was not statistically significant ($p = 0.444$). The highest number of the respondents were found in the age range of 25 – 29 years comprising of 37 individuals (46.3%) in both the pre-eclamptic subjects and normotensive pregnant control groups as shown in **Table 1**.

The gestational age of the pre-eclamptic group ranges from 28 – 38 weeks with a mean gestational age of 33.24 ± 2.89 weeks, while that of the normotensive pregnant control subjects was 25 – 40 weeks with a mean of 33.41 ± 3.72 weeks. There is no statistically significant difference between the mean gestational ages of the two groups ($P = 0.74$) as shown in the **Table 1** below.

Table 1: Socio-demographic Characteristics of pre-eclamptic and normotensive pregnant control Subjects:

Variables	Pre-eclamptic subjects n=80 (%)	Normotensive pregnant control n=80 (%)	Total n=160	P-value
Age (Years)				
<20	2 (2.5)	2 (2.5)	4	
20-24	12 (15.0)	12 (15.0)	24	
25-29	37 (46.3)	37 (46.3)	74	
30-34	23 (28.8)	23 (28.8)	46	
35-40	6 (7.5)	6 (7.5)	12	
Mean \pm SD	28 \pm 3.82	27.54 \pm 4.32		P = 0.444
Gestational age (weeks)				
20 - 24	0	0	0	
25 - 29	9 (11.3)	9 (11.3)	18	
30 - 34	37 (46.3)	37 (46.3)	74	
35 - 40	34 (42.5)	34 (42.5)	68	
Mean \pm SD	33.19 \pm 2.88	33.42 \pm 3.68		P = 0.740

Ophthalmic artery Doppler velocimetric indices in the pre-eclamptic and normotensive control subjects.

The ophthalmic artery PSV, EDV, RI PI, P2 and PR ranges for pre-eclamptic and normotensive control subjects are shown in **Table 2**.

The mean PSV, EDV, RI PI, P2 and PR values on the right and left sides showed no statistically significant difference ($P = 0.99$), as shown in **Table 3**

The mean ophthalmic artery PSV, EDV, RI PI, P2 and PR for the pre-eclamptic subjects were 55.78 ± 20.4 cm/s, 22.36 ± 8.94 cm/s, 0.58 ± 0.09 , 0.89 ± 0.29 , 41.80 ± 15.9 cm/s and 0.78 ± 0.08 on the right side. The corresponding values for the left eye were 55.81 ± 20.11 cm/s, 22.81 ± 9.03 cm/s, $0.57 \pm$

0.09 , 0.88 ± 0.28 , 42.03 ± 15.85 and 0.75 ± 0.08 . Similarly, the mean ophthalmic artery PSV, EDV, RI PI, P2 and PR values for the normotensive control subjects were 69.59 ± 15.47 cm/s, 17.94 ± 6.60 cm/s, 0.74 ± 0.08 , 1.56 ± 0.35 , 40.06 ± 9.71 cm/s and 0.59 ± 0.12 in the right eye. The corresponding values on the left were 69.18 ± 14.77 cm/s, 17.94 ± 6.55 cm/s, 0.73 ± 0.08 , 1.56 ± 0.34 , 40.24 ± 9.65 and 0.59 ± 0.11 (**Table 4**).

The mean PSV, RI and PI values among the pre-eclamptic subjects were lower than those of the normotensive control subjects, while the EDV and PR values of the pre-eclamptic subjects were higher on both the right and left sides ($P < 0.001$). The P2 values for the pre-eclamptic and normotensive controls showed no statistically significant difference ($P = 0.400$), as shown in **Table 3**.

Table 2: The range of ophthalmic artery Doppler velocimetric indices between pre-eclamptic and normotensive control subjects.

Doppler Parameters	Pre-eclamptic subjects		Normotensive control subjects	
	RIGHT EYE	LEFT EYE	RIGHT EYE	LEFT EYE
PSV (cm/s)	12.00 – 88.50	13.00 – 88.00	43.13 - 96.70	43.33 - 96.50
P2 (cm/s)	8.69 – 69.9	8.70 – 69.20	23.8 -65.44	23.9 – 65.5
EDV (cm/s)	3.32 – 40.16	3.4 – 40.60	6.70 - 34.20	7.00 - 34.00
RI	0.35 – 0.79	0.34 – 0.78	0.56 – 0.91	0.56 - 90
PI	0.38 – 1.81	0.36 – 1.80	1.00 – 2.37	0.98 – 2.36
PR	0.52 – 0.85	0.52 – 0.86	0.31 – 0.79	0.32 – 0.79

Table 3: Comparison of means of Doppler velocimetric indices of pre-eclamptic and normotensive control subjects for the right and left side.

Doppler parameters	Pre-eclamptic (cases)		P-value	Normotensive (controls)		P-value
	Mean	SD		Mean	SD	
RIGHT_PSV	55.78	20.4	0.99*	69.59	15.47	0.99*
LEFT_PSV	55.81	20.11		69.18	14.77	
RIGHT_EDV	22.36	8.94	0.99*	17.94	6.60	0.99*
LEFT_EDV	22.81	9.03		17.94	6.55	
RIGHT_RI	0.58	0.09	0.99*	0.74	0.08	0.99*
LEFTT_RI	0.57	0.09		0.73	0.08	
RIGHT_PI	0.89	0.29	0.99*	1.56	0.35	0.99*
LEFTT_PI	0.88	0.28		1.56	0.34	
RIGHT_P2	41.80	15.95	0.99*	40.06	9.71	0.99*
LEFT_P2	42.03	15.85		40.24	9.65	
RIGHT_PR	0.75	0.08	0.99*	0.59	0.12	0.99*
LEFT_PR	0.75	0.08		0.59	0.11	

*Statistically significant at $p \leq 0.05$

Table 4: Comparison of means of Doppler velocimetric indices of pre-eclamptic and normotensive control subjects.

DOPPLER PARAMETERS	Pre-eclamptic (CASES)		Normotensive (CONTROLS)		P-value
	Mean	SD	Mean	SD	
RIGHT_PSV	55.78	20.4	69.59	15.47	<0.002*
LEFT_PSV	55.81	20.11	69.18	14.77	<0.003*
RIGHT_EDV	22.36	8.94	17.94	6.60	<0.003*

LEFT_EDV	22.81	9.03	17.94	6.55	<0.001*
RIGHT_RI	0.58	0.09	0.74	0.08	<0.001*
LEFTT_RI	0.57	0.09	0.73	0.08	<0.001*
RIGHT_PI	0.89	0.29	1.56	0.35	<0.001*
LEFTT_PI	0.88	0.28	1.56	0.34	<0.001*
RIGHT_P2	41.80	15.95	40.06	9.71	0.402*
LEFT_P2	42.03	15.85	40.24	9.65	0.383*
RIGHT_PR	0.75	0.08	0.59	0.12	<0.001*
LEFT_PR	0.75	0.08	0.59	0.11	<0.001*

*Statistically significant at $p \leq 0.05$

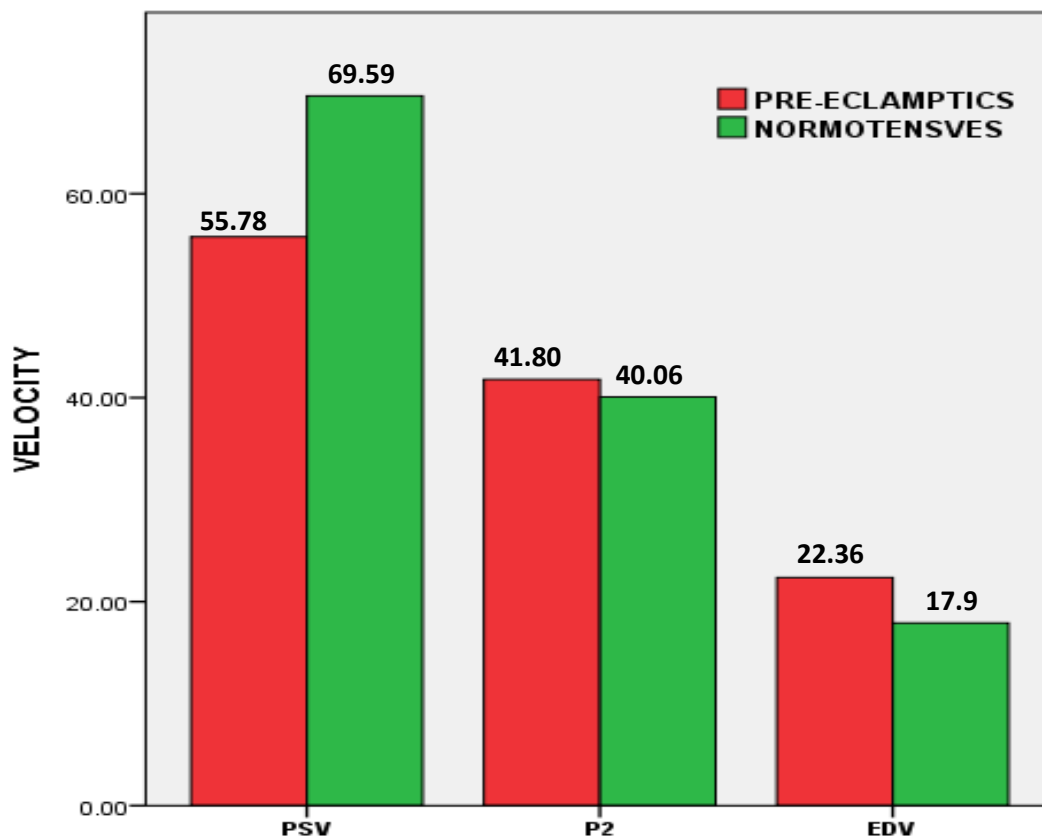


Figure 2: Bar chart showing means of PSV, P2 and EDV of the ophthalmic arteries of the right eyes for the pre-eclamptic and normotensive group.

Discussion

Pre-eclampsia (PE) is a complication of pregnancy that is associated with substantial maternal and foetal morbidity and mortality. Maternal endothelial dysfunction due to circulating factors of foetal origin from the placenta is a hallmark of pre-eclampsia.¹⁴ The occurrence, development, and intensity of PE can vary significantly in a natural context, with unpredictable timing, intensity, and severity. The commonly cited explanation for the observed pathology is that inadequate transformation of spiral arteries and excessive oxidative stress in the placenta leads to a systemic inflammatory reaction, characterized by extensive damage to the endothelium, where the placenta is considered the primary pathogenic agent in this process.¹

This study examined ophthalmic artery Doppler velocimetric indices in both normotensive pregnant women and those diagnosed with PE.

A total of 80 pre-eclamptic subjects were evaluated in this study with equal number of normotensive pregnant control group summing up to 160 participants. The mean age of 28 ± 3.86 years with an age range of 19 – 38 years for the pre-eclamptic subjects was similar, to that of the control group with a mean of 27.52 ± 4.36 years and a range 18 – 37. The modal age for both the study and control groups is 25 – 29 years. The difference between the mean age of the study and control groups was not statistically significant (P- value = 0.444), because they were matched. The mean age obtained in this study (27.52 ± 4.36 years) was similar to that derived by *Mustapha et al*¹⁵ in North-western Nigeria at 27.24 ± 4.16 . However, *Olatunji et al*¹² obtained higher mean age in a study in southwestern Nigeria where found a mean age of 32.4 ± 4.7 years. This difference was likely due to socio-cultural variation in terms of time of marriage between the two regions.

The mean gestational age of the pre-eclamptic group at 33.24 ± 2.89 , was similar to that of the control group (33.41 ± 3.72 weeks). The modal gestational age for the

two groups was 25 – 29 weeks. There was no statistically significant difference between the gestational age of pre-eclamptic subjects and their normotensive control groups (P value = 0.74). The modal gestational age presented in this study was similar to what was found by *Olatunji et al*¹² in southwestern Nigeria where gestational age of less 30 weeks was reported. The mean gestational age of the pre-eclamptic group was also similar to what was recorded by *Mustapha et al*¹⁵ in North-western Nigeria at 33.20 ± 3.74 weeks

The mean ophthalmic artery peak systolic velocity (PSV) value among the pre-eclamptic subjects was lower than that of the normotensive control subjects, and the difference was statistically significant (P < 0.001). Conversely, the end diastolic velocity (EDV) of pre-eclamptic subjects was higher than those of the normotensive controls on both the right and left sides (P < 0.001). The mean second peak systolic velocity (P2) value was slightly higher in the pre-eclamptic subject compared to that of the normotensive controls, however, not statistically significant (P= 0.400). This explained the statistically significant (P < 0.001) lower mean resistive index (RI) and pulsatility index (PI) values, with a higher peak ratio seen in the pre-eclamptic subjects. This pattern of reduced resistance with increase blood flow was explained by *Belfort et al*¹⁶ in the United States. They stated that pre-eclampsia as a placental disease is associated with increase placental vascular resistance and in order to improve placental perfusion, it may be hypothesized that there is compensatory production of vasodilator substances by the placenta. These circulating factors, as a secondary effect, dilate vessels in multiple organs, including aorta, myometrium and intracranial circulation compared to normotensive controls groups. *Pollyanna et al*¹⁰ in a systemic review of 14 studies and *Olatunji et al*¹² in Southwestern Nigeria reported similar pattern of low resistance among the pre-eclamptic subjects. They revealed that the mean RI, PI, and PSV were significantly lower in pre-eclamptic patients

than in the normotensive pregnant controls. While Mean P1, EDV, and PR were significantly higher in the pre-eclamptic group.

This study found no statistically significant difference between the mean PSV, EDV, RI PI, P2 and PR values on the right and left side ($P = 0.99$). This is in agreement with what was recorded by *Mustapha et al*¹⁵ in North-western Nigeria and *Olatunji et al*¹² in Southwestern Nigeria in their respective studies.

The mean ophthalmic artery PSV and EDV recorded in this study among the pre-eclamptic subjects were 55.78 ± 20.4 cm/s and 22.36 ± 8.94 cm/s respectively in the right eye and 55.81 ± 20.11 cm/s and 22.81 ± 9.03 cm/s respectively in the left eye. This was in agreement with what was obtained by *Kumari et al*¹⁷ in India. However, *Olatunji et al*¹² in Southwestern Nigeria recorded a lower mean PSV value, presumably due smaller sample size of 42 compared with 80 in this study. The mean ophthalmic artery PSV and EDV recorded in this study among the normotensive control was 69.59 ± 15.47 cm/s and 17.94 ± 6.60 cm/s on the right side, and 69.18 ± 14.77 cm/s and 17.94 ± 6.55 cm/s on the left side. The pattern of higher PSV and lower EDV among the control group compared to the study group was reported by *Kumari et al*¹⁷ in India and *Olatunji et al*¹² in Southwestern Nigeria.

Limitations of the study: Being a study conducted at a single centre, highlights the potential for selection bias due to its limited geographic scope. While the findings regarding ophthalmic artery Doppler parameters are significant, the results may not fully represent the broader population. Secondly the study is limited by lack of longitudinal follow-up, absence of diagnostic accuracy analysis and potential confounding variables.

Conclusion: Ophthalmic artery Doppler parameters showed significant differences between pre-eclamptic and normotensive pregnant subjects, and may serve as a useful adjunct in the evaluation of pre-eclampsia. Given its non-invasive nature, it holds

promise as an adjunctive tool for the evaluation and monitoring of pre-eclampsia, though larger, multi-centre studies are recommended to establish normative thresholds and refine its clinical utility.

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HISTOMORPHOLOGIC EVALUATION OF EPSTEIN–BARR VIRUS-ASSOCIATED CYTOPATHIC EFFECTS IN LYMPHOMAS: IMPLICATIONS FOR SCREENING AND DIAGNOSTIC UTILITY

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Abstract

Background: Lymphomas comprise a heterogeneous group of lymphoid malignancies with diverse etiological factors, including infection with Epstein–Barr virus (EBV). EBV-associated lymphomas include Hodgkin lymphoma, Burkitt's lymphoma, and other non-Hodgkin lymphomas. Despite substantial global evidence linking EBV infection to lymphomagenesis, there is a limited available data describing EBV-associated morphologic patterns in lymphomas, particularly in North-east Nigeria. The absence of well-defined histomorphologic indicators of EBV restricts its utility as a screening or diagnostic tool. **Objective:** To evaluate the histomorphologic features suggestive of EBV-associated cytopathic effects in archived lymphoma specimens in North-east Nigeria. **Materials and Methods:** A retrospective study was conducted involving thirty-one archived lymphoma cases retrieved from the Department of Histopathology, Modibbo Adama University Teaching Hospital, Yola. Formalin-fixed paraffin-embedded tissue sections were stained with haematoxylin and eosin using standard protocols. Relevant sociodemographic and clinical data were extracted from patients' medical records. **Results:** Among the 31 cases analysed, 45.2% (n=14) were females and 54.8% (n=17) were males. Hodgkin lymphoma accounted for 9.7% (n=3), Burkitt's lymphoma constituted 32.2% (n=10), while other non-Hodgkin lymphomas represented 58.1% (n=28). EBV-associated cytopathic effects such as multinucleated large atypical cells, Reed-Sternberg-like cells, starry-sky appearance, and diffuse populations of large cells with abundant cytoplasm were observed. **Conclusion:** These findings suggest that H&E histomorphologic evaluation may serve as a useful preliminary screening approach for identifying EBV-association lymphomas, particularly in resource-limited settings. However, further studies incorporating immunohistochemistry and molecular techniques are recommended to validate these findings and develop standardised morphologic scoring systems for predicting EBV status through multicentre retrospective and prospective investigations.

Keywords: Epstein–Barr virus; Lymphoma; Histomorphology; Haematoxylin and Eosin

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Introduction

Epstein-Barr virus (EBV) is a gamma herpesvirus that asymptotically infects and establishes life-long latency in B lymphocytes in more than 90% of the world population. In Africa, primary EBV infection commonly occurs in the first five years of life. Since its initial identification in 1964 in Burkitt's lymphoma, EBV has been implicated in the pathogenesis of several lymphoid malignancies, including Hodgkin lymphoma, Diffuse large B-cell lymphoma, extranodal natural killer (NK)/T-cell lymphoma, and post-transplant lymphoproliferative disorders (1–3).

Lymphomas represent a diverse group of haematological malignancies that are frequently diagnosed at advanced stages particularly in low-income countries. Therefore, contributing to poor clinical outcomes, terminal crisis, and increased disease-related mortality. Detection of EBV within lymphoma tissues could have important diagnostic, prognostic, and therapeutic implications. However, this detection may require advanced molecular and immunohistochemical techniques, which are not routinely available in many resource-limited environments. Consequently, histomorphologic evaluation using haematoxylin and eosin (H&E) staining makes a feasible preliminary screening and diagnostic modality. Histomorphologic features could provide valuable preliminary indicators with positive predictive value (PPV) to suggest EBV infection.

EBV-associated lymphomas typically demonstrate type I or type II EBV latency. These types of latencies are characterised by the expression of a limited viral markers including, Epstein-Barr encoded RNAs (EBERs), Epstein-Barr nuclear antigen-1 (EBNA-1), and latent membrane protein-1 (LMP-1) (4). These genes possess oncogenic properties and thus contribute to lymphomagenesis through multiple

mechanisms. For example, EBERs have been shown to be sufficient to induce and maintain cell proliferation and inhibit apoptosis compared to control cells (5–7). While LMP-1 is shown to be involved in activating cellular signalling pathways that lead to cell growth, survival, differentiation, and transformation (8).

Certain histomorphologic features observable on routine H&E staining have been associated with EBV-associated lymphomas. These features include architectural effacement of lymphoid tissues, diffuse, nodular, or angiocentric infiltration, geographic necrosis, presence of large immunoblast-like cells, starry-sky appearance, and polymorphous inflammatory backgrounds (3,9). Additionally, Reed-Sternberg-like cells and nuclear features of vesicular chromatin and prominent nucleoli are cytopathic effects linked to EBV-associated lymphomas (10). These histomorphologic characteristics are shown to have strong correlation with EBV-associated lymphomas, particularly endemic Burkitt's lymphoma and extranodal NK/T-cell lymphoma (11).

Lymphomas constitute a significant public health burden in Nigeria, where non-Hodgkin lymphoma ranks among the leading cancers, with an estimated 1,989 new cases and 920 deaths reported in 2022 (12). Both EBV prevalence and lymphoma subtype distribution exhibit marked geographic variation, influencing disease patterns and diagnostic predictive values (2,4). Burkitt's lymphoma, for instance, shows a strong epidemiological association with sub-Saharan Africa, including Nigeria (4). Despite this burden, there is an observed paucity of comprehensive data on haematological malignancies and EBV-associated lymphomas in Nigeria, particularly the North-eastern part of the country. Therefore, this study aimed to evaluate histomorphologic features

suggestive of EBV association in archived lymphoma histological specimens in Northeast Nigeria, with the objective of assessing the potential screening and diagnostic utility of the cytopathic observations.

Materials and Methods

A retrospective study was conducted at Modibbo Adama University Teaching Hospital (MAUTH), Yola. The study involved the review of archived tissue specimens and corresponding clinical records of patients previously diagnosed with lymphoma. Archived formalin-fixed paraffin-embedded (FFPE) tissue blocks of confirmed lymphoma patients were retrieved from the histopathology archives of MAUTH, and stained with H&E. Cases with insufficient tissue, poorly preserved specimens, or inadequate staining were excluded from the study. Relevant sociodemographic data such as, age, gender, place of residence, etc. were extracted from the patients' medical record. Clinical and behavioural variables potentially associated with lymphoma risk including smoking, alcohol consumption, presence of chronic diseases, and previous haematological disorders, co-infections were also obtained where available from the documented records.

The tissue blocks retrieved were previously fixed in 10% neutral buffered formalin for 24 h at room temperature and dehydrated through graded ethanol (50%, 70%, 95%, and 100%; 2 min each), cleared in two changes of xylene; 5 min each, and embedded in paraffin wax. Paraffin blocks were sectioned at 3 μ m thickness using a microtome. Sections were mounted on poly-L-lysine-coated glass slides and dried at 60 °C for 1 h. Sections were deparaffinised in two changes of xylene for 5 min each, and rehydrated through a descending alcohol series (100%, 95%, and 70%; 2 min each), followed by rinsing in distilled water. The slides were stained with

haematoxylin for 5 min and rinsed in running tap water for 5 min. Differentiation was performed using 1% acid alcohol (1% HCl in 70% ethanol) for 1 min, followed by immediate washing in distilled water. Bluing was achieved using tap water substitute for 1 min, followed by rinsing in running tap water for 5 min. The sections were counterstained with 1% eosin Y solution for 1 min, followed by brief rinsing in distilled water to remove excess stain. Stained sections were mounted using DPX mounting medium (Molechem) with glass coverslips. Stained sections were examined under a light microscope (Leica HistoCore BIOCUT). Representative images were captured using a digital imaging system attached to the microscope.

Descriptive statistics were performed using Microsoft Excel (Microsoft, Redmond, WA, USA). Graphs were generated using the same Microsoft Excel (Microsoft, Redmond, WA, USA), package. Ethical approval for the study was obtained from the Health Research Ethics Committee of Modibbo Adama University Teaching Hospital, Yola (Approval No MAUTHY/HREC/24/354 dated 17th October, 2024). Patient confidentiality was maintained throughout the study by anonymising all retrieved data.

Results

A total of fifty (50) Formalin-fixed Paraffin-Embedded (FFPE) lymphoma blocks were retrieved. Nine (9) cases were excluded due to unavailability of corresponding medical records at the time of data compilation. Additionally, ten (10) tissue blocks were deemed unsuitable for analysis owing to tissue deterioration during storage and hence, could not withstand sectioning or staining procedures. Consequently, thirty-one (31) FFPE lymphoma cases met the inclusion criteria and were included in the final analyses. The blocks/samples that met the inclusion criteria during the study period comprised of 45.2% (n=14) females and

54.8% (n=17) males (Figure 1). Among these, 64.3% (n=9) of females and 47.1% (n=8) of the males were married (Figure 1). The age of study participants ranged from 8 to 73 years, with a mean age of 35.2 years (Figure 2). Patients were seen from all senatorial zones of Adamawa State, including Mubi North, Mubi South, Maiha, Hong, Gombi, Song, Girei, Yola North, Yola South, and Mayo Belwa Local Government Areas, as well as neighbouring Jalingo in Taraba State, indicating a wide regional referral coverage.

The distribution of lymphomas in this study was found to vary based on sociodemographic parameters, such as age, gender. For instance, Burkitt's lymphoma constituted 32.2% (n=10) of the lymphoma cases reported in this study. Majority of these patients were males of ages between 8 – 19 years (Figure 2). Other NHL were found to be distributed across all age groups (10 – 73 years), while HL totals 9.7% (n=3) found in mid-age patients with 30 – 50 years old.

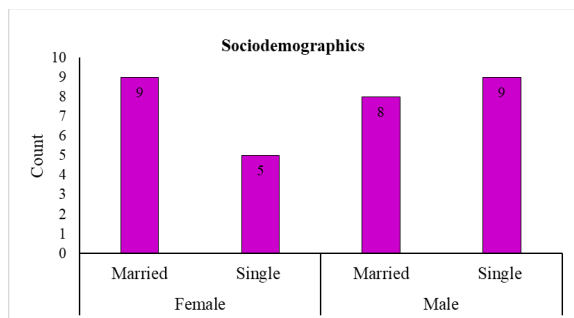


Figure 1: Gender and marital status of the study population

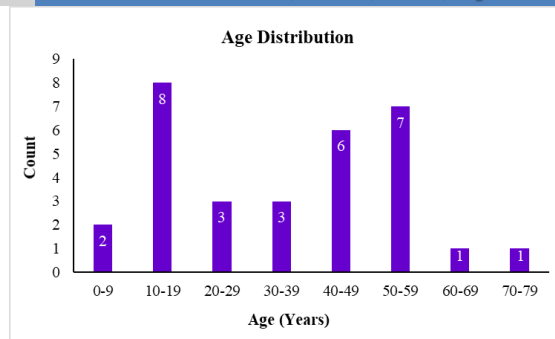


Figure 2: Age distribution of the study population

Based on the predefined morphological criteria observed in this study, 54.8% (n=17) of the cases were suggestive of EBV-associated lymphoma. These features include prominent large, multinucleated cells, some with large cytoplasm. Other features are Reed-Sternberg-like cells and angiocentric growth pattern, and starry-sky appearance. Co-infection with *M. tuberculosis* was detected in one of the cases. Most of the clinical diagnosis were linked to non-Hodgkin lymphomas (NHL), with 90.3% (n=28) cases. Of these, Burkitt's lymphoma made up a total of 32.2% (n=10), anaplastic large cell lymphoma 3.2% (n=1), follicular lymphoma 6.4% (n=2), and unclassified NHL constitute 48.4% (n=15) (Figure 3). Hodgkin lymphomas account for 9.7% (n=3) (Figure 3).

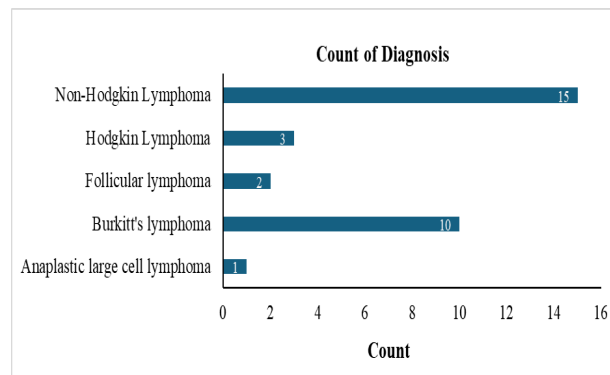


Figure 3: Clinical diagnosis of the study subjects

Burkitt's lymphoma cases were found predominantly in individuals aged ≤ 19 years.

While some of the tissue sections of Burkitt's lymphoma showed classical histomorphologic patterns consistent with EBV-associated cytopathic effects, others demonstrated typical morphology without obvious changes suggestive of EBV (Figure 4). The EBV-suggestive features observed in Burkitt's lymphoma included multinucleated large cells, Reed-Sternberg-like cells, and prominent starry-sky appearance (Figure 4). Furthermore, these children were shown to have normal range of monocytes including, neutrophils, lymphocytes, and eosinophils. Similarly, other non-Hodgkin lymphoma

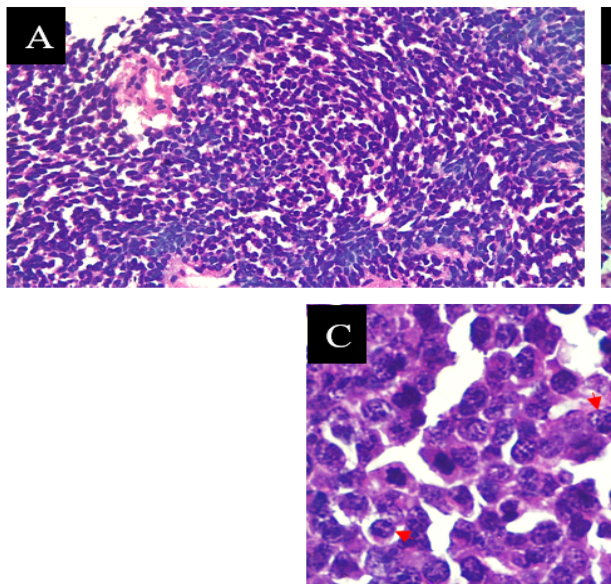


Figure 4: EBV morphologic features in Burkitt's lymphoma

A = showing no obvious EBV cytopathic effect (x100).

B = showing starry-sky appearance (x100).

C = showing multinucleated cells, and Reed-Sternberg-like cells (x400).

cases exhibited multinucleated atypical cells and Reed-Sternberg-like morphology (Figure 5), whereas a small proportion ($n = 3$) showed no obvious EBV-associated morphologic features. Hodgkin lymphoma (HL) accounted for 6.4% ($n=3$). All Hodgkin lymphoma cases demonstrated characteristic morphologic findings, including Reed-Sternberg-like cells, multinucleated large cells, and diffuse distribution of large atypical cells with abundant cytoplasm (Figure 6), consistent with features commonly reported in EBV-associated Hodgkin lymphoma (13).

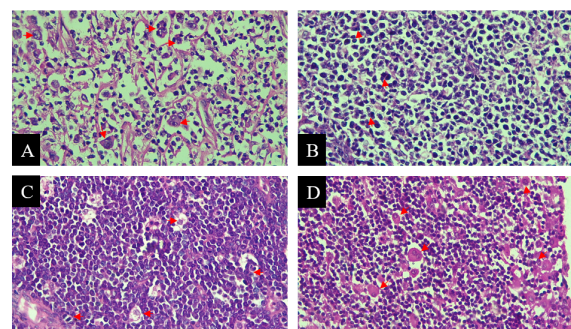


Figure 5: EBV morphologic features in non-Hodgkin lymphoma

A = showing Anaplastic large cell lymphoma (x100).

B = showing multinucleated large cells, and Reed-Sternberg-like cells (x100).

C = showing starry-sky appearance, and Reed-Sternberg-like cells (x100).

D = showing Anaplastic large cell lymphoma, cells with larger cytoplasm, and Reed-Sternberg-like cells (x100).

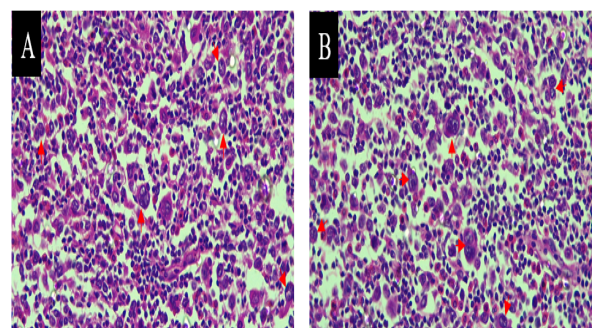


Figure 6: EBV morphologic features in Hodgkin lymphoma

A = showing wide-distribution of multinucleated large cells, and cells with large cytoplasm (x100).

B = showing wide-distribution of multinucleated large cells, and cells with large cytoplasm, and Reed-Sternberg-like cells (x100).

Discussion

Lymphomas constitute a significant source of malignancy-related morbidity and mortality globally and in Nigeria (14,15). Lymphomas, like most other malignancies, largely have uncertain aetiologies. However, strong empirical evidence has linked causality of some lymphoma to infection with Epstein-Barr virus. This variation in causality could be linked to the differences in environmental location among other sociodemographic parameters. EBV, a ubiquitous and oncogenic virus, is asymptotically carried by more than 90% of the human population (1,16). The virus preferentially and efficiently infects and establishes lifelong latency in lymphocytes (6,17). EBV-associated malignancies are characterised with high fatality risk. Estimates indicate that globally, approximately 239,700 - 357,900 people develop EBV-associated malignancies annually, with around 137,900 - 208,700 deaths (4). This represents ~ 60% fatality. EBV was first identified in the Africa region in 1964 in a case of Burkitt's lymphoma (1). The global picture reveals that haematological malignancies are ranked in the top 10% of all malignancies worldwide (12), and they are diagnosed in both males and females in developed and developing countries of the world (4,18). Nonetheless, the findings in this study and many previous literature imply an increased incidence risk of lymphomas in males than females (19,20). This gender inclination could be attributed to the direct anti-proliferative effects of estrogen on lymphocytes that express the estrogen receptor (19,20). Increasing lymphoma incidence observed worldwide

could partly be attributed to improved diagnostic capabilities, heightened disease awareness, and advances in tumour classification systems.

The distribution of lymphomas in this study varies considerably across sociodemographic factors, such as age, gender, marital status, geographical location, clinical presentations, treatment options and prognosis (2). For instance, Burkitt's lymphoma constituted one-third of the lymphoma cases reported in this study, comprises majority of male patients with ages between 8 – 19 years. Of this, paediatrics of ≤ 14 years constituted the majority. This findings conforms with many previous studies as compiled in a review article by Khan and colleagues (4). Similarly, in the present study, non-Hodgkin lymphoma (NHL) constituted the predominant lymphoma subtype in MAUTH compared with Hodgkin lymphoma (HL). This is consistent with epidemiological patterns reported globally and within Nigeria (15,21). It is also reported that married lymphoma patients are shown to have superior 5-year survival outcomes compared to their unmarried counterparts (22). This impact is observed in many haematologic malignancies and also multiple solid tumours (22,23). Although this observation is not yet biologically described, it could be attributed to social factors such as emotional and financial support, improved adherence of the long-term treatment regimens, and greater access to healthcare services (22,23). The increased number of married patients observed this study could be ascribed to the mentioned social factors that may lead the married patients have access to early and proper diagnosis.

We further evaluated the usefulness of H&E morphology as a screening tool for EBV in lymphoma cases. Our findings demonstrate that H&E-based assessment indicated moderate-to-high sensitivity and specificity,

with positive predictive value in specific Burkitt's lymphoma and other non-Hodgkin lymphoma. The morphologic features often predictive of EBV positivity were large, multinucleated cells with large cytoplasm, Reed-Sternberg-like cells, and angiocentric growth, and "starry-sky" patterns, etc. The "starry-sky" pattern and high mitotic activity observed in Burkitt's lymphoma correlated strongly with EBV positivity, especially in paediatric and endemic cases (24).

Although we found that the lymphoma biopsies at MAUTH express morphologic changes typical of EBV, we were not able to histopathologically investigate for EBV markers due to paucity of tools. Furthermore, efforts to screen for the EBV markers using PCR amplification proves abortive probably due to the nature of the biopsies as recovering DNA from the FFPE samples is very challenging. Therefore, it is recommended that future studies to perform histopathological screening for EBV markers in lymphoma biopsies in Northeast Nigeria, particularly at MAUTH.

While H&E morphology demonstrated potential positive predictive value, histologic assessment alone does not seem sufficient to establish EBV diagnosis. This is because EBV-positive lymphomas may exhibit overlapping morphologic features with EBV-negative counterparts, and thus, cases may lack distinctive morphologic clues. Though Epstein-Barr encoded RNA (EBER) *in situ* hybridisation remains the gold standard for detecting latent EBV infection in tissue sections due to its high sensitivity and specificity (7,25), its application for routine screening in resource-limited settings may not be feasible due to its high financial and infrastructural cost. We therefore support a realistic diagnostic approach in which morphologic prediction on routine H&E examination guides selective application of confirmatory EBV testing. Such targeted testing strategies may improve diagnostic efficiency and resource utilisation in many Nigerian hospitals.

Conclusion

This study demonstrates that routine haematoxylin and eosin histomorphologic evaluation may serve as a useful preliminary screening tool for identifying lymphomas with potential Epstein-Barr virus association, particularly in resource-constrained environments where advanced diagnostics are limited. However, the absence of standardised morphologic indicators may contribute to false-negative or indeterminate interpretations when morphology alone is relied upon. Consequently, confirmation of EBV involvement should incorporate ancillary diagnostic techniques such as EBER *in situ* hybridisation or immunohistochemistry. Establishing reproducible morphologic criteria capable of predicting EBV status on routine histology would facilitate prioritisation of cases for confirmatory testing and improve diagnostic accuracy. Therefore, future studies, are recommended to utilise both retrospective and prospective methods to standardised morphologic scoring systems for predicting EBV in lymphomas.

Limitation of the study

The limitations of this study include its retrospective design, relatively small sample size, and single-centre setting, which may limit generalisability of the findings. Therefore, multicentre studies involving larger cohorts and incorporating confirmatory EBV validation are recommended to develop and standardised histomorphologic scoring systems for predicting EBV status in lymphoma cases.

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Conflict of Interest

The authors declare no competing interests.

TRIPLE NEGATIVE BREAST CANCER IN MAIDUGURI, NORTH EAST NIGERIA: A FIVE YEAR REVIEW

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Abstract

Introduction: Breast cancer is the most common malignant neoplasm and a leading cause of cancer related deaths among women worldwide. Traditional breast cancer classification based on histopathologic features has limited prognostic and predictive value compared to the molecular classification. Currently, three biomarkers are commonly used to classify breast cancer including estrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor-2 (HER-2). Assessing these markers help to select patients appropriately for treatment targeted on these major molecular pathways of the disease. A breast cancer that fails to express ER and PR, and has absence of HER-2 overexpression is designated Triple Negative. Paucity of information on triple negative breast cancer from North Eastern Nigeria prompted this study. **Methods:** The study was a hospital based, descriptive and cross sectional one. One hundred and thirteen (n=113) archived tissue blocks from confirmed cases of breast cancer that fulfilled the inclusion criteria for the study were retrieved along with their request cards. Immunohistochemistry was performed on the tissue blocks using monoclonal mouse antibodies to human ER, PR and HER-2 (Novocastra post primary, Leica Biosystems REF7111, 7102 and 7101 respectively). The slides were evaluated using the J score. Equivocal HER-2 cases had FISH done on them at Unistel medical laboratories, South Africa using the IQFISH protocol. The slides were evaluated using the ASCO/CAP 2013 guidelines. **Results:** Out of the 1415 cancers diagnosed at the Department of Histopathology, University of Maiduguri Teaching Hospital (UMTH) over the study period, breast cancer accounted for 276 (19.5%) cases. Of the 113 breast cancer cases analysed by immunohistochemistry for the study, 78(69%) were triple negative breast cancer. TNBC was predominantly invasive carcinomas, 72 (92.3%) cases. The histological Grades 1, 2, and 3 recorded 1 (0.9%), 43 (38.1%), and 56 (49.6%) cases, respectively. **Conclusion:** The present study buttresses the fact that breast cancer in Nigeria is predominantly triple negative (69%) and have a high unfavourable molecular subclass (Basal-like). It also shows that triple negative /basal like tumours have high cases of grade 3 carcinoma (53.8%) which may partly explain the poor treatment outcomes being experienced. It also shows that FISH if available, can influence management decisions in cases that are HER-2 equivocal by immunohistochemistry.

Key words: Triple Negative Breast Cancer(TNBC), immunohistochemistry, FISH, Maiduguri

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Introduction

Breast cancer is a clinically heterogeneous disease.¹ It is the most common cancer among women worldwide.¹ More than two million cases occur annually worldwide.² GLOBOCAN 2022 data indicated that breast cancer is the most frequently diagnosed female cancer worldwide accounting for 11.6% of all diagnosed cancer.² It is also the most frequently diagnosed cancer in Africa (16.8%)³ and Europe (13.1%)⁴. An estimated 2.9 million women live with breast cancer in the United States of America.⁵ The incidence in the USA is higher among non-Hispanic whites but mortality is higher among African Americans. In Africa, breast cancer accounts for 27.6% of all cancers in females.⁵ The incidence varies with regions across the continent. In Nigeria, breast cancer has been reported to be the most common cancer in females in many centres. Ezenkwa *et al*⁶ in a recent study in Northeastern Nigeria showed that breast cancer is the leading cancer accounting for 22.9% of all cancers in the region. Despite much research work in the field of cancer research, it is still a mystery why a neoplasm arising in an organ readily accessible to self-examination and clinical diagnosis, continues to exert such a heavy toll.⁷ Late presentation, lack of systemic screening programs, ignorance of the nature of disease, economic, sociocultural factors for breast cancer among many other limiting factors has hindered the management of breast cancer, with up to 90% of cases diagnosed at stage III-IV of the disease in Africa.⁸ Seeing that patients with early breast cancer can present with metastasis, breast cancer is now considered a systematic disease from the outset and the approach toward clinical assessment and management of breast cancer has substantially changed over the past few decades to reflect the emerging reality.⁸ The trend is toward a more conservative surgical approach and use of chemotherapy and hormonal therapy. The use of adjuvant therapy has clearly proven beneficial by helping eradicate metastatic deposits.¹ Breast cancer has traditionally

been classified on the basis of its histopathological features which have been shown to have low prognostic and predictive value.⁹ A more recent molecular classification that is based on hierarchical clustering analysis of gene expression profiling has been proposed. This microarray based molecular classification has better prognostic value and is of predictive value therapeutically.¹⁰ The molecular classification has been shown to bear striking similarity to those of immunohistochemically defined schemes using antibodies to known breast markers.¹¹ These markers are used as surrogates for the molecular classification. Immunohistochemistry as an adjunct in assessing molecular pattern of breast cancer has contributed to prognostication of the disease.¹² Currently, three biomarkers are commonly used to classify breast cancer including estrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor-2 (HER-2)¹² Assessing these markers help to select patients appropriately for treatment targeted on these major molecular pathways of the disease.

A breast cancer that fails to express ER and PR, and has absence of HER-2 overexpression is designated “Triple Negative.”¹³ Triple negative breast cancer (TNBC) compared with other groups of breast cancer describes a subtype of this malignant disease with worse prognosis and dismal survival outcomes.¹⁴ It is associated with unfavorable and aggressive clinicopathological features including onset at a younger age, high grade, pushing borders, poorer Nottingham prognostic index, much frequent node positivity, higher incidence of recurrence, distant metastasis, and poorer survival.¹⁵ The TNBC is described also as a heterogeneous disease because molecular panels such as basal keratin and other markers (Ck5/6, Ck14, Ck17, 34BE112, CD117, EGFR, P53, and SMA) have been used in subtyping TNBCs into two groups.¹⁶ Positivity for these stains describes the basal TNBCs, to differentiate it

from the non-basal subtype. The former constitute the majority of TNBCs and has a worse prognosis than the latter.¹⁷ This study is aimed to determine the proportion of TNBCs in 113 patients who had immunohistochemical studies (ER, PR and HER-2) and FISH (fluorescent in situ hybridization) as well as their relationship to histological type and histological grade.

Methods

The study was conducted at UMTH, Maiduguri which is the apex referral centre in the Northeastern region of Nigeria. The study was a hospital based and descriptive. One hundred and thirteen (113) breast cancer cases that fulfilled the study criteria had their archived tissue blocks along with their request cards retrieved (over a five-year period, 2010-2014). The histologic diagnosis and tumour grade were retrieved from the reports.

Immunohistochemistry was performed on the tissue blocks using monoclonal mouse antibodies to human ER, PR and HER-2 (Novocastra Post Primary Leica Biosystems REF711, 7102 and 7101 respectively).¹⁸

Sections from the tissue blocks were initially stained with haematoxylin and eosin (H&E) to determine their adequacy for immunohistochemistry. Four micrometer thick sections were taken from each tissue block and mounted on adhesive coated glass slides preparatory to immunohistochemical staining.

Sections were deparaffinised in xylene for 10 minutes, rehydrated in grades of alcohol followed by blocking of endogenous peroxidase activity using 0.5% hydrogen peroxide. Heat induced epitope retrieval was achieved using microwave incubation in citrated buffer (0.1M: PH6.0). Antigen localisation was achieved by incubating sections with primary antibody followed by application of primary antibody enhancer. The indirect avidin-biotin complex procedure using 3,3-aminobenzidine tetrahydrochlorate

(DAB) as substrate chromogen was applied for detection of bound antibodies.¹⁹

The scoring system for ER and PR status was based on J score which score the percentage of tumor cells with nuclear staining: Score 0, no stained cells; Score 1+, stained cells $\leq 1\%$; Score 2+, $1\% < \text{stained cells} < 10\%$; and Score 3+, stained cells $\geq 10\%$. Scores 0 was classified as negative; Scores 1 and 2 as intermediate; and Score 3 as positive. HER-2 staining was scored based on membrane staining pattern (intensity and completeness)-Hercept test: score 0, when no staining is observed, or is seen in $< 10\%$ of tumor cells; Score 1+, when staining is faint/barely seen in $> 10\%$ of tumor cells; Score 2+, when a weak/moderate complete staining is observed in $> 10\%$ of tumor cell; and Score 3+, when a strong complete staining is detected in $> 10\%$ of tumor cells. Score 0 and 1+ were classified as negative; Score 2+ as inconclusive (weakly positive); and Score 3+ as positive.²⁰ Specimens that fail to be positive for ER, PR, and HER-2 earned the triple negative designation.

Equivocal HER-2 cases had FISH done using the standard IQFISH protocol at Unistel Medical Laboratory, Stellenbosch University, South Africa and reported using the 2013 American Society of Clinical Oncologists /College of American Pathologists (ASCO/CAP) guideline.²¹

Results

A total of 113 cases of breast cancers were eligible for the study having fulfilled the inclusion criteria and all had immunohistochemistry done on them. Out of these, a total of 78 (69%) cases were negative for all three immunohistochemical markers and included in the study. Two biopsies were initially equivocal by immunohistochemistry and over amplified on doing FISH.

Invasive carcinoma (NST) constituted the vast majority of histological types of breast cancer, accounting for 100(88.5%) cases. The TNBC was predominantly invasive

carcinomas, 72 (92.3%) cases. The remaining 6 (7.7%) cases of TNBC were invasive lobular carcinomas. (Table 2)

The histological Grades 1, 2, and 3 recorded 1 (0.9%), 43 (38.1%), and 56 (49.6%) cases, respectively (Table 3). The association between histological grade and TNBC status for Grades 1, 2, and 3, were 1 (1.4%), 28 (38.8%), and 42 (58.3%) of cases, respectively.

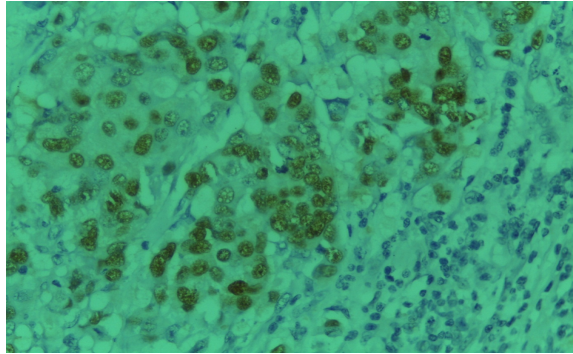


Figure 1: Photomicrograph of ER positive breast cancer
The section shows nuclear staining in about seventy percent of the tumour cells (J- Score) (X200)

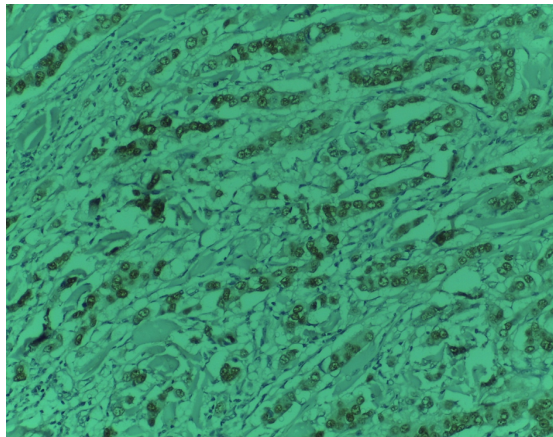


Figure 2: Photomicrograph of PR positive breast cancer
The section shows nuclear staining that is visible in sixty percent of the tumour cells (J-Score) (X200)

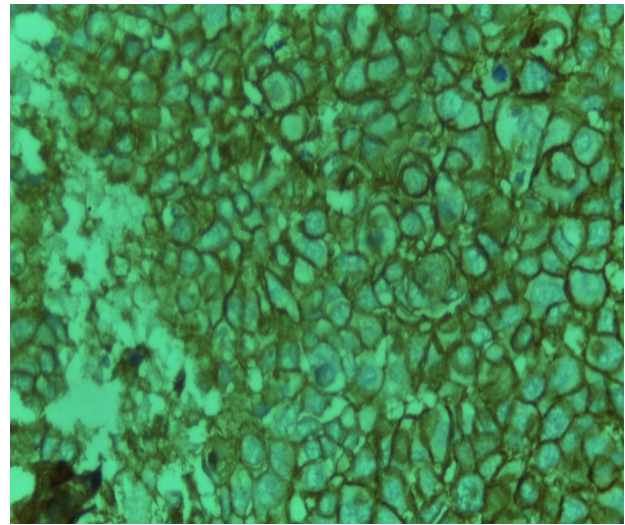


Figure 3: photomicrograph of HER-2 positive breast cancer
The section shows complete, strong membrane staining in 90% of tumour cells. (X200)

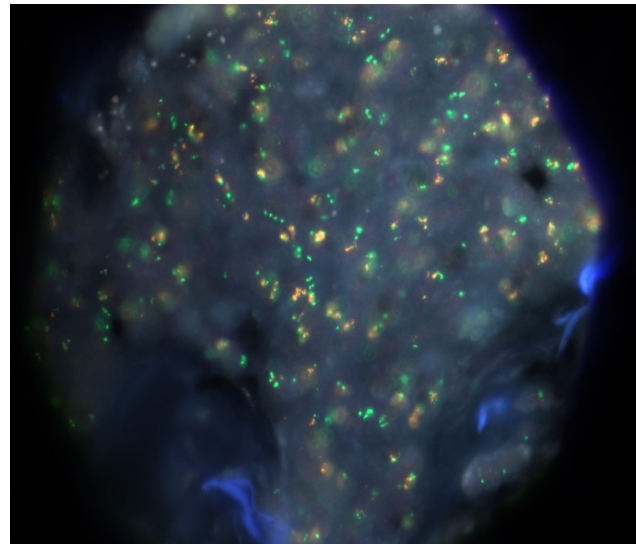


Figure 4: fluorescent in situ hybridization photomicrograph.
The photomicrograph shows amplification of HER-2. The orange signal represents *HER2* and the green signals chromosome 17(*CEP17*). The HER-2/cep 17 ratio was 3.49 and the average HER-2 copy number equals 12.05

Table I: Frequency Distribution of ER, PR and HER-2 among individual Breast Cancer Cases (N=113)

Immunohistochemical markers	Frequency distribution	Percentage (%)
ER, PR, HER-2 negative	78	69
ER, PR, HER-2 positive	0	0
ER, PR positive	10	8.8
ER, HER-2 positive	1	0.9
PR, HER-2 positive	1	0.9
ER positive	12	10.6
PR positive	1	0.9
HER-2 positive	10	8.8
Total	113	100.0

Table II: Frequency Distribution of Breast Cancer according to histologic types

Histologic Type	Frequency(%)	Frequency in TNBC(%)
Invasive Carcinoma NST	100(88.5)	72(92.3)
Invasive lobular Carcinoma	12(10.6)	6(7.7)
Mucinous Carcinoma	1(0.9)	-

Table III: Frequency Distribution of Breast Cancer according to histologic grade

Histologic Grade	Frequency(%)	Frequency in TNBC(%)
1	1(0.9)	1(1.4)
2	43(38.1)	28(38.8)
3	56(49.6)	42(58.3)
Special Types	12(10.6)	1(1.4)

Discussion

There were a total of 1415 histologically diagnosed cancers in the diagnosis register of Histopathology department UMTH during the five year study period (2010-2014). Out of this number, breast cancer constituted 276 cases accounting for 19.5% of all cancers diagnosed during the study period. This figure is higher than the 13.9% reported by Nggada *et al.*²² in the same centre 2001-2005. This may be attributable to more awareness on breast cancer and its screening methods as well as increased access to health care facilities by the rural dwellers in the region that were displaced by insurgency to Maiduguri the state capital.

The Index study observed the frequency of hormone receptors (ER and PR) and HER-2/neu (as shown in table I to be 24 (21.2%) for ER, 11(9.7%) for PR and 13 (11.5%) for HER-2 while 78 (69%) were negative for all three markers. The total frequencies are in agreement with most studies from other parts of Nigeria that show a low hormone receptor and HER-2 positivity and high triple negativity.²³⁻²⁹ Minoza *et al.*²⁵ in the same facility in 2016, reported triple negative breast cancers of 52.6% while Mandong *et al.* in Jos recorded TNBC of 41.3%.⁸

Stark *et al.*¹² in Ghana compared hormone receptor and HER status between White Americans, African Americans and Africans (Ghanaians) breast cancer patients and recorded ER of 22.8%, PR of 30.8% and HER-2 of 5.3% among Ghanaians. Their findings show a low hormone receptor and HER-2 positivity similar to the index study.

In two comparative studies between Nigerian and British breast cancer women, Agboola *et al.*^{26,27} reported ER of 72% and 51%, PR of 58.3% and 38.7% and HER-2 of 12.5% and 14.7% respectively among the British cohort. These findings are at variance with the index study and most other studies from Africa.

The results for hormone receptors ER and PR in the index study are similar to other studies

in Nigeria and Africa where breast cancer cases are more likely to be hormone receptor negative.²³ Some studies have shown that there is significant difference in oestrogen signaling and levels between Blacks and Caucasians with blacks having a decreased level of the protective *ERα* isoform.^{23,30}

The index study observed that invasive carcinoma NST was the most prevalent histological variant accounting for 100(88.5%) cases out of which 72(92.3%) are TNBC. This finding is similar to those of other researchers in Nigeria. Mandong *et al.*⁸ in Jos, recorded 92.3% of triple negative breast cancer cases being invasive carcinomas. Ohehe-Yeboah *et al.*³¹ recorded TNBC/basal-like subtype of 42.7% in Ghana,

Using the modified SBR (Nottingham) grading system, the index study observed that out of the 113 cases analysed, there was 1 (0.9%) case of grade 1 carcinoma, 43 (38.1%) cases of grade 2 carcinoma and 56 (49.6%) cases of grade 3 carcinoma as shown in table IV. Thirteen (11.5%) cases were special type carcinomas out of which 12 (10.6%) cases were invasive lobular carcinoma and 1 (0.9%) case a mucinous carcinoma. The findings from this study corroborates those of other studies from other centres in Nigeria and Africa where breast cancers from this part of the world are predominantly high grade and poorly differentiated. Minoza *et al.*²⁶ reported 63.2% of grade 3 cancers in Maiduguri. Other studies observed 60%, 69.7 70%, and 65% and in Uganda, Ife, Jos, and Gombe respectively.^{23,24,32,33} Studies from Switzerland, India and Oman reported lower prevalences of grade 3 cancers accounting for 27.1%, 22.9% and 30.2% respectively.^{34,35,36} Their findings are similar to those of Caucasians who are more likely to present with lower grade tumours (grade 1 and 2) which in this study accounted for 0.9% and 38.1% respectively. Studies have shown that histological grade alone or as a component of Nottingham prognostic index can be used to predict biological behaviour and outcome of breast cancer management.³⁵ Grade 3

tumours have been shown to have poor prognosis. Preponderance of grade 3 cancers in this study may further assert findings from other studies in Nigeria as cited above, that breast cancers in our setting are mainly high-grade tumours.

Studies have observed significant differences among molecular subtypes relating to tumour grade.³⁵ The index study showed that triple negative/Basal-like tumours showed high prevalence of grade 3 tumours 58.3% with well and moderately differentiated tumours constituting 1.4% and 38.8% respectively. Spitale *et al.*³⁵ reported similar findings with 75.9% of TNBC/basal-like tumours being high grade. They also alluded to the fact that other studies in Carolina, California and Poland showed poorly differentiated carcinoma constituting 82%, 71.1% and 72% of basal-like subtype respectively.³⁵

Immunohistochemical panels such as basal keratin Ck5/6 have been used in subtyping TNBCs into two groups.¹⁶ Positivity for these stains describes the basal TNBCs while negativity describes the non-basal subtype. The current study did not assess for CK5/6. It is also known that majority of TNBC arise in women with BRCA1 mutation.⁸ However, our study did not assess the status of BRCA1.

Conclusion

This study buttresses the fact that breast cancer in Nigeria is predominantly triple negative. The results show low hormone receptor and HER-2 positivity with an over representation of triple negative breast cancer which predicts poor response to hormonal therapy. The study suggests that empirical use of anti-hormonal therapy without prior receptor status testing in this environment be discouraged. It also shows that triple negative/basal like tumours have high cases of grade 3 carcinoma (53.8%) which may partly explain the poor treatment outcomes being experienced.

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Conflict Of Interest

The authors declare no conflicts of interest with respect to this research.

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GIANT SUBMANDIBULAR SIALOLITH: A CASE REPORT AND REVIEW OF THE LITERATURE

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Abstract

Background: Sialolithiasis refers to the presence of calcified structures within the ducts of salivary glands and is the most common disorder affecting these glands. It is the most common obstructive pathology of the major salivary glands, with the submandibular gland being most frequently affected. Giant sialoliths (>15 mm) are rare and often present with atypical or prolonged symptoms. It can be diagnosed through clinical examination, conventional radiography, computed tomography, and ultrasonography.

Case Presentation: We report a 39-year-old female who presented to the Maxillofacial Surgery Clinic of Yobe State University teaching hospital in Damaturu with a 5-month history of persistent pain and swelling in the right floor of the mouth. Clinical and radiological evaluation revealed a giant submandibular duct sialolith measuring 3 × 2 cm. Initial conservative management was unsuccessful, necessitating surgical removal under general anaesthesia via a transoral approach. Postoperative recovery was uneventful, with complete resolution of symptoms.

Conclusion: This case underscores the importance of early diagnosis and appropriate imaging in suspected salivary gland obstruction. Surgical excision remains the definitive treatment for giant sialoliths when minimally invasive modalities are not feasible.

Keywords: Sialolithiasis; Submandibular gland; Giant sialolith; Salivary gland obstruction; Transoral excision.

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Introduction

Sialolithiasis refers to the formation of calcified structures (sialoliths) within the salivary glands or their ducts. It may develop either in the parenchyma or the ductal system of a salivary gland [1]. It accounts for approximately 30–50% of all salivary gland diseases and represents the leading cause of obstructive sialadenitis [2]. The submandibular gland is most commonly affected, with 80–90% of stones occurring within Wharton's duct. This is followed by the parotid gland (19%) and the sublingual gland (1%) [3]. This predilection is attributed to anatomical and physiological factors, including the long, upward course of the duct and the viscous, mucin-rich, alkaline nature of submandibular saliva [4,5].

Most sialoliths measure less than 10 mm in diameter. Stones exceeding 15 mm are classified as giant sialoliths and account for less than 1% of reported cases [4]. These giant calculi pose unique diagnostic and therapeutic challenges due to their size, chronicity, and association with ductal damage, secondary infection, and gland dysfunction.

The pathogenesis of sialolithiasis is multifactorial. Calcium salts precipitate around an organic nidus composed of desquamated epithelial cells, bacteria, or mucous plugs [7]. Predisposing factors include reduced salivary flow, dehydration, ductal stenosis, smoking, and systemic conditions such as gout and nephrolithiasis [8,9].

Clinically, sialolithiasis typically presents with salivary colic—pain and swelling during meals. Prolonged obstruction may result in chronic sialadenitis, abscess formation, or glandular atrophy [10]. While small stones may pass spontaneously or respond to conservative measures, giant sialoliths rarely do and usually require surgical intervention [6].

Diagnostic imaging plays a critical role in evaluation. Plain radiographs can identify most radiopaque stones, whereas ultrasonography and computed tomography (CT) offer superior sensitivity for radiolucent or posteriorly located calculi. CT remains the gold standard for assessing stone size, location, and associated glandular pathology [11].

Management strategies have evolved considerably over recent decades. Minimally invasive techniques such as sialendoscopy, extracorporeal shock-wave lithotripsy (ESWL), and combined endoscopic–transoral approaches are now widely employed [12,13]. However, giant stones often require open transoral excision due to their size, impaction, and limited response to fragmentation [12]. Given the rarity of sialoliths exceeding 30 mm, documentation of such cases remains clinically valuable.

Case Presentation

A 39-year-old female presented at the Maxillofacial Surgery Clinic of Yobe State University teaching hospital in Damaturu with a 5-month history of progressive pain and swelling in the right floor of the mouth. The pain was exacerbated during meals and partially relieved by analgesics. There was no associated dysphagia or systemic illness.

Clinical examination revealed a firm, hard mass palpable in the right floor of the mouth along the course of Wharton's duct. Oral hygiene was fair, and mouth opening was unrestricted. Plain radiography demonstrated a well-defined radiopaque mass consistent with a large submandibular duct sialolith (Fig. 2)

An initial attempt at stone milking under local anaesthesia was unsuccessful. The patient was therefore scheduled for transoral sialolith removal under general anaesthesia after adequate counselling and taking informed consent. With the patient in the supine position and orotracheally intubated, a stay suture was placed on the anterior two-

thirds of the tongue to facilitate retraction. After infiltration with 2% lignocaine containing adrenaline, the surrounding tissues were gently dilated using a curved haemostat. The calculus was delivered intact (Figure 3). The cavity was irrigated with saline, followed by debridement of epithelialised and chronic granulation tissue. Haemostasis was achieved, and the defect was closed with 4-0 Vicryl sutures (Figure 4). Estimated blood loss was approximately 3 mL

A yellowish, kidney-shaped, rough-surfaced calculus measuring 3×2 cm was removed and sent for histopathological evaluation. The postoperative course was uneventful, with complete symptom resolution after 3 months of periodic review and follow-up.

Discussion

This report documents a giant submandibular sialolith measuring approximately 30–35 mm, far exceeding the size of typical salivary calculi encountered in routine practice. Liu et al. reported similar giant stones but emphasised their extreme rarity, while Bodner noted that such calculi constitute less than 0.5% of all sialolithiasis cases [5,16].

The clinical presentation of pain and swelling during meals in this patient is consistent with classical descriptions of sialolithiasis [10]. However, the prolonged duration of symptoms before presentation exceeds that seen in most routine cases. Leung and Katz observed that delayed diagnosis increases the risk of recurrent infection, ductal stenosis, and gland fibrosis [8]. In the present case, timely surgical intervention prevented irreversible gland damage.

Although minimally invasive techniques such as sialendoscopy, extracorporeal shock-wave lithotripsy (ESWL), and combined endoscopic-transoral approaches were documented in the literature [12, 13], transoral excision remains a cornerstone in the management of giant submandibular stones. While Marchal and Dulguerov

documented a historical reliance on gland excision, modern practice increasingly favours gland-preserving approaches [12]. Although sialendoscopy and ESWL are effective for smaller or mobile stones, Capaccio et al. and Koch et al. demonstrated that large, impacted calculi often necessitate open transoral removal [13,14], as was appropriate in this case.

Radiographic evaluation using plain imaging was sufficient due to the stone's radiopaque nature and anterior location. Although CT provides superior anatomical detail, Madani and Beale noted that basic imaging remains adequate for clearly calcified anterior stones [11].

In a case report by Nupur Agarwal et al in northern India of submandibular sialolith in a 50-year-old man, it was reported to measure about 1.5×0.8 cm in dimensions and another 0.4 cm in diameter using CBCT. [15] Importantly, reports from Nigeria and other African settings confirm that giant submandibular sialoliths occur regionally and may reach dimensions comparable to those described here [17,18]. A case from Port Harcourt documented a 40×25 mm submandibular calculus, while another Nigerian report described a “megalith” measuring 37×16 mm. These regional reports, together with global literature, demonstrate that although rare, very large calculi are encountered in African practice and can be managed successfully with appropriate surgical intervention. The present case adds to this limited but growing body of regional evidence.

Conclusion

This case highlights successful transoral removal of a rare giant submandibular sialolith measuring approximately 3 cm, without the need for gland excision. Early diagnosis, appropriate imaging, and an individualised surgical approach are essential for optimal outcomes. Continued reporting of

similar cases will improve understanding of the epidemiology and management of giant salivary calculi. outcomes for giant salivary stones.



Figure 1. Clinical Photograph of the patient with the stone insitu



Figure 2. Periapical Radiograph of the patients showing the stone around the right submandibular region.

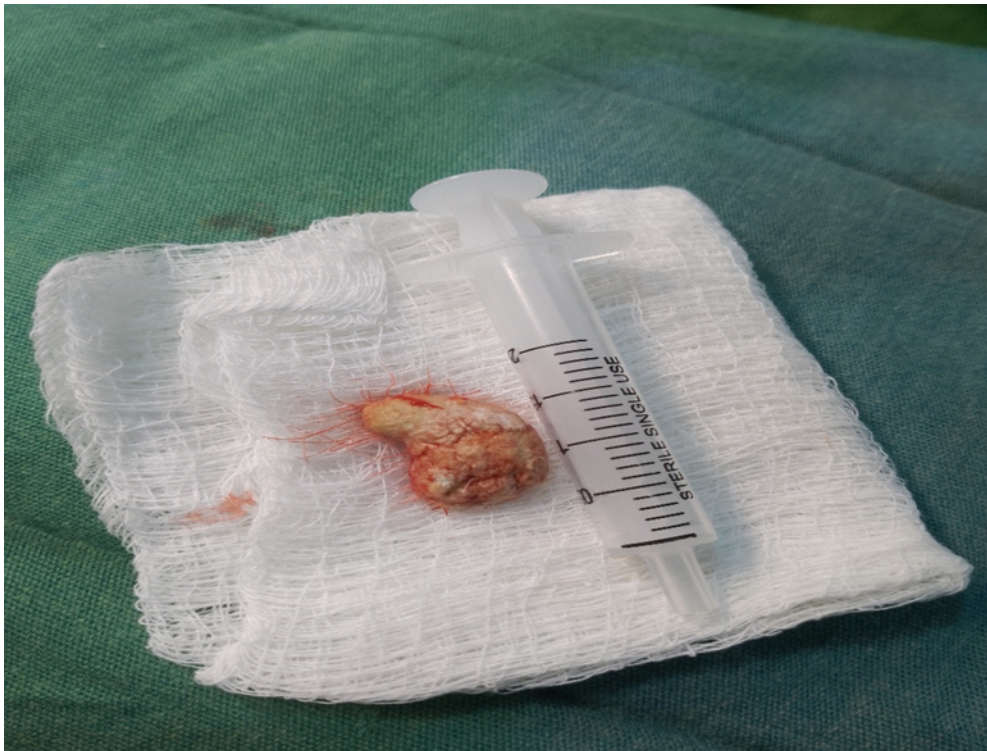


Figure 3. Clinical Photograph of the stone removed

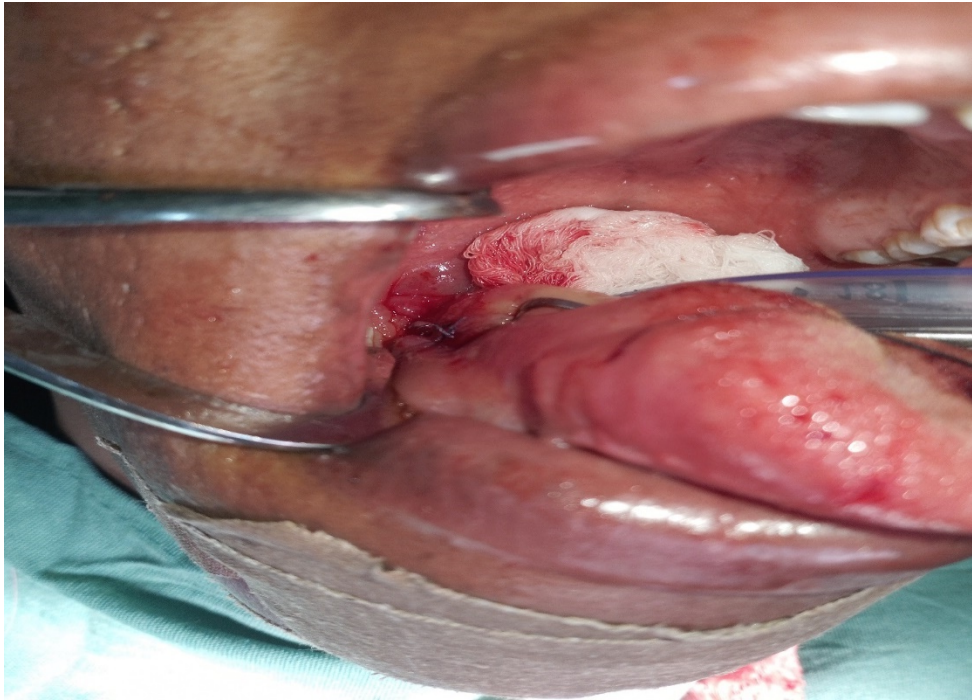


Figure 4. Clinical Photograph of the patient with the surgical site sutured

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COMMUNICATING HYDROCELE IN AN ADULT: CASE REPORT AND REVIEW OF LITERATUREBashir Musa Umar¹, Idowu Gabriel Ajiboye¹, Isa Hassan Muhammad²¹Department of Surgery, Gombe State University/State Specialists Hospital, Gombe State, Nigeria²Department of Radiology, Yobe State University/Yobe State University Teaching Hospital Damaturu, Yobe State, Nigeria³Department of Surgery, Bayero University Kano/Aminu Kano Teaching Hospital, Kano State, Nigeria**Corresponding Author:** Dr Bashir Musa Umar, Email: ymbashiru@gmail.com

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Abstract

Background: Communicating hydrocele is uncommon in adults and often results from an unrecognized or a neglected childhood patent processus vaginalis (PPV). Recurrence occurs when misdiagnosed and treated as vaginal hydrocele, underscoring the importance accurate pre-operative diagnosis. **Case report:** We present a case report of a 41-year-old man who presented to us with communicating hydrocele and was managed by PPV ligation and Lord's placation via a trans-inguinal approach. **Conclusion:** Communicating hydrocele should be considered in adults presenting with inguinoscrotal swelling, especially when clinical features are atypical. A carefully planned surgical approach minimizes recurrence. Groin approach alone may be sufficient in selected patients.

Keywords: Communicating hydrocele, Patent processus vaginalis, Adult, Case report**Cite this article:** Umar BM, Ajiboye IG, Muhammad IH. **Communicating hydrocele in an adult: case report and review of literature.** Yob Med J.2026;2(1):60-65

Introduction

Hydrocele is the accumulation of fluid within the tunica vaginalis. A communicating hydrocele occurs when fluid from the peritoneal cavity passes through a patent processus vaginalis (PPV) which is a developmental structure, and accumulates within the tunica vaginalis.¹ Vaginal hydrocele on the other hand, which primarily intra-scrotal, is the fluid accumulation due to an imbalance of fluid production and absorption within the epithelial lining of the tunica.²

Because of its rarity, communicating hydrocele is easily missed. The approach in a misdiagnosed communicating hydrocele (scrotal approach) does not give access to the PPV, leading to recurrence. Therefore, recognition of this uncommon clinical entity is important for better treatment outcomes.³

Case report

A 41-year-old man presented to us with the complaint of right scrotal swelling which was noticed about 2 years prior to presentation. The swelling increases during day time but does not reduce completely when lying supine or when manipulated. It was painless. He also noticed that the scrotal swelling occasionally extends to the groin area. The patient could not remember noting a swelling in the groin or scrotum during childhood. No symptoms suggestive of intestinal obstruction and no lower urinary tract symptoms. No abdominal swelling or chest symptoms and no known co-morbidities.

Abdominal examination was normal. He has normal male external genitalia with a normal testis in the left scrotum. There was a right inguinoscrotal swelling which has a palpable cough impulse. The swelling was soft, non-tender and has no differential warmth. The swelling was not reducible and the ipsilateral testis could not be separated from the swelling. A clinical diagnosis of non-reducible right inguinoscrotal hernia was made keeping in mind the possibility of a communicating hydrocele. Abdominal ultrasonography reported normal study. Groin and scrotal ultrasound scan showed fluid within the scrotum and extending into the

inguinal region, suggesting a communicating hydrocele. The serum electrolytes, urea and creatinine were within normal limits. Full blood count parameters were also adequate.

Informed consent for surgery was obtained.

The patient was placed in a supine position after spinal anaesthesia was given. Surgical access was via an oblique right groin incision. A fluid-filled sac was noticed upon opening of the anterior wall of the inguinal canal, consistent with an encysted hydrocele of the cord. However, when the sac was gently separated from the cord structures it was noticed to be continuous with fluid in the tunica vaginalis in the scrotum medially and to the peritoneal cavity at the deep ring laterally (Figure 1). The deep ring was also wide. Fluid from the tunica could be forced through the sac into the peritoneal cavity. The patient was instructed to cough and there were no bowel loops herniating into this transparent sac.

The processus was double clamped and high-ligated using vicryl 1 suture. It was then excised (Figure 2). The lateral end of the cut processus retracted into the peritoneal cavity through the deep ring. The patulous deep ring was tightened using nylon 1 suture. The fluid in the right scrotum was suctioned out and the testis was brought to the groin wound. The tunica was then everted (Lord's placcation) and the testis returned to the scrotum. The wound was closed in layers followed by application of scrotal support.



Figure 1: Demonstration of the Patent Processus Vaginalis

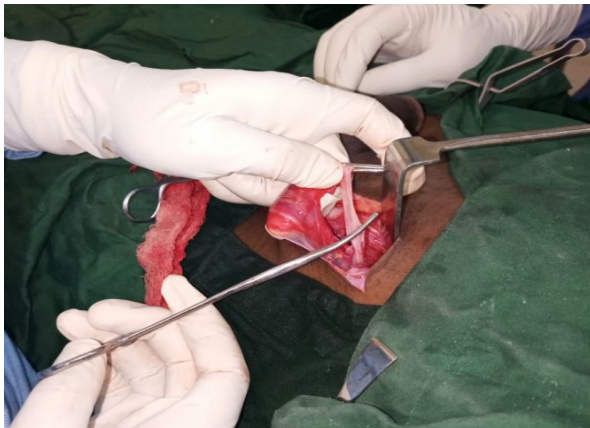


Figure 2: Clamping of the Patent Processus before ligation

The patient recovered satisfactorily; the scrotal support was removed on postoperative day 5. Histopathology of the excised processus showed a benign wall lined by a single layer epithelium. He is currently on follow up at the surgical outpatient clinic.

Discussion

Communicating hydrocele in the adult is an uncommon clinical entity seen in patients with patent processus vaginalis (PPV).¹ A PPV is a communication between the peritoneal cavity and the scrotum occurring due to failure of closure of this developmental structure. During intrauterine life, the parietal peritoneum is drawn into the

inguinal canal and the scrotum by the descent of the testes from the posterior abdominal wall. It normally obliterates before or shortly after birth; it may persist and result in communicating hydrocele or hernia. It is proposed that transforming growth factor beta1 (TGF β 1), a potent fibrogenic agent stimulates fibrosis and closure of the processus vaginalis.² The processus is patent in 80-90% of term male infants at birth and by age 2 years it remains un-obliterated in about 25-40% of these children. Despite this high proportion, hydroceles are only clinically observed in 1-5% of children.^{2,3}

Adult communicating hydrocele has a general prevalence of about 1% of adult males, mostly following an unrecognized or neglected PPV during childhood.⁴

Risk factors for failure of closure of the processus vaginalis include low birth weight, breech presentation, prematurity and maternal use of progestin.¹ Hydroceles have been classified as primary and secondary. Primary hydroceles are those without primary pathology of the testes; they are commonly of congenital origin and may be divided into communicating or non-communicating types (i.e. with or without patency between peritoneum and scrotum, allowing peritoneal fluid to flow particularly during Valsalva maneuver). Secondary hydroceles are caused by conditions such as testicular torsion, torsion of the appendix testis, infections/infestations (e.g. epididymitis or filariasis), previous surgery (e.g. varicolectomy) or malignancy.^{2,3} Thus, while hydroceles are benign swellings, they should be evaluated thoroughly, as they can be associated with underlying scrotal pathology. Less commonly, a non-communicating, isolated fluid collection may occur along the pathway of the processus in form of encysted hydrocoele of the cord in males, or as cyst of the canal of Nuck in females.⁵

The diameter of PPV is typically much smaller than that seen with an indirect inguinal hernia, and therefore only peritoneal fluid passes into the scrotum without accompanying intraabdominal organs. These patients presents with painless scrotal swelling that increases over the course of the day and reduces or even disappear while sleeping or assuming recumbent position, as fluid returns to the peritoneal cavity as in the case of our patient.³ Often, PPV enlarges over time and results in herniation of a viscus. The chance of developing an inguinal hernia is four times higher in children with unobliterated and untreated PPV than in children without it. In some patients the size remains small and develops into adult type communicating hydrocele as in the case of our patient.⁶

Egharevba et al reported a case of a 36-year-old Nigerian man with a recurrent left-sided giant communicating hydrocele which developed after 2 previous attempts at open drainage by hydrocelectomy via scrotal approach. This type of presentation raises the suspicion of a possible unresolved PPV or an unidentified testicular pathology. The authors confirmed the diagnosis by untrasonography and the patient had surgery through both groin and trans-scrotal approaches.⁷

A close differential diagnosis of a communicating hydrocele is the abdominoscrotal hydrocele which is the collection of fluid in the tunica vaginalis that extends from the scrotum to the abdominal cavity in a blind ending sac. The hydrocele sac is often tense and produces a dumbbell or hourglass shape.³ Khalili et al reported a case of a slow growing mass in lower abdomen of a small boy whose abdominal ultrasonography and CT scan demonstrated a large intraabdominopelvic cystic swelling extending to the inguinal canal and the scrotum. At operation a large abdominals scrotal hydrocele was found and excised.⁸

Confirming the diagnosis of communicating hydrocele by ultrasonography is important for planning treatment and for identifying complications. Complications of hydroceles include infection (e.g. pyocele), haematocele, testicular atrophy, infertility, hydrocele rupture and hernia formation.^{9, 10} Ultrasonography of the groin and scrotum is highly sensitive. Common features include anechoic fluid collections anterior to the testis with a cephalic narrow peritoneal communication. Occasionally, low-level echoes, suggests protein aggregates or cholesterol crystals and not necessarily superimposed infection or hemorrhage. It is important to perform ultrasound examinations in both standing and supine positions, as communicating hydroceles may reduce when the patient is laying down.^{10, 11}

When a diagnosis of a communicating hydrocele is missed, a '*scrotal approach*' alone will be adopted and this will not give access to the PPV in the inguinal canal. This may leading to recurrence.^{1, 7} The choice of a surgical approach depends on the specific characteristics of the hydrocele. With *groin approach* the PPV is separated, ligated and excised. This takes care of the communication. A second incision is normally made in the scrotum to take care of the scrotal component.¹² In the case of our patient, the scrotal fluid was drained through the inguinal incision and the testis was brought into the wound where the tunica was everted (Lord's placcation). This obviated the need for a second scrotal incision.

Lord's placcation is a favored technique for thin-walled hydroceles as in the case of our patient. This serves to prevent the development of a non-communicating hydrocele in future. Tightening the enlarged internal ring is recommended if it is noticed to be enlarged as in our patient.⁵ Another indication for inguinal approach is the presence of suspicion for concomitant malignancy. In this case, an inguinal

approach will for allow control of the spermatic cord in preparation for radical orchiectomy. The combination of groin and scrotal approaches is a safer means of addressing communicating hydrocele especially in recurrent or giant hydroceles which is not the case in our patient.^{5, 7, 12}

In the *trans-scrotal approach*, the hydrocele is accessed through either a median raphe or a transverse unilateral scrotal incision. The sac is dissected and delivered intact. An opening in the sac is made away from the testis, epididymis, and cord structures and the fluid is drained. The hydrocele sac is then opened and repaired by one of the following techniques: (i) The Jaboulay “bottle-neck” technique; it is useful for large, floppy, long-standing, thick-walled, hydrocele sacs. It is performed by excising the sac and leaving a larger margin of excision between the edge of the sac and the testis to allow for sewing the edges of the sac together behind and without compressing the cord. (ii) Lord's Plication technique is suitable for thin-walled hydroceles, with no redundant sac be left in the scrotum. It is performed by cauterizing or oversewing the cut edges of the sac, and using interrupted, radially placed sutures to plicate the sac. The scrotal skin is then closed with or without drain.^{12, 13, 14}

Follow up of patients after surgery for hydrocele is essential. At least one postoperative follow-up visit is recommended for straight forward hydroceles.⁵ In patients managed for long standing or recurrent hydroceles, patients with hydrocele due to significant testicular pathology, and in infants, a more prolonged follow-up evaluation is indicated: bi-weekly, monthly, or 2 to 3 monthly to ensure optimal recovery and restoration or maintenance of normal testicular size and architecture.^{2, 5}

Conclusion

Communicating hydrocele is uncommon in adults. It mostly follows an unrecognized or neglected childhood PPV. All hydroceles

should be evaluated thoroughly. Accurate pre-operative diagnosis is important in determining choice of surgical approach which is key to preventing recurrence.

Consent: Written informed consent to publish this case including clinical photographs was obtained from the patient prior to writing of this manuscript.

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Conflict of interests: None

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PRIMARY NON-GESTATIONAL UTERINE CHORIOCARCINOMA MIMICKING LEIOMYOMA IN A POSTMENOPAUSAL WOMAN: AN UNUSUAL CASE REPORTHaruna Usman¹ Abdullahi Muhammad Ahamad² Usman Abba³¹Department of Obstetrics and Gynecology Rasheed Shekoni Federal University Teaching Hospital Dutse- Nigeria²Department of pathology, Bayero University Kano/Aminu kano Teaching Hospital, Kano-Nigeria³Department of Obstetrics and Gynecology, Yobe State University Damaturu-Nigeria**Corresponding Author:** *Usman Abba*, Email: usmanabbagdm@gmail.com

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Abstract**Background:** Gestational trophoblastic neoplasia (GTN) is a rare cause of postmenopausal bleeding that can be easily missed, leading to delayed treatment.**Case report:** We report a 50-year-old postmenopausal woman, 9 years after menopause and last delivery, who presented with 7 months of recurrent vaginal bleeding and anemia requiring 5 units of blood transfusion. Intraoperative findings revealed a bulky uterus with necrotic bleeding lesions and hemoperitoneum. Total abdominal hysterectomy with bilateral salpingo-oophorectomy was performed, and histopathology confirmed GTN.**Conclusion:** This case underscores the need for a high index of suspicion for GTN in women with abnormal uterine bleeding regardless of menopausal status. Early use of beta-hCG testing can reduce diagnostic delays and enable prompt treatment, especially in resource-limited settings.**Cite this article:** Haruna Usman¹ Abdullahi Muhammad Ahamad² Usman Abba³. Primary non-gestational uterine choriocarcinoma mimicking leiomyoma in a postmenopausal woman: an unusual case report. Yob Med J.2025;2(1):66-69

Introduction

Gestational trophoblastic neoplasia encompasses a diverse group of interrelated but distinct tumors that include choriocarcinomas, placental-site trophoblastic tumors, and epithelioid trophoblastic tumors¹

Choriocarcinoma is classified into two types depending on the pathogenetic mechanisms underlying it. Gestational Choriocarcinoma (GC) has an antecedent history of pregnancy, abortion or a hydatidiform mole, and therefore has both paternal and maternal DNA. Non-gestational Choriocarcinoma (NGC) is much rare compared to gestational Choriocarcinoma. NGC is not linked to any form of pregnancy and is the rarer subtype, originates from trophoblastic differentiation of germ cell tumors in the gonads or as a somatic component of another histologically different tumor such as teratoma, yolk sac tumor, embryonal carcinoma, and endometrioid adenocarcinoma hence, non-gestational choriocarcinoma contains only the patient's genetic material^{2 3}.

The occurrence of NGC in the ovary has been well documented. However, its occurrence in postmenopausal uterus is rare.⁴

The clinical features and prognosis of gestational and NG Choriocarcinoma are very different. Therefore, it is imperative to be able to make the distinction.

In this case report, we document a case of post-menopausal woman who presented with abnormal vaginal bleeding, that was subsequently diagnosed as NGC.

Case Report

We present a 50-year-old postmenopausal woman whose last menstrual period was 9 years ago that presented with an abnormal vaginal bleeding of 7 months. Her last childbirth was also 9 years ago. The vaginal bleeding was recurrent with passage of clots, but there was no history of passage of vesicles. She has been transfused with five pints of blood over the past seven months. There was history of abdominal pain and dizziness, but no history of syncopal attacks. Abdominal examination revealed uterine size of 24 weeks gestation, nodular and firm in

consistency. Pelvic examination revealed blood-Smeared female external genitalia. There were vaginal and suburethral haemorrhagic deposits measuring about 1.5x1.5cm, 1 x 1cm and 0.5cm x 0.5cm. Abdominopelvic ultrasound scan revealed a bulky uterus with anteroposterior diameter of 64mm. There were fairly oval shaped mixed echogenic masses in the posterior uterine wall measuring 65 x 43mm and similar mass measuring 39mm x35mm in the cervical region all consistent with huge solitary uterine and cervical fibroids. Colposcopy revealed type II transformation zone with atypical vascular pattern. No aceto-whitening, but poor iodine uptake.

A provisional clinical diagnosis of Uterine leiomyoma was made.

She underwent a total abdominal hysterectomy with bilateral salpingoophorectomy. Intraoperatively, there was 1 liter of hemoperitoneum with a bulky uterus to the size of a 24-week pregnancy, doughy in consistency with multiple cystic nodules and large necrotic area on the fundus oozing blood with bowel attached to it. No obvious metastatic deposit seen in the peritoneal cavity, both ovaries were atrophied. The specimen was sent to the Pathology department for histopathologic analysis.

The specimen received was an enlarged and distorted uterus with salpingo-oophorectomy measuring 17 x 16x 9 cm and weighed 820g. There was a rupture at the apex 10cm across. Cut section shows a huge submucous mass with ulcerated surfaces protruding into the endometrial cavity. The tumor has necrotic to grayish white hemorrhagic surfaces which were extensively sampled. Histological sections showed a predominantly hemorrhagic areas with sheets of syncytiotrophoblasts and cytotrophoblast cells having pleomorphic and hyperchromatic nuclei. Several areas of infiltration into the myometrium were also seen. (Figures 1 and 2) Given the histologic features as well as the increased beta human chorionic gonadotrophin (beta- HCG) level of 346,231mIU/ml, a diagnosis of Non

gestational Choriocarcinoma was made. The patient was being optimized for commencement of chemotherapy, when her condition deteriorated and she started having irrational talks and became delirious. She passed away on the fourteenth post-operative day.

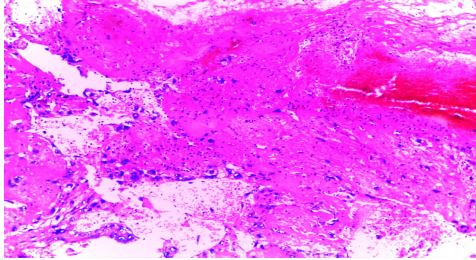


Figure 1 Section shows predominantly areas of hemorrhage and necrosis (Hematoxylin and Eosin X100)

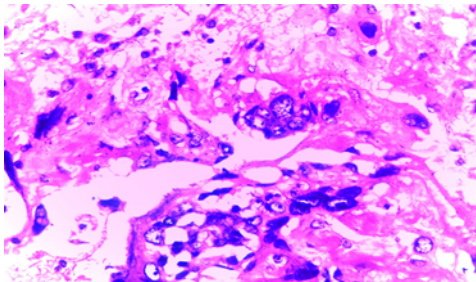


Figure 2 Clusters of malignant cells disposed singly and in a syncytium. The cells have pleomorphic and occasional hyperchromatic nuclei with moderate to abundant cytoplasm (A), Similar malignant cells are seen infiltrating into the myometrial fibers. (B) (Hematoxylin and Eosin X400)

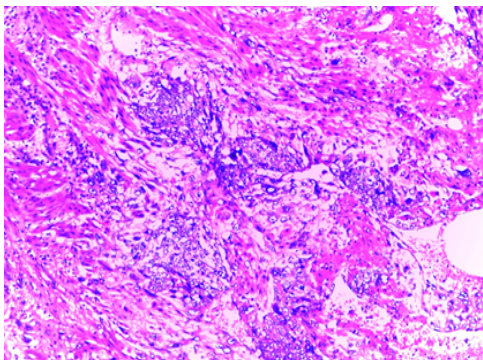


Figure 2 Clusters of malignant cells disposed singly and in a syncytium. The cells have pleomorphic and occasional hyperchromatic nuclei with moderate to abundant cytoplasm (A), Similar malignant cells are seen infiltrating into the myometrial fibers. (B) (Hematoxylin and Eosin X400)

Discussion

In this case report, the presentation of the postmenopausal woman with abnormal vaginal bleeding and the finding a uterine mass led to the presumptive diagnosis of uterine leiomyoma. This is not unusual given the fact that most patients with uterine leiomyoma have similar presentation. The other possible differential diagnosis of an endometrial cancer was not considered due to absence of endometrial thickening on the ultrasound scan. The diagnosis of a choriocarcinoma was only considered after the specimen was sent for histopathological analysis and histologic features consistent with choriocarcinoma were observed. It was this initial observation that prompted the request to review the presumptive clinical diagnosis by assaying serum beta HCG level. However, being a postmenopausal woman this finding was consistent with that of Wang and Hirata but contrary to the findings by Sano where the reported case was that of a premenopausal woman ^{1,6,7}. GCC arises from chorionic cells from a previous pregnancy. NGCC, however, arises from pluripotent germ cells or originates from poorly differentiated somatic carcinomas⁷. Primary uterine non gestational choriocarcinoma is characterized by abnormal uterine bleeding, suprapubic swelling and pain this was corroborated by another researcher ⁶. This presentation made the diagnosis very difficult and diagnosis of leiomyoma was entertained. Patient later deteriorated exhibiting some neuropsychiatric symptoms, this may not be unconnected to likely brain metastasis. This presentation was the reason why serum beta HCG level was not requested for until after the histopathological diagnosis. The diagnostic dilemma was the reason why chemotherapy was not commenced till the demise of the patient. Had the serum level of beta HCG was determined earlier this index case would have salvaged however, there was no justification to have assayed the Serum beta HCG prior to histopathological finding. Similar case was reported by Sano et. al but that case was in a premenopausal woman.

There were few case reports of primary non-gestational choriocarcinoma exhibiting myoma symptomatology^{1,6,7}.

Conclusively it was a difficult experience managing such a patient with diagnostic dilemma leading to delays in commencing appropriate treatment for the patient especially in resource constraint setting. Therefore, high index of suspicion can go a long way in assisting the managing physician to request for appropriate investigations and commence appropriate treatment promptly.

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PERFORATED COLONIC LYMPHOMA PRESENTING AS GENERALIZED PERITONITIS IN AN 8-YEAR-OLD GIRL: A CASE REPORT.

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Abstract

Perforation of gastrointestinal tract (GIT) lymphoma is an uncommon cause of peritonitis. Diagnosis of this condition is mostly at surgery. Adequate resection, histological confirmation, and appropriate chemotherapeutic regimen are essential in ensuring survival of these patients. We report case of an 8-year-old girl who presented to our hospital with clinical features of generalized peritonitis who found to have a perforated tumour of the transverse colon, the histology of which revealed gastrointestinal tract –associated B Cell lymphoma.

Keywords: Gastrointestinal tract lymphoma, perforation, peritonitis

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Introduction:

Primary Gastrointestinal lymphoma is a rare disease, accounting for only 1-4% of gastrointestinal tract (GIT) malignant tumours, although the incidence is rising.¹ Gastrointestinal tract is the commonest site of extra-nodal involvement in lymphomas, constituting 5%-20% of all of all GI lymphomas.^{2,3} Perforation peritonitis from a GIT –associated lymphoma is a rare occurrence and the identification of this condition is mostly at laparotomy. Diffuse large B-cell lymphoma is the most common subtype associated with perforations.⁴

Case report:

We present a case report of an 8-year old girl who presented to the emergency pediatric unit of our hospital with complaints of fever of 7 days duration, multiple episodes of bilious vomiting and central abdominal pain which became generalized two days before presentation. There was no history of similar episodes of abdominal pain in the past however, the patient was noticed by her parent to have significant weight loss in the preceding few months. No other symptoms were present. Her past medical history was unremarkable.

Examination revealed mild palor and dehydration. No significant peripheral lymphadenopathy. The patient had a distended abdomen with generalized tenderness and guarding. Bowel sounds were absent on auscultation. A diagnosis of generalized peritonitis from viscus perforation was made, likely typhoid intestinal perforation given the symptomatology and the endemic nature of typhoid fever and its complications in our environment. The patient was resuscitated with intravenous fluids, parenteral antibiotics and analgesics. Nasogastric tube and urethral catheter were inserted. The serum electrolytes and creatinine were within normal limits but urea was 9.2 mmol/L. Full blood count showed Hemoglobin of 10.2 g/dL, total white cell count of 11.8×10^9 /L

(Neutrophils: 82%, Lymphocytes: 16%, Granulocytes: 2%) and platelet count of 154×10^9 /L. Total protein was 58.6g/L with albumin of 34.4 g/L and globulin of 24.2 g/L. Retroviral and hepatitis B and C screening tests were negative. Erect chest X-ray showed a rim of air under right hemidiaphragm. Following adequate resuscitation, consent for laparotomy was obtained from the care givers. The abdomen was entered through a long midline incision. The intra-operative findings were feculent fluid in the peritoneal cavity (about 1,500 ml), fibrinoid adhesions and a friable grayish mass in the mid-transverse colon about 4 cm x 3 cm in size with a perforation about 1cm wide on the antimesenteric border at the edge of the mass. There were enlarged lymph nodes in the transverse mesocolon. No perforations were found on the small bowel, vermiform appendix, stomach or the gallbladder. No nodules were noted on the surface of the liver, no carcinomatosis peritonii. The spleen appeared grossly normal. A transverse colectomy (oncologic resection) was performed with colocolic end-to-end anastomosis. She recovered adequately and was discharged home on the 7th postoperative day.

Histopathology of the resected transverse colon reported a neoplasm composed of lymphoid cells arranged in sheets. The cells were larger than the size of small normal mature lymphocytes, with vesicular pleomorphic nucleus. Mitosis was reported to be 1-2 per high power field with no areas of necrosis seen. The tumour was positive for CD-20 and negative for Cytokeratin and CD3 on immuno histochemistry. A histological diagnosis of Diffuse Large B cell Lymphoma was therefore made.

The patient was referred to the radio-oncology unit of the Federal Teaching Hospital Gombe, Nigeria, where she received adjuvant chemotherapy consisting of Cyclophosphamide, doxorubicin (Hydroxyldaunorubicin), vincristine

(Oncovin) and Prednisone (CHOP regimen) as a total of six cycles. After the last cycle of chemotherapy, she was seen in our hospital monthly for 3 months and thereafter 3 monthly for 1 year. During this period of follow up there were no signs of recurrence in the abdomen and no evidence of chest or superficial nodal disease. Contrast-enhanced thoraco-abdominal CT scan at 6 month post-operatively was normal. She is still being followed up.

Discussion

Generalized peritonitis is a common surgical condition in our environment which requires adequate resuscitation and prompt surgical intervention. Common etiologies in children in our environment include typhoid intestinal perforation, ruptured appendix/appendiceal abscess, perforation due to intussusception, volvulus or adhesive intestinal obstruction. Others are perforated necrotizing enterocolitis and abdominal trauma.^{5, 6}

Peritonitis from a perforated GI lymphoma is a life-threatening complication. Mechanisms of perforation may include localized tumor replacement of the bowel wall, which lacks of normal gut tissue integrity resulting in tumor necrosis and full thickness perforation; it may also occur after prolonged obstruction, which leads to distention, ischemia and necrosis. Occasionally, perforation may result from treatment (e.g., steroids) or from complications of chemotherapy (e.g., severe dehydration, decreased bowel perfusion).^{7, 8} The pre-operative diagnosis of a perforated GI tumour is difficult due to its rarity and the non-specific nature of its presentation. Often, the diagnosis is established at surgery and confirmed after histology. In a few patients however, pre-operative diagnosis may be possible when non-specific symptoms of weight loss, abdominal discomfort, nausea, vomiting and loss of appetite lead to a diagnosis of intraabdominal tumour through abdominal ultrasound scan, CT or MRI followed by laparoscopic or open biopsy.⁹

The clinical presentation of our patient was that of a generalized peritonitis. The possibility of a tumour was not brought forward due to absence of preceding abdominal pain or bowel symptoms. Other aetiologies were therefore considered (typhoid intestinal perforation, ruptured appendix and perforated volvulus). This is often the typical clinical scenario.⁷

Establishment of the diagnosis primary gastrointestinal lymphoma (extranodal) in our patient followed the Dawson’s criteria¹⁰ (1961) (see Table 1).

Table 1: Definition of primary gastrointestinal lymphoma as described by Dawson et al.

Absence of palpable lymphadenopathy on clinical examination
Absence of mediastinal lymphadenopathy
Normal range of total and differential white cell count
Involvement of only regional lymph nodes, discovered on surgery
Liver and spleen remain without disease

This emergency presentation of a perforated GI lymphoma in our index patient is similar to other reports. Vaidya et al analyzed the clinicopathologic features of patients with biopsy-proven lymphoma of the GI tract using the Data Base of the Mayo Clinic Lymphoma and the University of Iowa/Mayo SPORE Data Base in a retrospective review of 1975 to 2012 data. They noted that 92 of the 1062 patients had intestinal perforation at presentation or during the course of chemotherapy. Lymphoma was primarily of GI origin in 72 patients and secondary from systemic lymphoma in the remaining 20 patients. The small bowel was the commonest site perforations (59%), followed by the stomach (16%) and the colon (22%).⁴ Similar findings were reported by Ara et al in their case series of eight patients

managed for bowel perforations from lymphoma where 6 of the 8 perforations occurred in the small bowel and only 2 involved the large bowel.¹¹ Ahmed A et al reported similar pattern of perforation in a study on 240 patients with intestinal lymphoma. The ileum was the most common site of perforation compared to other parts of the GI tract. Perforation occurred at presentation, during induction, during maintenance chemotherapy, or at relapse.¹²

Reports of GIT lymphomas presenting as perforation peritonitis also include adult patients. Abdul Rehaman et al¹³ in Calicut, India, Love et al¹⁴ in Chicago, USA, Warsinggih et al⁸ in Makassar, Indonesia, and Tian Y et al¹⁵ reported perforation peritonitis as first presentation of various forms of Primary GI lymphomas.

Our patient had perforation in her transverse colon. Perforation of the colon is less common possibly because (i) its wall is thicker than that of the small bowel and (ii) it is less frequently involved in GIT lymphomas. Gastric lymphomas, although more prevalent than small bowel and colonic lymphomas, are less likely to perforate due to thickness of the gastric wall.⁴

Definitive risk factor(s) for the lymphoma in our patient could not be established from the basic investigations carried out: she tested for negative retroviral disease (HIV), *Helicobacter pylori*, and hepatitis B virus (HBV). Genetic studies could not be carried out due to lack of these tests in our hospital and the nearby teaching hospital. Other risk factors for lymphoma in the literature include celiac disease, infection with Epstein-Barr virus (EBV), *Campylobacter jejuni* and T-cell lymphotropic virus-1 (HTLV-1), inflammatory bowel disease, immunosuppression, Wegener's granulomatosis, and rheumatoid arthritis.^{2, 3, 8} Treatment strategies for GI lymphoma have changed over the last two decades.¹² The most widely used modalities are cytotoxic

chemotherapy or immunochemotherapy, radiotherapy and treatment of any identified underlying aetiology. Surgery as treatment modality is now reserved only for those with complications such as perforation, obstruction, fistula or bleeding. For intestinal Diffuse B Cell lymphoma, surgery is still a component of treatment in localized disease. A recent study recommends surgical resection followed by chemotherapy as an effective treatment strategy for localized intestinal DLBCL. The extent of lymph node dissection include regional lymph node dissection equivalent to colon adenocarcinoma or resection only of lymph nodes with suspected lymphoma involvement. Some centres uses R-CHOP (with Rituximab) as chemoimmunotherapy especially in more aggressive diffuse B-Cell lymphomas.^{16, 17, 18, 19} Our patient was offered transverse colectomy, taking out all lymphovascular supply of the middle colic artery. This is to ensure oncologic clearance²⁰ since the histologic nature of the tumour was known at the time of surgery. A diverting ileostomy should have been created as there was no pre-operative bowel preparation however, proximal stoma was not made as the bowels were only slightly edematous and the patient was generally preserved. In addition, the pre-operative serum albumin was 34g/L (marginally low).

Our patient was followed up monthly for the first 3 months, then 3 monthly for 1 year and there were no clinical evidence of recurrence in the abdomen or chest and no superficial nodal disease. Contrast-enhanced thoraco-abdominal CT scan was performed at 6 months which was within normal limits. She is still being followed up.

The National Comprehensive Cancer Network (NCCN) guidelines for the surveillance for NHL include physical examination (to look for lymph nodes, liver and splenic enlargement), complete blood count, CT scans with contrast of the chest, abdomen, and pelvis every 3–6 months for the first 2 years, then every 12 months for every subsequent years for 2 years after

treatment for patients in complete remission.^{17, 21} PET/CT is not included in the NCCN recommendations. The European Society of Medical Oncology guidelines also discourage the use of PET/CT in routine surveillance after complete remission.²²

‘Next-generation’ approaches for detection of minimal residual disease in Hodgkin and non-Hodgkin lymphoma area novel serologic assessments which may provide opportunity to identify relapse early and intervene prior to progression of clinical disease. These include lactate dehydrogenase and absolute lymphocyte count.¹²

Conclusion and Recommendations:

Primary gastrointestinal lymphoma should be considered in children presenting with peritonitis, especially when clinical features are atypical for common causes such as typhoid perforation. To ensure good outcome, high index of suspicion, early surgical intervention, thorough peritoneal assessment, adequate tumour resection, histological confirmation, appropriate chemotherapy and prudent surveillance are essential.

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