



**NIGERIAN MEDICAL
ASSOCIATION
BAYELSA STATE BRANCH**



**VOL. 4 ISSUE 2,
April — June, 2025**

Niger Delta Journal of Medicine & Medical Research

**A PUBLICATION OF
NIGERIAN MEDICAL ASSOCIATION
BAYELSA STATE BRANCH**

<http://www.ndjmmronline.com>

NIGER DELTA JOURNAL OF MEDICINE AND MEDICAL RESEARCH

Vol. 4 No. 2, April – June 2025

Published by the Nigerian Medical Association, Bayelsa State Branch,
Nigeria.

Contents

Editorial Board	ii
Editorial Note	iii
Aims and Scope	iv

Articles

The interface between depression and common cardiovascular risk factors at the grass root community level in Southwestern Nigeria. Oni OO, Ogunwobi O, Akinwusi PO, Owolabi JI, Odeyemi AO, Israel GM, Ala O, Akande JO, Israel OK, Ajibola I, Aremu AO, Shitu AO.....	42
Evaluation of the effects of <i>Pleurotus ostreatus</i> and <i>Calocybe indica</i> on the liver and kidney function of Wistar albino rats. Deborah Etin-Osa, Brenda Isichei-Ukah, Endurance Ophori.....	52
Postpartum infective endocarditis, a challenge to improve clinical skills. Nwade B, Offiah E, Uwanuruochi K.	62
Accidental formalin ingestion in a child: A rare case report. Okonkwo CJ, Udah CA, Onyeagwara NC.....	66
Perception of Caesarean delivery by patients and their care-givers in the ultra-short stay versus the traditional post-operative management protocol, following uncomplicated Caesarean delivery: A randomized controlled trial. Oyeyemi N, Onwudiegwu U, Pughikumo DT, Oyeyemi AS.....	70

Editorial Board

Editor-in-Chief

Dr. Orij, Peter Chibuzor

+234 7064233209

Email: ndjmmrbayelsa@gmail.com

Deputy Editor-in-Chief

Dr. Yeibake, Weriwoyinipre Silver

Website: www.ndjmmr.org

Associate Editors

Dr. Patrice Appiah

Dr. Hilda Afakwu-Adimoha

Dr. Doubara Morowei

Editorial Advisors

Prof. T. C. Harry

Prof. I. Jeremiah

Prof. F. O. Akinbami

Dr. E. Chapp-Jumbo

Dr. A. Oyeyemi

Prof. P. J. Allagoa

Prof. E. N. Etebu

Prof. D. Ogoina

Prof. D. O. Allagoa

Dr. J. E. Omietimi

Dr. E. Young-Dede

Dr. P. Alabrah

Dr. N. Osegi

Dr. F. Meme

Dr. O. Oguche

Dr. C. Duru

Dr. P. Abonyi

Dr. D. Jesu-Orobo

Dr. V. O. Ndu

Dr. E. I. Obi

Dr. Marcus Ifeh

Dr. Patrick Igwe

Dr. Abimbola Afolayan

Dr. Michael Ogba

Dr. Victor Madu

Editorial Office

Nigeria Medical Association

Secretariat,

Okaka Housing Estate, Yenagoa,

Bayelsa State, Nigeria.

Executive Council of the Nigerian Medical Association, Bayelsa State Branch (2024/2026).

Chairman – Dr. Izibeya Wilcox

Vice Chairman – Dr. Ebier Disi

General Secretary – Dr. Stephen Umuwe

Asst. General Secretary – Dr. Oru Oru Inetsol

Treasurer – Dr. Lilian Tabowei

Financial Secretary – Dr. Romeo T. Mbooh

Public Relation Officer – Dr. Tokoni Torunana

Chairman CME/Editor – Dr. Peter Chibuzor Orij

Immediate Past Chairman – Dr. Oyintonbra Koroye

Editorial Note

We are pleased to welcome you to this edition of the *Niger Delta Journal of Medicine and Medical Research (NDJMMR)*. The *NDJMMR* serves as the official publication of the Nigerian Medical Association, Bayelsa State Branch, Nigeria. The journal is released quarterly, specifically in January – March, April – June, July – September, and October – December.

The *NDJMMR* publishes open-access, peer-reviewed content, including original research articles, review papers, case reports, letters to the editor, short communications, commentaries, viewpoints, book reviews, medical educational resources, and scholarly articles addressing socioeconomic, political, or legal issues related to medical practice.

Unless otherwise indicated, all opinions expressed in the articles are solely those of the respective authors and do not represent the official position of the *Niger Delta Journal of Medicine and Medical Research*, or the Nigerian Medical Association, Bayelsa State Branch.

No portion of this publication may be reproduced, transmitted in any form or by any means, or stored in any retrieval system without prior written permission from the editorial board.

Copyright Notice © 2025

Articles published in the *Niger Delta Journal of Medicine and Medical Research* are covered under the Creative Commons Attribution (CC BY) 4.0 International License. For further information, please refer to Creative Commons. Under this licence, third parties are permitted to use the authors' work in accordance with the stated terms.

Privacy Statement

The names and email addresses provided on this journal's website, or used in any correspondence with the journal, will be utilised solely for the purposes specified and will not be disclosed for any other use or to any third party.

Fees and charges for submission of manuscripts.

For the time being, and pending further review, no fees will be charged for the publication of articles in the *NDJMMR*. The journal's website remains accessible, and PDF versions of all published articles can be downloaded at no cost.

For all correspondence, kindly contact the editor-in-chief:

Dr. Oriji, Peter Chibuzor

Nigeria Medical Association Secretariat,
Okaka Housing Estate, Yenagoa, Bayelsa State,
Nigeria.

+234 7064233209

Email: ndjmmrbayelsa@gmail.com

Website: www.ndjmmr.org

Aims and Scope

The *Niger Delta Journal of Medicine and Medical Research (NDJMMR)* aims to publish high-quality research papers, reviews, case reports, and short communications across all fields of medicine and medical science. In addition to traditional full-length research articles and short communications, the journal also welcomes submissions covering every stage of the research process, including study protocols, pilot studies, and pre-protocols.

NDJMMR is an open-minded, peer-reviewed medical periodical dedicated to promoting both conventional scientific work and innovative, groundbreaking research, provided the submissions are technically sound and scientifically justified.

The journal covers a wide range of clinical and biomedical disciplines, including immunology,

anaesthesia, cardiovascular medicine, dentistry, pathology, pharmacology and therapeutics, physiology, human anatomy, dermatology, respiratory medicine, rheumatology, otolaryngology, emergency medicine, infectious diseases, neurology, nutrition and metabolism, obstetrics and gynaecology, endocrinology, gastroenterology, genetics, geriatric medicine, haematology, oncology, ophthalmology, paediatrics, psychiatry, radiology, renal medicine, sexual health, urology, epidemiology, health policy, forensic medicine, environmental medicine, and public health.

NDJMMR publishes four issues per year. Each issue operates on a rolling basis, and all officially accepted manuscripts are made available online immediately after acceptance.

TYPES OF ARTICLES

Research Articles: Primary research papers covering the full spectrum of medical and biomedical sciences.

Case Reports: Well-documented case descriptions intended for educational purposes or to highlight unusual presentations, treatment outcomes, disease transmission, or control measures. Authors must obtain written and signed consent from patients or their guardians. Case reports may include clinical images.

Case Studies: Detailed analyses of major healthcare interventions, primarily from a public health perspective. Favourable consideration is given to case studies that include rigorous assessments of intervention processes, outcomes, and recommendations for future practice. Case studies must not describe individual patients; such descriptions belong in the case report category.

Commentaries: Short, focused, and opinion-driven articles addressing timely issues or recent research findings within the journal's scope. Typically, around 800 words.

Reviews: Comprehensive reviews covering all aspects of medicine. While some reviews are commissioned, unsolicited submissions are welcome and undergo peer review. Reviews are not limited in length but must follow the journal's overall house style.

Opinion Articles: Brief, opinion-focused pieces on contemporary medical topics, including meeting reports or responses to recently published articles of relevance to NDJMMR readers. Both commissioned and unsolicited submissions are accepted and peer-reviewed.

NDJMMR also encourages scholarly engagement through "Comments," which allow readers to critically discuss previously published articles. All comments are moderated and remain linked to the original publication.

Original Article

THE INTERFACE BETWEEN DEPRESSION AND COMMON CARDIOVASCULAR RISK FACTORS AT THE GRASS ROOT COMMUNITY LEVEL IN SOUTHWESTERN NIGERIA

Oni OO^{1*}, Ogunwobi O², Akinwusi PO³, Owolabi JI⁴, Odeyemi AO³, Israel GM¹, Ala O³, Akande JO⁵, Israel OK⁶, Ajibola I⁷, Aremu AO⁷, Shitu AO¹

¹Department of Medicine, Ladoke Akintola University of Technology, Ogbomosho.

²Department of Medicine, Bowen University, Iwo.

³Department of Medicine, Osun State University, Osogbo.

⁴Department of Radiology, Bowen University, Iwo

⁵Department of Chemical Pathology, Ladoke Akintola University of Technology, Ogbomosho

⁶Department of Community Medicine, Ladoke Akintola University of Technology, Ogbomosho.

⁷Department of Community Medicine, Bowen University, Iwo

*Corresponding author: Dr O. O. Oni; +234(0)8060450458; opeyemi.oni@bowen.edu.ng; oniopeyemi64@gmail.com; ORCID number: 0000-0002-2790-9834

Abstract

Background: Depression is a major cause of morbidity and mortality globally. There is a reciprocal relationship between depression and cardiovascular risk factors. However, the prevalence of depression in the rural areas and the attending cardiovascular risk factors have not been well described.

Methodology: A cross section study of the Ejigbo community was done through convenient sampling. Data was obtained using the Patient Health Questionnaire-9, WHO STEPS and a standard proforma. Ethical approval was obtained from the relevant authorities. Data analysis was done with SPSS version 25.

Results: Two hundred and twenty-five subjects were recruited with 25.8% being males. The total prevalence of depression is 23.2%, with prevalence of mild, moderate and major depression was 12.9%, 7.6% and 2.7% respectively. Those with depression were younger, taller, with higher Body mass index (BMI), higher estimated glomerular filtration rate and a shorter QRS duration. Chest pain, palpitation, breathlessness and intermittent claudication were also more common among the subjects with depression. Those with depression were more likely students, unemployed- unable to work and had a worse New York Heart Association functional score($p=0.001$). Diabetes mellitus and Obesity tend to be commoner in those with depression. Depression correlated inversely with age, height, total cholesterol, High Density Lipoprotein cholesterol and directly with BMI, chest pain, palpitations, breathlessness and intermittent claudication. Age, BMI and palpitations were independent determinants of depression in this study.

Conclusion: Depression is prevalent within the community and has significant association with cardiovascular risk factors and symptoms.

Keywords: Depression, Cardiovascular risk, Chronic kidney disease, Diabetes Mellitus, Cholesterol

Cite this article: Oni OO, Ogunwobi O, Akinwusi PO, Owolabi JI, Odeyemi AO, Israel GM, et al. The interface between depression and common cardiovascular risk factors at the grass root community level in Southwestern Nigeria. Niger Delta J Med Med Res. 2025;4(2):42–51.

INTRODUCTION

Depression is a major cause of morbidity and mortality. Depression is not only a risk factor for cardiovascular disease, but it also a correlate of mortality and re-hospitalization in those with preexisting heart disease.[1]

Depression has been found to causally related to a wide spectrum of cardiovascular disorders, including atrial fibrillation, stroke and coronary heart disease. The prevalence of depression in patients with heart failure is about 20%, rising from about 10% in asymptomatic to

40% in those with functional impairment.[2] The incidence of suicide, a marker of major depression, has risen in most parts of the world and has been found to be strongly associated with depression, with a 14-fold increase in the odds of suicide in those with major depression.[3] In the developing world, data is generally poorly kept. In addition, cultural stereotypes regarding suicide and depression may discourage reporting of such events.

Studies have shown a bidirectional relationship between depression and cardiovascular disease. For instance, the prevalence of myocardial infarction is twice as much in those with depression than those in the normal population.[4] However, the prevalence of depression in the community as well as its association with cardiovascular risk factors have been poorly described.

We therefore set out to evaluate depression in the local community, determine its prevalence and its correlation with cardiovascular risk factors

METHODOLOGY

Ejigbo is a rural community in South-West Nigeria. It lies along Latitude 7.54°N Longitude 4°18'54" E /Latitude 7.90000° Longitude 4.31500°E. It is about 426 meters above sea level and it receives a depth of about 133 cm of rain annually. It has an estimated population of 138,357 as at 2023 and is strategically placed among four major towns and is served by a secondary health care centre and many primary health care centres. The populace are all blacks, largely made up of traders and farmers, with teachers, commercial drivers and other professions composing the rest of its inhabitants. The study was conducted at the field adjacent to Baptist Medical Centre, Ejigbo, Osun State. This study is a cross-sectional, descriptive study.

SAMPLE SIZE DETERMINATION

Using Leslie Kish formula, a minimum sample size of 84 was estimated for the study. Prevalence of depression (5.2%) in a previous study was used.[5] Tolerable margin of error was set at 5% and a non-response rate of 10% was envisaged among the respondents and corrected for.

STUDY POPULATION

The study population was made up of people in the community, estimated at 138,357 people. About seven hundred people presented for the study but two hundred and fifty-five subjects gave informed consent and were subsequently recruited for the study. Subjects below 18 years of age and females who were pregnant were excluded from the study. High blood pressure was defined according to WHO/ISH guideline: A systolic blood pressure $SBP \geq 140$ mmHg and/or diastolic blood pressure ≥ 90 mmHg or being on treatment.[6]

Blood pressure (BP) was taken using the mercury sphygmomanometers with appropriate cuff sizes. Blood pressure was taken after allowing at least 5 minutes rest and after ensuring that patients had not taken coffee or smoked cigarettes within 30 minutes of taking BP. Systolic BP and DBP would be taken as Korotkoff's sound I and V (disappearance) respectively. The BP readings were recorded to the nearest 2 mmHg. Three BP readings were taken at a 2 minutes interval and the average reading calculated. The average reading was used for statistical analysis

ETHICAL APPROVAL

The ethical approval was obtained from the Bowen University Teaching Hospital ethical review board. A signed letter of informed consent was obtained from all subjects participating in the study.

SUBJECT ASSESSMENT

Patients' information was obtained using a standard proforma containing questions on demographic, socio-economic status and habits of the subjects (sex, age, family status and educational levels, smoking and alcohol use etc) under the supervision of the investigator. Patient Health questionnaire-9 was used to assess depression. Patients having at least five out of the nine domains were said to have depression. Severity of depression was classified as follows: 5-9 points - Mild depression; 10-19 points - Moderate depression; ≥ 20 points - Severe depression.

The functional status of patients was evaluated using the New York Heart Association algorithm. Each patient had

his/her weight (kg) measured using a standard hospital weighing scale. Subject was in minimal clothing with shoes off. Height was measured against a graduated height scale (stadiometer) with patients in erect position and unshod. The height was in metres (m).

Body mass index (BMI) was calculated from the weight and height as follows: $BMI = \text{weight (kg)}/\text{Height}^2 \text{ (m}^2\text{)}$.

Body surface area was calculated using the DuBois formula:[7]

$$BSA = \text{Height(cm)}^{0.725} * \text{Weight(Kg)}^{0.425} * 71.84/10000$$

LABORATORY ANALYSIS AND ESTIMATED GLOMERULAR FILTRATION RATE

Venous blood was collected into Fluoride Oxalate and Lithium Heparin, for glucose analysis and other parameters respectively, from each participant using standard technique of phlebotomy. Plasma from each participant was analyzed in batches using standards and controls for all the biochemical parameters.

Enzymatic end point was used for lipid profile (Total Cholesterol, HDL-Cholesterol and Triglycerides) parameters except Low density lipoprotein cholesterol (LDL-Cholesterol). Low density lipoprotein cholesterol was calculated using Friedewald formula.[8] Dyslipidemia classification for the cut off points are derived from the American heart association as follows: Total cholesterol >5.2 mmol/L, Triglycerides >1.7 mmol/L, Low density lipoprotein >3.4mmol/L, and High density lipoprotein <0.9 mmol/L.[9]The definition of Dyslipidemia used in this study is an abnormality in at least one of the above domains. The estimated ten-year global cardiovascular disease risk and estimated vascular age of all subjects was calculated using the 2008 Framingham Risk score calculator.

Glucose was determined enzymatically using the glucose oxidase method. Serum Creatinine (SCr) was determined using colorimetry by the kinetic method. Urea was determined by colorimetric end point, Urease-Berthelot method. Uric Acid was determined by enzymatic colorimetric Method. All the analyses were done using kits from Randox Laboratories Limited, Crumlin, UK. The estimated glomerular filtration rate (eGFR) was calculated using the equation from the CKD-EPI.[10]

Chronic kidney disease was defined as $eGFR \geq \text{Stage 3}$ (i.e $eGFR \leq 60 \text{ ml/min}/1.73 \text{ m}^2$)

ELECTROCARDIOGRAM

Electrocardiography (ECG) – 12 lead resting ECG was done on all the subjects (using Nihon Kohden cardiofax Q-9130K and Cardimax FX-3101 devices). Left ventricular hypertrophy was defined using standard criteria.

DATA MANAGEMENT AND ANALYSIS

All data obtained were entered into a standard proforma. Continuous variables were expressed as mean \pm standard deviation (SD) while categorical variables were expressed as count (percentages). Data analysis was done by IBM SPSS Statistics for Windows, Version 25.0.

The Shapiro-Wilks test was used to assess the normality of the distribution of variables. The means of continuous variables was compared using the Student's *t*-test for independent groups. For categorical variables, Chi square and/or Fisher's exact test was applied to test the equality of distributions between the two groups. The demographic, anthropometric and electrocardiographic characteristics of subjects were evaluated between those with and without depression using Independent *t*-test.

The correlational analysis was done to determine the relationship between these variables and outcomes of depression. Variables with significant relationships were entered into a model to evaluate for correlates of depression using binary logistic regression. A two tailed *p*-value of less than or equal to 0.05 was said to be significant.

RESULTS

A total of two hundred and twenty-five subjects were recruited for the study. The prevalence of depression in this study is 22.6%, with 12.9%, 7.6% and 2.7% having mild, moderate and severe depression respectively. There was no significant difference in the prevalence of depression between males and females, though females tend to have a higher prevalence (26.3% vs 15.5%). Those with depression were younger, shorter and had higher body mass index, than those without depression. According to the International

Monetary poverty index, 26.4% of those that were depressed were poor (earning less than 11,460 naira per month as at the year 2020). The BMI groups were not different between those with or without depression. When the obesity groups were combined in one and the analysis done again, it still did not show any difference between those with and without depression. ($P=0.199$). Diabetes Mellitus had a prevalence of 16% in those depressed as compared to 7.5% in those who were not depressed ($p=0.072$). There was no difference of anti-diabetic or anti-hypertensive use between those depressed and not depressed. Insulin was used only by 2 people in the study, and they were not depressed. Other details are seen in Table 1.

The second table showed that palpitations, chest pain, breathlessness and intermittent claudication were more in those that were depressed. Those with depression also had higher estimated glomerular filtration rate and have lower Total cholesterol and high-density lipoprotein cholesterol levels. Several voltage criteria for left ventricular hypertrophy including Sokolow Lyon voltage (3.0 ± 0.9 vs 3.0 ± 1.0 ; $p=0.674$), Cornell (1.5 ± 0.6 vs 1.5 ± 0.8 ; $p=0.861$) and Gubner Ungerleider (1.2 ± 0.7 vs 1.2 ± 0.7 , $p=0.762$) were

not different between those with and without depression. There was no difference between the PR interval (162.0 ± 24.3 vs 168.7 ± 24.9 ; $p=0.113$), P wave duration in lead II (103.2 ± 21.5 vs 105.4 ± 17.4 ; $p=0.498$), corrected QT interval (424.0 ± 37.4 vs 415.7 ± 40.0 ; $p=0.215$) or Heart rate (82.9 ± 16.2 vs 80.6 ± 13.7 ; $p=0.348$) in those with and without depression. Further details are seen in Table 2.

Depression was shown to correlate directly with early morning hyperglycaemia, chest pain, palpitations, intermittent claudication, a worse New York Heart Association functional classification and higher body mass index. Depression was however found to correlate inversely with height, age, total cholesterol, High density lipoprotein and serum creatinine. Details are seen in Table 3.

Using binary logistic regression, palpitations and BMI were the independent determinants of depression in this study. Early morning glucose showed a trend towards being a significant determinant. When NYHA status was added to the model, the model became slightly stronger, with age becoming an independent correlate of depression (in addition to Body mass index and palpitations).

Table 1: Shows the distribution of the anthropometric, clinical and laboratory variables between study subjects with and without depression

Variables	Depression (n=53)	Not Depressed (n=172)	P value
Age(years)	52.7±17.1	60.4±15.8	0.003
Sex			
Male	9(17)	49(28.5)	0.094
Female	44(83)	123(71.5)	
Weight (Kg)	71.1±17.5	68.1±14.2	0.214
Height (cm)	156.5±8.4	160.0±8.8	0.015
Waist Circumference (cm)	90.6±13.2	88.4±11.8	0.263
Hip circumference (cm)	102.2±11.4	99.8±11.9	0.193
Body surface area (m²)	1.71±0.2	1.71±0.2	0.869
Body mass index (kg/m²)	29.1±6.7	26.8±6.4	0.031
Systolic BP (mmHg)	133.7±23.2	134.8±22.0	0.754
Diastolic BP (mmHg)	81.1±14.0	81.1±13.9	0.996
Pulse pressure (mmHg)	52.6±15.8	53.7±16.0	0.664
Current smokers	1(1.8)	8(4.7)	0.690
Ever consumed alcohol	12(24.5)	46(27.2)	0.703
Education status			
>12 years in school			
Yes	9(19.6)	54(34)	0.062
No	37(80.4)	105(66)	
Poverty index			
Poor	14(26.4)	71(41.2)	0.101
Not poor	25(47.2)	72(41.9)	
Refused to answer	14(26.4)	29(16.9)	

Malaria within the last 3 months	33(63.5)	79(47.3)	0.115
Marital status			
Never Married	5(9.4)	8(4.7)	0.108
Currently Married	28(52.8)	107(62.6)	
Separated	3(5.7)	2(1.2)	
Divorced	1(1.9)	1(0.6)	
Widowed	16(30.2)	53(31)	
Work			0.019
Govt Employee	2(3.8)	17(10)	
Non-Govt Employee	3(5.7)	13(7.6)	
Self employed	35(66)	88(51.8)	
Student	3(5.7)	3(1.8)	
Homemaker	0	2(1.2)	
Retired	6(11.4)	39(22.9)	
Unemployed (able to work)	0	6(3.6)	
Unemployed (unable to work)	4(7.6)	2(1.2)	
Hypertension			0.339
Yes	33(71.7)	102(64.2)	
No	13	57	
Diabetes Mellitus			0.072
Yes	8	12	
No	42	149	
Obesity class	19(37.3)	38(23.6)	0.055
Body Mass Index groups			0.149
Underweight	0	6	
Normal	14	57	
Overweight	16	58	
Obese stage 1	10	26	
Obese stage 2	9	12	

Table 2: Distribution of clinical, laboratory and electrocardiographic variables between those with and without depression

Variables	Depressed n=53	Not Depressed n=171	P value
Packed cell volume(%)	38.3±3.9	38.6±4.3	0.729
Total cholesterol(mmol/L)	4.7±1.4	5.4±1.8	0.027
Triglycerides(mmol/L)	0.9±0.5	1.1±0.9	0.087
HDL(mmol/L)	1.4±0.6	1.6±0.7	0.011
LDL(mmol/L)	2.9±1.3	3.1±1.6	0.372
Total cholesterol: HDL ratio	4.3±2.9	5.0±14.6	0.766
High Total cholesterol	14(29.8)	63(43.2)	0.104
High Triglycerides	3(6.4)	26(17.8)	0.063 ^F
Elevated LDL cholesterol	16(34)	57(39)	0.539
Low HDL cholesterol	8(20.5)	20(13.7)	0.574
Dyslipidemia	23(48.9)	93(63.7)	0.072
Urea(mmol/L)	3.6±2.0	3.4±1.5	0.562
Creatinine(µmol/L)	79.8±27.6	97.3±38.6	0.004
eGFR(ml/min/1.73m²)	82.4±27.2	66.1±26.3	0.000
Uric acid(mmol/L)	0.3±0.4	0.2±0.4	0.601

Glucose(mmol/L)	6.2±1.9	5.5±1.7	0.018
Diabetes Mellitus	8(16)	12(7.4)	0.072
P amplitude in lead II(mV)	0.02±0.06	0.07±0.2	0.045
QRS duration(msec)	80.3±9.4	84.3±12.4	0.047
Chest pain	22(43.1)	42(26.4)	0.024
Palpitations	36(72)	54(33.3)	0.000
Intermittent Claudication	19(51.4)	38(27.9)	0.007
Breathlessness	26(51)	28(18.7)	0.000
New York Heart Association			
1	37	131	0.001
2	12	15	
3	3	0	
4	1	0	
Fatigue after sleep			0.000
Always	5	7	
3-4 times per week	6	7	
1-2 times per week	15	22	
1-2 times per month	3	2	
Never	20	80	
Chronic kidney disease stages			0.001^F
1	16	28	
2	21	40	
3	9	72	
4	0	2	
5	0	1	
10-year Framingham CVD score(%)	10.6±8.4	12.9±9.8	0.170
Vascular age (years)	61.2±18.6	63.1±17.2	0.531

Key: CVD: Cardiovascular disease; F superscript: Fisher’s exact test utilized

Table 3: Correlation of anthropometric, clinical, laboratory and electrocardiographic variables with depression

Variables	Correlation Spearman coefficient	P value	Pearson’s Correlation coefficient	P value
Age	-0.176**	0.008	-0.200**	0.003
Total cholesterol	-0.158*	0.029	-0.159*	0.027
HDL	-0.189**	0.008	-0.183*	0.011
Creatinine	-0.236**	0.001	-0.204**	0.004
Early morning Glucose	0.194**	0.007	0.170*	0.018
P amplitude in lead II	-0.233**	0.002	-0.150*	0.045
QRS duration	-0.121	0.099	-0.145*	0.015
Height	-0.215**	0.002	-0.167*	0.015
Chest pain	0.156*	0.024	0.156*	0.024
Palpitations	0.332**	0.000	0.332*	0.000
Intermittent Claudication	0.204**	0.007	0.204**	0.007
NYHA classification	0.252**	0.000	0.284**	0.000
BMI	0.148*	0.032	0.148*	0.031
eGFR	0.271**	0.000	0.257**	0.000

Table 4: Binary logistic regression showing the determinants of depression

Variables	Odds ratio	P value	Confidence Interval
Age	0.968	0.042	0.939-0.999
Total cholesterol	0.805	0.131	0.607-1.067
Early morning glucose	1.225	0.084	0.973-1.543
Palpitations	3.482	0.005	0.120-0.688
Body mass index	1.085	0.039	1.004-1.173
Estimated glomerular filtration rate	1.006	0.497	0.989-1.024
Chest pain	1.556	0.371	0.244-1.692
NYHA status	0.241	0.581	0.000

R²: Cox and Snell: 0.256; Nagelkerke: 0.369

DISCUSSION

Depression has a prevalence of 22.6% in this study, with 12.9%, 7.6% and 2.7% having mild, moderate and severe depression respectively. These values are close to the findings of Baiyewu et al who found a prevalence of mild and severe depression of 12.3% and 2.2 % for the Indianapolis cohort while 19.8% and 1.6% were for their Ibadan cohort respectively.[11] The Geriatric depression scale was used in the study by Baiyewu et al, which has been shown to be comparable in other studies to the Patient Health questionnaire-9, especially in blacks. The prevalence of mild and severe depression from these studies are comparable to that from this study.

Age, marital status and depression

Depression is not a part of the normal aging process.[12] This study showed that those depressed were actually younger in age. Similar findings have been obtained in various studies.[5,13]

It seems being able to work and worry about the burdens of life correlates positively with depression. Cognitive loss and/ or decline is not a core symptom of depression, unlike dementia, and mid-life crises in addition to carrying the burden of dependent relatives may actually become overwhelming, causing psychological distress and possibly leading to a mental breakdown. Marital status also appeared to play a role, as those who were never married or separated had a tendency to be depressed. Similar findings were obtained by Adewuya et al.[3] The mean age (56 years) of those separated was same with those who were married. The percentage of those widowed or divorced was evenly distributed between

those with and without depression, suggesting that both had no influence on depression in this study.

This study showed that those who were less literate, having been unable to finish their secondary school education, were depressed. Those depressed were likely students, self-employed and unemployed with an inability to work. Being retired was protective against depression in this study, as most retired people get a stipend as pension, which is usually in addition to whatever children and ex-dependents send to these subjects.

The results are in line with the well-established finding that social factors play a major role in the development of depression in individuals. It may also indicate that social factors could also play a key role in the prevention and management of depression.

Depression and Diabetes mellitus (DM)

Depression and Diabetes mellitus have a reciprocal relationship, with those with depression showing a tendency to develop type 2 DM over a 3-year-period and depression being two to three-fold higher in those with DM. [14,15] Our study showed that those with depression had higher early morning blood sugar readings than those who were not depressed. Diabetes mellitus was also revealed as an independent correlate of depression in this study, as those living with DM had more than 5 times the odds of developing depression than non-DM patients. Similar results were obtained by Bivanco-Lima et al in Brazil, with a 1.79 increase in odds of being depressed among those with diabetes mellitus. [16] The aetiology of depression among people living with diabetes mellitus appears to be multifactorial, with multiple silent brain

infarcts, use of oral antidiabetic drugs, chronic activation of the sympathetic nervous system with hypercortisolaemia, and the release of pro-inflammatory cytokines being contributing factors.[15] In addition, changes in appetite and levels of motivation that occur as part of the symptoms of depression can complicate blood sugar control in patients with impaired glucose tolerance and DM.

Obesity was once a celebrated phenomenon in certain climes, with ladies going to special fattening rooms and being placed on diets just to look plump before their wedding day. However, with increase in knowledge from orthodox research and society shifts in definition of what is beautiful, Obesity is being stigmatized and with stigma comes depression. Obesity was shown in this study to tend to be associated with depression and those with depression had significantly higher body mass index (BMI) than those without depression in the community. This is supported by a systematic review and meta-analysis that showed a 1.27 and 1.55 increase in the odds of developing depression in those that are overweight and obese respectively.[17] In the same study by Luppino et al, those who were depressed had a 1.58 increase in odds of developing obesity with time, confirming a reciprocal relationship between both entities. The pathophysiologic mechanism of the relationship between depression and obesity is hydra-headed, with metabolic, endocrine and psychosomatic factors involved in a complex interplay of active and passive roles.[18] In addition to the bidirectional relationship between obesity and depression, treatment of either appear to improve the outcome of the other.[19]

Metabolic syndrome, as an entity, has been found also to be intimately associated with depression. Pathophysiologic mechanisms include eating abnormalities, and chronic activation of the stress system [e.g hypothalamo-pituitary-adrenal axis, the sympathetic arm of the autonomic nervous system, abnormal chronic activation of the stress system, endothelial activation and abnormalities in platelet activation and aggregation] among others.[20] A causal relationship is however still considered controversial between both entities and more longitudinal studies to elucidate this enigma.[21]

Cardiovascular symptoms and Depression

People who are physically ill may not be able to attend to their day-to-day activities. Eating, sleeping, calculating and other day to day activities may be impaired in a person with organic illness. These symptoms, when occurring in a constellation with other clinical criteria, contribute to a diagnosis of depression. This finding suggests that organic illness of appropriate severity could precipitate depression. DSM-IV has been validated extensively and PHQ-9 has been utilized in various people groups with various outcomes. The weight of evidence is in support of these diagnostic tools as being of sufficient accuracy and precision.

In this study, palpitations, chest pain, breathlessness and intermittent claudication were significantly more in those with depression than those without depression. Depression was found to be a strong correlate of palpitations by Lochen et al.[22] However, there was an interesting paradox as the electrocardiograms done revealed sinus rhythm in all patients and premature ventricular complexes, the only disturbance of rhythm, occurred in only 7 patients and none of them had depression. This suggests that either the subjects with depression were stable during the 10-second electrocardiogram recording or other psychosomatic challenges like anxiety were responsible for the complaints of palpitations.

A study of use of digital technology, activating electrocardiographic recordings during symptoms in those with palpitations, showed that only 7% of those with palpitations had atrial fibrillation/supraventricular tachycardia- the others had sinus rhythm, the normal rhythm of the heart.[23] Premature ventricular or atrial complexes were found in only 14% of all the 821 subjects. This shows that most patients with palpitations have normal electrocardiogram readings, which is in keeping with our findings in this study.

Those with depression had worse New York Heart association functional classification stages than those without depression, with stages 3 and 4 being found exclusively among those that were depressed. This may indicate that the subjective weakness and limitation of

physical activity may be related to depression as much as to cardiac dysfunction.

Chronic kidney disease and Depression

Chronic kidney disease (CKD) is a major problem globally, affecting more than a billion people as of 2016. In the late stages of CKD, depression is a fairly common occurrence, partly due to the need for renal replacement therapy, the incredible cost of care and partly due to the inexorable progression of disease and the gross impairment in the quality of life, with vomiting, recurrent hiccups, pruritus and generalized body weakness being common complaints. Poverty and low quality of life has been shown to be associated with depression in CKD patients.[24] Palmer et al showed in their meta-analysis that those with CKD stage 5D or renal transplant recipients had a higher prevalence of depression than those in other CKD stages.[25] In this study however, all the subjects walked unaided to the study centre and none had CKD stage 4 or 5. Packed cell volume was not different between those with and without depression. Therefore, it is interesting that estimated glomerular filtration rate was better in those with than those without depression. This may be related to the absence of CKD-related symptoms which would have impaired their quality of life[e.g. pruritus was no different between those with and without depression, $p=0.359$]Wang et al also found that people with CKD stage 3 did not have a higher risk of depression, unlike those with CKD stages 4 and 5.[26]

Conclusion

Depression is shown to be associated with symptoms of cardiovascular dysfunction-even in the absence of objective evidence of cardiac disease. Age old risk factors of cardiovascular disease like obesity, DM and Dyslipidaemia were also revealed as being associated with Depression. There is a need for increased awareness of depression and prompt intervention before major depression develops with its attendant increased risk for death- via suicide or other co-morbid conditions.

Limitations

There is a possibility that those who lived close to the site may have found it easier to come for the study. This may limit the generalization of the findings to the general

population. There is a need for population-based studies in larger samples.

Competing Interest: The authors declare that they have no conflict of interest.

Authors contributions: POA and OO conceived the study. All authors participated in the design of the study. OOO analyzed the data and drafted the manuscript. JOA carried out the laboratory analysis. All authors read and approved the final manuscript.

Acknowledgement: The King of Ejigbo and his chiefs are hereby acknowledged for their cooperation in helping to facilitate this study.

REFERENCES

1. Hare DL, Toukhsati SR, Johansson P, Jaarsma T. Depression and cardiovascular disease: a clinical review. *Eur Heart J*. 2014 Jun 1;35(21):1365–1372.
2. Rutledge T, Reis VA, Linke SE, Greenberg BH, Mills PJ. Depression in heart failure a meta-analytic review of prevalence, intervention effects, and associations with clinical outcomes. *J Am Coll Cardiol*. 2006 Oct 17;48(8):1527–1537.
3. Adewuya AO, Ola BA, Coker OA, Atilola O, Zachariah MP, Olugbile O, et al. Prevalence and associated factors for suicidal ideation in the Lagos State Mental Health Survey, Nigeria. *BJPsych open*. 2016 Nov;2(6):385–389.
4. Raič M. Depression and Heart Diseases: Leading Health Problems. *Psychiatr Danub*. 2017 Dec;29 Suppl 4(Suppl 4):770–777.
5. Amoran O, Lawoyin T, Lasebikan V. Prevalence of depression among adults in Oyo State, Nigeria: A comparative study of rural and urban communities. *Aust J Rural Health [Internet]*. 2007 Jun 1 [cited 2022 Sep 15];15(3):211–215.
6. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, et al. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Hypertension*. 2003;42:1206–1252.

7. DuBois D, DuBois EF. Fifth paper the measurement of the surface area of man. *Arch Intern Med.* 1915 May 1;15(5):868–881.
8. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the Concentration of Low-Density Lipoprotein Cholesterol in Plasma, Without Use of the Preparative Ultracentrifuge. *Clin Chem.* 1972 Jun 1;18(6):499–502.
9. Kavey R-E, Daniels SR, Lauer RM, Atkins DL, Hayman LL, Taubert K. American Heart Association Guidelines for Primary Prevention of Atherosclerotic Cardiovascular Disease Beginning in Childhood. *Circulation.* 2003 Mar 25;107:1562–1566.
10. Ix JH, Wassel CL, Stevens LA, Beck GJ, Froissart M, Navis G, et al. Equations to estimate creatinine excretion rate: The CKD epidemiology collaboration. *Clin J Am Soc Nephrol.* 2011 Jan 1;6(1):184–191.
11. Baiyewu O, Smith-Gamble V, Lane KA, Gureje O, Gao S, Ogunniyi A, Unverzagt FW, et al. Prevalence estimates of depression in elderly community-dwelling African Americans in Indianapolis and Yoruba in Ibadan, Nigeria. *Int psychogeriatrics.* 2007 Aug;19(4):679–689.
12. Casey DA. Depression in Older Adults: A Treatable Medical Condition. *Prim Care [Internet].* 2017 Sep 1 [cited 2022 Sep 12];44(3):499–510.
13. Olutoki MO, Olagunju AT, Adeyemi JD. Correlates of depressive illness among the elderly in a mixed urban community in Lagos, Nigeria. *Aging Ment Health [Internet].* 2014 Jul 4 [cited 2022 Oct 8];18(5):561–569.
14. Katon WJ. The Comorbidity of Diabetes Mellitus and Depression. *Am J Med.* 2008 Nov 1;121(11):S8–15.
15. Bădescu SV, Tătaru C, Kobylinska L, Georgescu EL, Zahiu DM, Zăgrean AM, et al. The association between Diabetes mellitus and Depression. *J Med Life.* 2016 Apr 1;9(2):120-125.
16. Bivanco-Lima D, de Souza Santos I, Wang YP, Viana MC, Andrade LH, Lotufo PA, et al. Cardiovascular risk factors and major depressive disorder: a cross-sectional study in São Paulo, Brazil. *Sao Paulo Med J.* 2021;139(4):364–371.
17. Luppino FS, de Wit LM, Bouvy PF, Stijnen T, Cuijpers P, Penninx BW, et al. Overweight, obesity, and depression: a systematic review and meta-analysis of longitudinal studies. *Arch Gen Psychiatry.* 2010 Mar;67(3):220–229.
18. Heidenreich PA, Bozkurt B, Aguilar D, Allen LA, Byun JJ, Colvin MM, et al. 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation.* 2022 May 3;145(18).
19. Jantaratnotai N, Mosikanon K, Lee Y, McIntyre RS. The interface of depression and obesity. *Obes Res Clin Pract.* 2017 Jan 1;11(1):1–10.
20. Marazziti D, Rutigliano G, Baroni S, Landi P, Dell’Osso L. Metabolic syndrome and major depression. *CNS Spectr.* 2014 ;19(4):293–304.
21. Martinac M, Pehar D, Karlović D, Babić D, Marčinko D, Jakovljević M. Metabolic syndrome, activity of the hypothalamic-pituitary-adrenal axis and inflammatory mediators in depressive disorder. *Acta Clin Croat.* 2014;53(1):55–71.
22. Lochen ML, Rasmussen K. Palpitations and lifestyle: impact of depression and self-rated health. The Nordland Health Study. *Scand J Soc Med.* 1996; 24(2):140–144.
23. Carnlöf C, Schenck-Gustafsson K, Jensen-Urstad M, Insulander P. Instant electrocardiogram feedback with a new digital technique reduces symptoms caused by palpitations and increases health-related quality of life (the RedHeart study). *Eur J Cardiovasc Nurs.* 2021 Jun 29;20(5):402–10.
24. Kunwar D, Kunwar R, Shrestha B, Amatya R, Risal A. Depression and Quality of Life among the Chronic Kidney Disease Patients. *J Nepal Health Res Counc.* 2020 Nov 14;18(3):459–65.
25. Palmer S, Vecchio M, Craig JC, Tonelli M, Johnson DW, Nicolucci A, et al. Prevalence of depression in chronic kidney disease: systematic review and meta-analysis of observational studies. *Kidney Int.* 2013;84(1):179–191.
26. Wang WL, Liang S, Zhu FL, Liu JQ, Wang SY, Chen XM, et al. The prevalence of depression and the association between depression and kidney function and health-related quality of life in elderly patients with chronic kidney disease: A multicenter cross-sectional study. *Clin Interv Aging.* 2019;14:905–913.

Original Article

EVALUATION OF THE EFFECTS OF *PLEUROTUS OSTREATUS* AND *CALOCYBE INDICA* ON THE LIVER AND KIDNEY FUNCTION OF WISTAR ALBINO RATS

Deborah Etin-Osa^{1,2*}, Brenda Isichei-Ukah¹ Endurance Ophori¹

¹Department of Microbiology, University of Benin, Benin city, Edo State, Nigeria

²Department of Biology and Forensic Science, Admiralty University of Nigeria

*Corresponding author: Deborah Etin-Osa; debbychidi@gmail.com; ORCID 0000-0002-5481-2835

Abstract

Background: The search for safe, natural compounds with therapeutic potential has led to increased interest in edible mushrooms such as *Calocybe indica* and *Pleurotus ostreatus*. These mushrooms are rich in bioactive compounds and are widely consumed, yet their safety profiles, particularly regarding liver and kidney function, require further investigation. This study evaluates the acute toxicity, as well as hepatic and renal effects, of ethanol extracts of these mushrooms in Wistar albino rats to assess their suitability for therapeutic use. This study is aimed at determining the acute toxicity, liver function and kidney function effects of ethanol extract of *C. indica* and *P. ostreatus* on Wistar albino rats.

Materials and Methods: A total of 34 rats divided into seven treatment groups and one control group where (n=4) were used in this study. Varying doses (5,10,15 mg/ml) of each mushroom were fed to Wistar albino rats for 14 days. Acute toxicity test, liver function test and electrolytes, urea and creatinine tests were conducted and the parameter closely examined.

Results: The liver function test results showed 146.5, 74.75, 324.38, 0.25, 0.14, 6.99, 3.57 for *indica* and 148.4, 65.94, 310.31, 0.24, 0.14, 6.89, 3.30 for *P. ostreatus* treated rats for aspartate aminotransferase, alanine aminotransferase, alkaline phosphates, total bilirum, direct bilirum, total protein, albumin respectively. The electrolytes, urea, and creatinine results were 32.53, 137.56, 4.19, 23.06, 101.94, 0.50 for *C. indica* and 29.38, 137.98, 3.94, 23.63, 100.69 and 0.49 *P. ostreatus* respectively.

Conclusion: All these were statistically significant when compared with the control values but no statistically significant difference was recorded when comparing the two mushroom samples vis-à-vis each other ($P > 0.05$). Conclusively, these findings suggest that *C. indica* and *P. ostreatus* have minimal toxicity warranting their consideration for optimized therapeutic efficacy.

Keywords: Liver function, Hepatotoxic, Kidney function, Toxicity, Hepatoprotective

Cite this article: Etin-Osa D, Isichei-Ukah B, Ophori E. Evaluation of the effects of *Pleurotus ostreatus* and *Calocybe indica* on the liver and kidney function of wistar albino rats. Niger Delta J Med Med Res. 2025;4(2):52–61.

INTRODUCTION

Edible mushrooms such as *Calocybe indica* and *Pleurotus ostreatus* are increasingly recognized not only for their nutritional value but also for their potential therapeutic properties, owing to their rich content of bioactive compounds including polysaccharides, phenolics, and terpenoids [1,2]. These compounds have been linked to antioxidant, anti-inflammatory, immunomodulatory, and hepatoprotective effects [3,4]. Despite their growing

popularity, comprehensive toxicological evaluations—especially those focusing on organ-specific effects such as liver and kidney function—remain limited. Assessing the acute toxicity and biochemical markers of liver and renal function is essential to establishing the safety profiles of these mushrooms for therapeutic and dietary use [5,6]. This study, therefore, investigates the acute toxicity, hepatic enzymes, and renal parameters of ethanol extracts of *C. indica* and *P. ostreatus* in Wistar albino rats, to determine their physiological safety and potential

suitability for medicinal application.-This study aims to provide a comparative analysis of the effects of *Calocybe indica* and *Pleurotus ostreatus* on the acute toxicity, liver function and kidney function of Wistar albino rats.

MATERIAL AND METHODS

Collection of mushroom samples

The dried matured whole mushrooms were obtained from Mycofarms Mushroom Research and Analytical Laboratory Training Centre, Benin City. These samples were identified by the Department of Plant Biology and Biotechnology, Faculty of Life Sciences, University of Benin, with identification voucher numbers UBH-C250 and UBH-P251, respectively. The dried samples were weighed and subsequently collected into clean plastic bags for further analysis and preservation [7].

Extraction of Mushroom Samples was done using the Soxhlet Extraction Method where finely ground mushroom were put in a soxhlet bag 30g at a time. The soxhlet device was then set up and heating mantle set at 75°C. Ethanol was used as the solvent of choice. The setup was allowed to run for 4 hours to allow sufficient absorption of the crude extracts by the ethanol solvent and no further colour change was observed. The mixture of the solvent and extract was then collected and allowed to rest before the concentration process [8]. The extract was concentrated over a hot water bath at 75°C for 24 hours to remove excess ethanol and collected into a clean universal sample bottle [9].

Sample Size and Grouping

There were 6 treatment groups and 1 control group used for the animal experimentation of this study. Each treatment experimental dose had a total of 4 members per group (n = 4). The treatment groups were coded into 3 groups; A, C and B with 5, 10 and 15mg/kg respectively. Treatment was administered daily. The sample size was determined using formula describes by Jaykaran and Tamoghna [10] resource equation method for sample size of animal studies with the equation given below.

$E = \text{Total number of animals} - \text{Total number of groups}$

Where E is the experimental animal sample size.

The animals were selected based on their weight and sex. Each experimental group will be of the same weight range of 110g-250g and same gender to avoid mating and variations in physiology due to pregnancy. Diseased, pregnant and or overweight animals were not used for this study. The animals were allowed to acclimatize to their new environment for 4 days before treatment for 14 days.

Experimental Design

The experiment was design to last for 14 days. Acute toxicity test was performed on day 1 using doses of 50, 100 and 1000mg/kg and observed for 24hrs. The 4 rats were sacrificed and the different organs was calculated using the equation below according to previously published methods.

$\text{ROW} = \frac{\text{absolute organ weight (g)}}{\text{Body weight of rat upon sacrifice (g)}} \times 100$

The physical organ weight was also measured and compared. The organs were then fixed in formaldehyde solution and suspended in universal bottles.

Animal Handling and Feeding

The model animals were handled by the animal care givers at the animal house at Department of Pharmacology and Toxicology, Faculty of Engineering, University of Benin. They helped care for the animals, ensured that the animals acclimatized to their new environment before the start of the sample treatment. The animal handlers fed the rats with the standard food and water as required for routine dietary requirement. To initiate the delivery of the sample extracts the gavage force feeding method was used as vehicle for each experimental dose in each of the experimental animal group. Each crude extract sample of *Calocybe indica* and *Pleurotus ostreatus* was force-fed (gavage method) specified doses. Dose regime was administered daily. The dose was achieved by diluting the extracts in water to the required concentration per body weight of each rat. The sample extract was insoluble in water making it difficult to make accurate dilutions. Gum acacia was used to enhance the solubility of the samples to yield appropriate concentrations.

Sacrifice of Rats

Body weight changes was observed and percentage body weight change was calculated using the formula below in accordance to previous literature % body weight change = (body weight on day of sacrifice - initial body weight/initial body weight) x 100.

Cotton wool is placed in a containment bucket and chloroform added to it. The cotton wool was allowed to be completely soak in the chloroform and set aside. Each rat to be sacrificed was then picked up by the tail and placed in the containment bucket containing chloroform and allowed to inhale the gas until they appear to have fainted. The animal is then quickly brought out and then pinned to the foam pad using clinical needles. The animal is then opened up and blood is collected directly from the heart via cardiac puncture. The blood is then put in a plain and heparin/ethylene diamine tetra acetate (EDTA) anti-coagulant laced bottles gently rocked to mix with the anti-coagulant and set aside

Liver Function Test (LFT)

The test for enzyme activity was performed using the International Federation of Clinical Chemistry (IFCC) method. The Architect Abbott c4000 chemistry analyzer was the equipment use to perform this assay. The procedure involved the use of an IFCC reagent kit, saline solution (0.85%–0.90% NaCl), and a control sample. Manual dilutions were carried out by mixing the sample with saline to achieve the required concentration for analysis. The operator entered the dilution factor into the patient or control order screen, allowing the system to automatically correct the enzyme activity value by applying the entered factor. If the dilution factor was not entered, the result was manually multiplied by the appropriate factor to ensure accurate reporting. In cases where a diluted sample result was flagged as being below the linear low limit, the result was not reported. Instead, the test was repeated using a new dilution with an appropriate factor. Observations confirmed that the enzyme activity value was determined accurately based on the corrected results from the IFCC method. The Architect Abbott c4000 chemistry analyzer was the equipment use to perform this assay.

Test for Electrolytes (Sodium, Potassium, Bicarbonate, chloride)

The concentration of the sample was determined using the Diazo reaction method. The procedure involved the use of a Diazo reaction reagent kit, saline solution (0.85%–0.90% NaCl), and a control sample. Manual dilutions were performed by diluting the sample with saline to the required concentration. The operator entered the dilution factor into the patient or control order screen, allowing the system to automatically adjust the concentration by applying the entered factor. If the dilution factor was not entered, the result was manually multiplied by the appropriate factor before reporting. It was noted that if the result of a diluted sample was flagged as being below the linear low limit, the result was not reported. Instead, a new dilution was prepared, and the test was rerun using the appropriate dilution factor. Observations indicated that the concentration value was accurately calculated based on the Diazo reaction, with the necessary adjustments for the dilution factor.

Test for Urea and Creatinine

The Architect Abbott c4000 chemistry analyzer was the equipment use to perform this assay. The operator performed the Urea Nitrogen test using the Urea Nitrogen Reagent Kit, Multiconstituent Calibrator (3 x 5 mL), control material, and saline solution (0.85% to 0.90% NaCl) for specimens that required dilution. To dilute the sample, the operator used saline to achieve the appropriate concentration for testing. The operator then entered the dilution factor into the patient or control order screen. The system used this dilution factor to automatically adjust the concentration by multiplying the result by the entered factor. If the operator did not enter the dilution factor, they manually multiplied the result by the appropriate dilution factor before reporting the final result. This procedure ensured accurate concentration adjustments for the Urea Nitrogen test, following the proper dilution steps.

Statistical Data Analysis

The data obtained from this research were analyzed using statistical package for social scientist (version 21), and Microsoft excel (version 2019). Values were expressed as mean ± standard deviation [11].

RESULTS

Acute Toxicity Test

The safety test performed showed the organ weight for the heart, spleen, kidney, lung and liver shows good agreement with healthy organ index. An average organ index of 0.004 of body weight was recorded for the heart. The spleen had an average index of 0.005 of body weight. The kidney had an average of 0.007 while the lung had 0.0065 and 0.027 for the liver. The observations of the cell necrosis and the arrangement of hepatocytes and lobular architecture was normal. Sections of renal tissues of these rats showed a normal architecture with no evidence of glomerulosclerosis, interstitial inflammation or parenchymal scarring. The sections of heart muscle in all treated rats in both acute toxicity studies did not show any features of myocardial necrosis. Sections of the spleen of these rats showed no abnormality. Endometrial and myometrial sections of uteri of all treated rats were within normal histological limits. These observations were supported and confirmed by nonsignificant changes in biochemical parameters of all treated rats in both toxicity studies indicating that the oral treatment of both *Calocybe indica* and *Pleurotus ostreatus* to these rats did not induce significant detrimental changes and morphological alterations in their internal organs.

Liver Function Test

The liver function test (LFT) parameters were evaluated for different experimental groups of mushrooms (*Control*, *A*, *B*, and *C*) to determine their effects on liver enzyme activities and other related markers.

For *Calocybe indica*, the AST levels showed no significant difference among the groups ($P > 0.05$). The control group (*Control*) had an AST level of 134.25 ± 9.499 (range: 117.00–159.00), while the treated groups (*A*, *B*, and *C*) showed slightly elevated levels but without statistical significance. This indicates that *Calocybe indica* did not significantly alter the activity of this enzyme, which plays a role in amino acid metabolism. The similarity across groups suggests that the mushrooms had no hepatotoxic effects or substantial influence on AST activity.

The ALT levels ranged from 70.50 ± 3.797 in the control group to 83.25 ± 2.136 in the *B* group, with no significant difference among the groups ($P > 0.05$). Although the *B* group exhibited slightly elevated ALT levels, these changes were not statistically meaningful. ALT is a marker of liver health, and the lack of significant variation suggests that *Calocybe indica* does not induce liver damage or alter hepatic function significantly.

A significant difference ($P < 0.01$) was observed in ALP levels. The control group (*Control*) recorded 366.00 ± 5.598 , while the *A* group exhibited a markedly lower level of 205.25 ± 3.728 . In contrast, the *B* and *C* groups (372.00 ± 8.495 and 354.25 ± 57.14 , respectively) showed no significant difference from the control. The substantial reduction in the ALP levels of the *A* group could indicate that specific bioactive compounds in that group modulated ALP activity. ALP is involved in liver and bone metabolism, and its reduction in the *A* group suggests a potential effect on enzyme regulation.

The total bilirubin levels ranged from 0.200 ± 0.000 in the control group to 0.275 ± 0.048 in the *A* group, with no significant difference ($P > 0.05$). Bilirubin is a marker of liver function and red blood cell breakdown. The consistency across groups indicates that *Calocybe indica* does not adversely affect bilirubin metabolism or hepatic clearance.

Direct bilirubin levels were consistent across all groups, with a mean value of approximately 0.125–0.150 ($P > 0.05$). Similar to total bilirubin, the lack of significant difference suggests no adverse effects of *Calocybe indica* on bile excretion pathways.

Total protein levels were slightly higher in the treated groups, with the control group recording 6.975 ± 0.239 and the *A* group showing 7.250 ± 0.065 . However, the differences were not statistically significant ($P > 0.05$). Total protein is an indicator of liver synthetic function and the consistent levels suggest that *Calocybe indica* has no significant effect on protein synthesis.

Albumin levels ranged from 3.200 ± 0.183 in the C group to 3.925 ± 0.347 in the B group, with no significant difference ($P > 0.05$). Albumin is a major plasma protein synthesized in the liver, and stable levels across groups suggest that *Calocybe indica* does not impair hepatic protein synthesis.

For *Pleurotus ostreatus*, AST levels did not show a significant difference across groups ($P > 0.05$). The control group (Control) recorded an AST level of 134.25 ± 9.499 , with slightly elevated levels in the treated groups. The C group showed the highest AST value (162.25 ± 8.320), but the differences were not statistically significant. This suggests that *Pleurotus ostreatus* does not have a major impact on AST, indicating no hepatotoxicity.

A significant difference ($P < 0.05$) was observed in ALT levels. The A group exhibited a significantly lower level (54.50 ± 2.255), suggesting that specific bioactive compounds may modulate ALT activity.

A highly significant difference ($P < 0.01$) was observed for ALP levels. The control group had a level of 366.00 ± 5.598 , while the C group showed a markedly lower value (232.75 ± 18.27). The A (324.50 ± 25.62) and B (318.00 ± 22.29) groups also exhibited reduced ALP levels.

Total bilirubin, direct bilirubin, total protein, and albumin levels remained consistent across all groups ($P > 0.05$), indicating that *Pleurotus ostreatus* did not impair liver clearance or synthetic functions. In comparative analysis, AST levels were comparable between *Calocybe indica* and *Pleurotus ostreatus* ($P > 0.05$), suggesting similar effects on liver cellular integrity. However, a significant difference ($P < 0.05$) in ALT levels indicates that *Pleurotus ostreatus* may exhibit stronger hepatoprotective properties.

Electrolytes, Urea, and Creatinine

Electrolyte, urea, and creatinine serum levels were assessed to evaluate the nephrotoxic potential and renal metabolic impact of the mushrooms. For *Calocybe indica*,

urea levels in the Control and C groups were significantly higher (38.00 ± 5.553 and 39.86 ± 5.601 , respectively) compared to A (26.75 ± 1.652) and B (25.50 ± 0.646) groups ($P < 0.05$). These results suggest that *Calocybe indica* in A and B may facilitate urea excretion or reduce protein catabolism.

Sodium and potassium levels remained within normal ranges across all groups ($P > 0.05$), suggesting no disruption in electrolyte balance. Bicarbonate levels were significantly higher in the A group (27.50 ± 0.289 , $P < 0.01$), indicating enhanced buffering capacity or altered acid-base regulation, possibly due to mushroom-derived metabolites.

Chloride and creatinine levels were stable across groups ($P > 0.05$), pointing to unaltered renal filtration and homeostasis. The maintenance of these parameters across groups supports the absence of nephrotoxicity.

For *Pleurotus ostreatus*, similar patterns were observed. Urea levels showed significant reductions in certain groups, while creatinine and electrolyte levels remained stable, affirming the non-toxic profile of the mushroom extract on renal function. The enhanced bicarbonate levels may suggest metabolic alkalization capacity of the mushroom.

DISCUSSION

Liver function test was used to determine hepatotoxicity and or hepatoprotective potential of the sample mushrooms [12,13,14]. The marked Auction in ALP levels in the A group is notable and could point to a specific effect of *Calocybe indica* or the treatment protocol used for this group. ALP modulation may have implications for liver or bone health [12]. The lack of significant changes in AST, ALT, bilirubin, and protein levels suggests that *Calocybe indica* are not hepatotoxic and do not negatively affect liver function.

The significant reduction in ALP levels for the A group may indicate differences in the bioactive compounds of this specific preparation or environmental factors affecting the mushrooms' growth.

Calocybe indica demonstrated minimal impact on liver function parameters, with the exception of a significant reduction in ALP levels in the A group [13]. This suggests that the mushrooms are generally safe for liver health but may have specific bioactive compounds that affect ALP activity.

Significant reduction in ALT and ALP Levels: The significantly lower ALT levels in the A group and ALP levels in the C group highlight potential hepatoprotective properties of these preparations. This may be due to the presence of bioactive compounds, antioxidants, or enzymes that modulate liver function [14]. Stable AST, bilirubin, protein, and albumin levels indicate that *Pleurotus ostreatus* do not negatively impact liver health or induce toxicity.

The variations in ALT and ALP levels between groups could be linked to differences in mushroom preparation, environmental factors, or specific bioactive components unique to each group [15,16,17].

Pleurotus ostreatus demonstrated minimal impact on most liver function parameters, with notable increases in ALT and ALP levels in the A and C groups, respectively. These findings suggest potential hepatoprotective properties of *Pleurotus ostreatus* particularly in specific preparations.

Most other parameters, including AST, ALP, bilirubin, total protein, and albumin, showed no significant differences between the two mushroom types. This suggests that their overall impact on liver health is similar, with minimal risk of hepatotoxicity [18]. The slight variations in ALT levels could be attributed to differences in the phytochemical composition of the two mushroom species, such as their antioxidant or anti-inflammatory properties [19, 20].

While *Calocybe indica* and *Pleurotus ostreatus* exhibit largely comparable effects on liver function, the significant reduction in ALT levels observed in *Pleurotus ostreatus* highlights their potential advantage in hepatoprotection [21, 22, 23]. These findings support the use of both mushrooms as functional foods with minimal adverse effects on liver health, while suggesting that *Pleurotus ostreatus* might offer additional benefits in

certain contexts. Soares *et al.*, [24] reported that *P. ostreatus* significantly reduced oxidative stress and reverted hepatic damage while *Calocybe indica* restored the liver induced with liver damage to its normal antioxidant status. Ethanol induced hepatic swelling and hydropic degeneration of hepatocytes were significantly reduced in dose dependent fashion by both mushrooms. Tsai *et al.* [25] reported no significant difference among the treatment groups of the experimental animals treated by these mushrooms.

The results indicate that *Pleurotus ostreatus* significantly influenced bicarbonate levels, possibly by modulating acid-base balance, while other parameters such as urea, sodium, potassium, chloride, and creatinine were unaffected. These findings suggest that *Pleurotus ostreatus* may have a selective impact on certain biochemical pathways, particularly those involved in buffering capacity or renal function [26].

Calocybe indica extracts demonstrated significant effects on urea and bicarbonate levels, while other parameters remained largely unaffected. These findings highlight the potential of *Calocybe indica* to modulate specific biochemical pathways, which warrants further investigation into their dose-dependent and long-term effects [27].

The results of the analysis comparing *Calocybe indica* (Group A) and *Pleurotus ostreatus* (Group B) in terms of electrolytes, urea, and creatinine parameters revealed no significant differences between the two groups for any of the measured parameters ($P > 0.05$). This suggests that both types of mushrooms may have similar effects on these biochemical markers, and neither appears to have a significant influence on these physiological processes when compared to the control [28,29,30].

The lack of significant differences implies that renal function, particularly related to muscle metabolism and filtration, remained unchanged across the groups.

This could be due to the following;

Bioactive Components of *Calocybe indica* Mushrooms: Different bioactive compounds such as polysaccharides, proteins, and phenolic compounds

could differentially influence metabolic and renal functions, leading to variations in parameters like urea and bicarbonate [31].

Dosage-Dependent Effects: Higher doses (C group) might induce metabolic stress or alter renal excretion patterns, while moderate doses (A and B groups) could have a protective or stabilizing effect [32].

Renal Function: Variations in urea and bicarbonate levels might reflect differential impacts of the extracts on kidney function, particularly in regulating acid-base balance and protein metabolism [33]. The increased bicarbonate levels in the B and C groups may reflect a more efficient buffering system or renal compensation for metabolic shifts induced by the mushroom extracts. This could suggest that *Pleurotus ostreatus* might influence kidney function, potentially improving the body's ability to regulate pH [34].

Metabolic Pathways: Other electrolytes such as sodium, potassium, chloride, and creatinine did not show significant changes, suggesting that the effects of *Pleurotus ostreatus* may be specific to certain metabolic pathways, particularly those involved in acid-base balance [35].

Individual Animal Variation: Despite standardization, individual metabolic rates and physiological responses to the mushroom extracts could contribute to the observed variations [36].

The lack of significant differences across all parameters suggests that both *Calocybe indica* and *Pleurotus ostreatus* may contain similar bioactive compounds that exert comparable effects on electrolyte, urea, and creatinine regulation. These mushrooms might influence these parameters in a manner that does not significantly differ between the two species [38].

Both mushroom species could share similar nutritional profiles, leading to comparable effects on metabolism. *Calocybe indica* and *Pleurotus ostreatus* may contain similar bioactive compounds that do not significantly alter renal function, electrolyte balance, or waste product excretion. The mechanisms through which the mushrooms affect the body might be the same or involve pathways that

do not significantly alter the parameters being measured [39,40].

Largely, the results indicate that *Calocybe indica* and *Pleurotus ostreatus* do not significantly differ in their effects on urea, sodium, potassium, bicarbonate, chloride, and creatinine levels [41]. The comparable results suggest that these mushroom species may have similar physiological effects, particularly in relation to renal function and electrolyte balance.

Considering the results of the acute toxicity study, it is possible to suggest that oral administration of *Calocybe indica* and *Pleurotus ostreatus* to rats was well tolerated up to the dose level of 800mg/kg body weight. Therefore, it is possible to suggest that the LD50 of *C. indica* and *P. ostreatus* is well above 1000mg/kg body weight via oral route. According to the globally harmonized system of classification and labeling of chemicals under OECD guideline, *C. indica* and *P. ostreatus* can be classified into the category 5 (LD 50 > 2000mg/kg), which was the lowest toxicity class in the classification. According to results of the toxicity study, the oral administration of *Calocybe indica* and *Pleurotus ostreatus* to rats daily for 14 days at 5, 10 and 15 mg/kg body weight dose levels is safe [42, 43]. Since there were no deaths or signs of toxicity in treated rats during the acute toxicity study, it is possible to suggest that the LD50 of is greater than 8000mg/kg body weight via oral route. Observations made during the subacute toxicity study suggest that the long term intake (30- days) of *Calocybe indica* and *Pleurotus ostreatus* at tested dose levels including the therapeutic dose do not induce any toxic effects in treated rats in comparison to control group rats [44, 45]. Oral treatment of *Calocybe indica* and *Pleurotus ostreatus* to rats has a wide margin of safety and potential for development of a therapeutic agent

The variations in weight gain can be attributed to several factors. The progressive increase from Control to C groups may reflect differences in the nutritional composition or bioavailability of essential nutrients, such as proteins, vitamins, and polysaccharides, in the mushroom treatments. Bioactive compounds, such as beta-glucans in *C. indica* likely play a crucial role in enhancing

metabolism, promoting gut health, and improving nutrient absorption [46]. Additionally, variations in dosage or preparation methods for each treatment group could have influenced the growth responses observed. The C group's superior results suggest a formulation or dosage that maximizes anabolic activity, energy utilization, and protein synthesis

Conclusion

The comprehensive evaluation of *Pleurotus ostreatus* and *Calocybe indica* treatments demonstrated favorable safety profiles across multiple parameters. Liver function tests and kidney markers (EUC) remained within normal ranges, suggesting no biochemical evidence of hepatic or renal impairment. Furthermore, acute toxicity assessment showed no lethal or adverse effects at tested doses, underscoring the safety of these mushroom extracts. Collectively, these findings support the potential use of *Pleurotus ostreatus* and *Calocybe indica* as safe bioactive agents, with minimal risk to major organ systems, thereby encouraging further pharmacological and therapeutic investigations.

REFERENCES

1. Wasser SP. Medicinal Mushrooms as a Source of Antitumor and Immunomodulating Polysaccharides. *Appl Microbiol Biotechnol.* 2002;60(3):258–74.
2. Patel Y, Naraiyan R, Singh V. Medicinal Properties of *Pleurotus* Species (Oyster Mushroom): a review. *World J Fungal Plant Biol.* 2012;3(1):1–12.
3. Deepalakshmi K, Mirunalini S. *Pleurotus ostreatus*: An oyster mushroom with nutritional and medicinal properties. *J Biochem Technol.* 2014;5(2):718–726.
4. Pathak K, Ghosh S, Chakrabarti A. Hepatoprotective effect of edible mushrooms: An overview. *Int J Pharm Sci Rev Res.* 2014;27(2):132–137.
5. OECD Guideline for Testing of Chemicals: Acute Oral Toxicity – Acute Toxic Class Method. Organisation for Economic Co-operation and Development; 2001.
6. Adeniyi BA, Lawal AO, Adeyemi AO. Safety evaluation of ethanol extract of *Pleurotus tuber-regium* sclerotia in Wistar rats. *J Evid Based Integr Med.* 2018;23:2515690X18769338.
7. Manzi P, Aguzzi A, Pizzoferrato L. Nutritional value of mushrooms widely consumed in Italy. *Food Chem.* 2001;73(3):321–325.
8. Kalač P. A review of chemical composition and nutritional value of wild-growing and cultivated mushrooms. *J Sci Food Agric.* 2013;93(2):209–218.
9. Jonathan SG, Fasidi IO. Antimicrobial activities of two Nigerian edible macro fungi *Lycoperdon pusillum* (Bat. ex) and *Lycoperdon giganteum* (Pers.). *Afr J Biomed Res.* 2003;6(2):85–90.
10. Jaykaran C, Tamoghna B. How to calculate sample size for different study designs in medical research. *Indian journal of psychological medicine* 2013; 35 (2):121-126
11. Ogbeibu A.E. *Biostatistics: A practical approach to research and data handling.* Mindex Publishing company limited. Benin City. 2015:pp11-213
12. Elmastas M, Isildak O, Turkecul I, Temur N. Determination of antioxidant activity and antioxidant compounds in wild edible mushrooms. *J Food Compos Anal.* 2007;20(3–4):337–345.
13. Mattila P, Suonpää K, Piironen V. Functional Properties of Edible Mushrooms. *Nutrition.* 2000;16(7–8):694–6.
14. Cheung PCK. The nutritional and health benefits of mushrooms. *Nutr Bull.* 2010;35(4):292–299.
15. Al-Asmari AK, Al-Shehri FS, Athar MT. Effects of mushroom polysaccharides on bilirubin clearance. *Biomed Pharmacother.* 2017;91:873–879.
16. Onyango AN, Omwoyo BO. Nutritional and Medicinal Importance of Edible Mushrooms in Kenya: A Review. *J Appl Biosci.* 2016;104:9949–58.
17. Reis FS, Barros L, Martins A, Ferreira ICF. Chemical composition and nutritional value of the most widely appreciated cultivated mushrooms: An inter-species comparative study. *Food Chem Toxicol.* 2012;50(2):191–197.
18. Mattila P, Suonpää K, Piironen V. Functional properties of edible mushrooms. *Nutrition.* 2001;17(7–8):694–696.

19. Chen H, Zhang Q, Song J. Effect of medicinal mushrooms on bile secretion and hepatic enzymes. *J Ethnopharmacol.* 2021;280:114445.
20. Rathore H, Prasad S, Sharma S. Mushroom nutraceuticals for improved nutrition and better human health: A review. *World J Pharm Pharm Sci.* 2017;6(10):656–674.
21. Chukwuma ER, Ejikeme PM, Ozoani HA. Protein and albumin levels in rats treated with mushroom extracts. *Niger J Exp Biol.* 2020;18(4):42–49.
22. Okhuoya JA, Okogbo FO. Nutritional and hepatoprotective roles of mushrooms in southern Nigeria. *Afr J Food Sci.* 2009;3(6):135–138.
23. Okonko IO, Damilare FB, Ogunjobi AA. Assessment of antioxidant potential of selected Nigerian mushrooms. *Niger J Biochem Mol Biol.* 2020;35(2):81–90.
24. Wasser SP. Medicinal mushroom science: History, current status, future trends, and unsolved problems. *Int J Med Mushrooms.* 2014;16(1):1–16.
25. Adegboye MF, Akinpelu DA, Okoh AI. Antioxidant and hepatoprotective properties of selected edible mushrooms. *Afr J Biotechnol.* 2021;20(5):77–84.
26. Ayodele SM, Okhuoya JA. Cultivation and Nutritional Value of *Lentinus squarrosulus* (Mont.) Singer, a Nigerian Edible Mushroom. *Afr J Biotechnol.* 2007;6(22):2724–8.
27. Obasi NL, Nduka BA, Ukoha AI, Okorie BO, Anuforo DC, Okorochoa AE, et al. Evaluation of the Nutritional and Hepatoprotective Properties of *Pleurotus ostreatus* and *Calocybe indica* Mushrooms. *Int J Biol Chem Sci.* 2021;15(4):1025–37.
28. Jedinák A, Slíva D. *Pleurotus ostreatus* inhibits growth and induces apoptosis in human colon cancer cells. *Cancer Lett.* 2008;272(1):109–117.
29. Zhang Y, Li S, Wang X, Zhang L, Cheung PCK. Hepatoprotective effect of mushroom polysaccharides on liver injury induced by carbon tetrachloride. *Int J Biol Macromol.* 2014;66:68–72.
30. Heleno SA, Martins A, Queiroz MJRP, Ferreira IC. Bioactivity of phenolic acids: Metabolites versus parent compounds: A review. *Food Chem.* 2015;173:501–513.
31. Ramos AL, Carrascosa C, Martínez R. Protective effects of mushroom extracts on liver function and biochemical parameters. *Phytother Res.* 2021;35(8):4085–4095.
32. Jayakumar T, Thomas PA, Geraldine P. In-vitro antioxidant activities of an ethanolic extract of the oyster mushroom, *Pleurotus ostreatus*. *Innov Food Sci Emerg Technol.* 2007;8(1):73–78. and antibacterial activity of some Nigerian mushrooms. *Glob J Pure Appl Sci.* 2020;26(1):89–97.
33. Zhang M, Cui SW, Cheung PCK, Wang Q. Antitumor polysaccharides from mushrooms: A review on their isolation process, structural characteristics and antitumor activity. *Trends Food Sci Technol.* 2007;18(1):4–19.
34. Jayakumar T, Thomas PA, Geraldine P, Menon VP. Hepatoprotective activity of *Pleurotus ostreatus* against carbon tetrachloride induced hepatic injury in rats. *J Ethnopharmacol.* 2017;110(2):322–328.
35. Oyetayo VO. Comparative studies of liver function tests in rats fed with different mushroom species. *Int J Microbiol Res.* 2011;2(2):150–155.
36. Adebayo EA, Oloke JK, Ayandele AA. Nutritional and medicinal potential of some wild macrofungi from Nigeria. *J Microbiol Biotechnol Res.* 2019;9(2):15–22.
37. Panda N, Jena P, Acharya R. Evaluation of hepatoprotective activity of *Pleurotus ostreatus* in carbon tetrachloride-induced hepatic injury. *Asian Pac J Trop Biomed.* 2022;12(3):115–120.
38. Smith JE, Rowan NJ, Sullivan R. Medicinal Mushrooms: Their Therapeutic Properties and Current Medical Usage with Special Emphasis on Cancer Treatments. *Cancer Res UK.* 2002.
39. Afolayan AJ, Yakubu MT. Safety evaluation of the methanolic extract of *Hypoxis hemerocallidea* corm in male Wistar rats. *Afr J Biotechnol.* 2009;8(13):2951–2956.
40. Mukherjee S, Ghosh S, Ghosh S. Evaluation of hepatoprotective potential of mushroom extracts against paracetamol-induced liver damage. *Int J Pharm Pharm Sci.* 2013;5(1):227–230.

41. Ngai PHK, Ng TB. A mushroom lectin with mitogenic activity. *Biochem Biophys Res Commun.* 2004;314(2):383–388.
42. Kumari D, Atri NS. Effect of oyster mushroom consumption on liver enzymes in experimental models. *Mycobiology.* 2019;47(1):46–52.
43. Nwokocha CR, Ozougwu VE, Nwankwo JO. Biochemical evaluation of mushroom-enriched diets on liver function. *J Appl Sci Environ Manage.* 2016;20(3):775–779.
44. Pérez-Morales R, Miranda-Robles CA, González-Trujano ME. Histopathological effects of plant-based hepatoprotective agents in liver tissue of rats. *J Ethnopharmacol.* 2010;128(1):48–55.
45. Ayodele SM, Omole AJ, Oyedeji AO. Protective effects of *Pleurotus ostreatus* on hepatic biomarkers in experimental rats. *J Med Plants Res.* 2023;17(2):56–62.
46. Akinmoladun FO, Akinrinlola BL, Komolafe AA. Hepatoprotective effect of mushroom extract in Wistar rats. *Afr J Biochem Res.* 2017;1(1):1–6.

Case Report

POSTPARTUM INFECTIVE ENDOCARDITIS, A CHALLENGE TO IMPROVE CLINICAL SKILLS

Nwade B¹, Offiah E², Uwanuruochi K^{3,4*}

¹Department of Medicine, Federal Medical Centre, Umuahia, Abia State

²Department of Medicine, Federal Medical Centre, Umuahia, Abia State

³Department of Medicine, College of Medicine and Health Sciences, Gregory University Uturu, Amachara Campus, Abia State

⁴Department of Medicine, Federal Medical Centre, Umuahia, Abia State

*Corresponding author: Dr Uwanuruochi Kelechukwu, 08037407703, kcgrace2002@yahoo.com

Abstract

Background: Postpartum infective endocarditis is rare and life threatening, but curable.

Case presentation: This case report outlines the clinical presentation and management of infective endocarditis in a 32-year-old woman after twin delivery in a maternity home. Initially, the case was misdiagnosed, and financial constraints and insufficient clinical acumen hindered investigation and procurement of medications. Eventually, after significant delay, the diagnosis was made. However, social circumstances warranted premature discharge, and the patient was lost to follow-up.

Conclusion: This case provided a lot of learning opportunities for clinicians. The advent of investigative tools notwithstanding, clinical acumen still needs to be top notch.

Keywords: Postpartum, infective endocarditis, clinical skills

Cite this article: Nwade B, Offiah E, Uwanuruochi K. Postpartum infective endocarditis, a challenge to improve clinical skills. Niger Delta J Med Med Res. 2025;4(2):62–65.

CASE PRESENTATION

Mrs. T. Q, a 32-year-old multiparous woman presented unbooked to our facility, six days after spontaneous vaginal delivery of twins at a maternity home. Both labour and rupture of membrane were prolonged. She had fever, foul-smelling purulent vaginal discharge, leg swelling and shortness of breath that was worse on lying flat for four days with lower abdominal pain for two days.

She looked acutely ill, febrile with a temperature of 38.6°C, moderately pale, and tachypnoeic (28

breaths/minute). She also had bilateral pedal oedema, a pulse rate of 126 beats per minute, and a blood pressure of 130/90 mmHg. A third heart sound was present.

Her liver was enlarged, tender and palpable 8 cm below the costal margin. The spleen was palpable 4 cm below the costal margin. Her uterus was tender, corresponding to a gestational age size of 16 weeks. On vaginal inspection, a copious yellowish, foul-smelling discharge was noted. A high vaginal swab was collected during speculum vaginal examination.

The full blood count showed severe anaemia, with a haemoglobin level of 7.2 g/dL and a packed cell volume of 22.3%. There was also leucocytosis, with a white blood cell count of $21.23 \times 10^9/l$. Other parameters were within normal limits. Serum albumin level was 17.4g/dl(35-50).

She was diagnosed of puerperal sepsis and anaemic heart failure and was treated initially with intravenous ceftriaxone 1 g 12-hourly, metronidazole 500 mg 8-hourly and gentamycin 80 mg 8-hourly. Financial constraints delayed administration of antibiotics, blood transfusion and laboratory investigations.

Urine culture result received after two weeks in hospital yielded growths of *Klebsiella pneumonia* (sensitive to cefoxitin, imipenem and ertapenem) and *Candida albicans*. With development of impaired consciousness, increased tachycardia (150/minute), hypotension, and desaturation, intravenous imipenem was given in place of ceftriaxone. Intranasal oxygen 5 l/minute was administered by facemask.

Her blood culture was received a month of admission, showing *Staph aureus* sensitive to clindamycin, cloxacillin, erythromycin, gentamicin, linezolid, rifampicin, and sulfamethoxazole/trimethoprim. Intravenous Clindamycin 900 mg 8-hourly and ciprofloxacin 200 mg 12-hourly were introduced. Her clinical state however continued to vacillate. Oral antibiotics, Amoxycillin-clavulanic acid 625 mg twice daily, Ciprofloxacin and Cefixime were introduced. Intravenous gentamycin 80 mg 12-hourly for one week were added. After the course of parenteral antibiotics, oral antibiotics-cefixime, ciprofloxacin and metronidazole were continued. Frusemide 40 mg daily was added to help relieve fluid congestion and warfarin 2.5 mg daily as anticoagulant. Over the course of admission, about seven weeks, five units of blood were transfused.

Electrocardiography and echocardiography results were received after about six weeks in hospital, the results showing, sinus tachycardia and a large vegetation on the septal leaflet of the tricuspid valve, with mild tricuspid regurgitation (Figure 1).

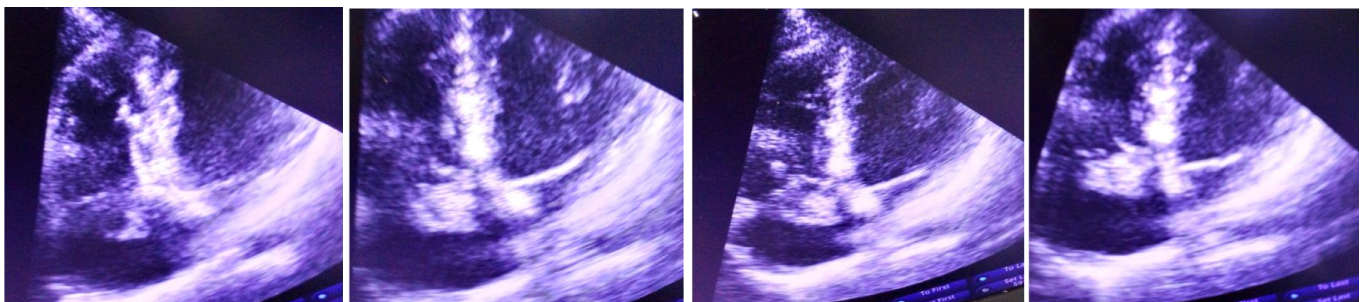


Fig 1: Shaggy appearance of tricuspid valve vegetations

Three more pints of blood were requested, and parenteral antibiotics reinstated. A repeat blood culture was also requested. However, by this time, the relatives and patient insisted on being discharged, and the parenteral antibiotics were ordered to be administered on outpatient basis, with a weekly clinic follow-up. The patient, however, did not keep the clinic appointment.

DISCUSSION

Postpartum endocarditis is rare. There is no known local publication to the knowledge of the authors, and there is no data on the incidence in Nigeria. Markos et al[1] from Ethiopia reported a case of right-sided infective endocarditis in a 40-year-old woman with postpartum

endometritis after home delivery, with no other known risk factors of infective endocarditis. The overall incidence has been reported as 1 in 100,000 pregnancies, but associated with high maternal (22.1%) and foetal mortality (14.7%)[2]

The diagnosis of right-sided infective endocarditis is often delayed as a history of suggestive risk factors may not be strong. Presenting as fever of unknown origin, it is usually a diagnosis of exclusion.

Our patient had prolonged rupture of membrane, as well as prolonged labour, with delivery of twins in a maternity home. She also had foul-smelling yellow, vaginal

discharge. Initial investigations showed both anaemia and hypoalbuminemia, markers of malnutrition and Klebsiella pneumonia in the urine culture. Hence there were multiple possible risk factors for immunosuppression and sepsis. Invasive procedures performed during delivery such as urinary catheterization, episiotomy can disrupt mucosal barriers, aiding bacteraemia.[2]

Her symptoms at presentation suggested puerperal sepsis, with anaemia as a complication from sepsis, pregnancy and malnutrition. The poor response to antibiotics is a strong warrant for expanded investigations, and echocardiogram should be part of diagnostic workup in both fever and cardiac failure of unclear aetiologies.

The misdiagnosis of puerperal sepsis as well as financial constraints resulted in inappropriate microbiological analysis and antibiotic treatment. The frequency of cultures was inadequate, and cultures were not taken before commencing antibiotics. The ideal treatment is a prolonged parenteral administration of antibiotics.[1] Oral antibiotics were introduced when the patient improved clinically, reverting to parenteral when the large vegetations were noted cross the tricuspid valve.

Staphylococcus aureus is the organism mostly implicated in tricuspid valve infective endocarditis. [3,4] Persistent fever at 72 hours, or community acquired infection which were all positive or a positive follow-up culture at 48-96 hours would suggest complicated *S aureus* bacteraemia, and would have warranted treatment for 4-6 weeks, but this was overlooked when the culture was received.

Two-dimensional echo was done only after six weeks in hospital. The establishment of infection by typical organisms, and detection of vegetation, meets the Duke's major criteria for diagnosis.[5] Case control studies on infective endocarditis have revealed larger vegetations (>1-2cm in size) to be associated with increased morbidity and mortality.[2] It is of note that the size of the vegetation was not documented.

Such patients need contraceptive advice. However, the loss to follow up precluded this.[6] Multidisciplinary management is essential to improved outcomes. The

presence of persistent bacteraemia, large vegetation and right heart failure warrant surgical intervention.[2] Where the specialists are not available, clinical acumen cannot be over-emphasized. A stronger index of suspicion comes with clinical knowledge. Risk factors for immunodeficiency and infection should be recognized, a sepsis should be improved, and microbiological vigilance is essential. As a preventive measure, delivery of multiple pregnancies should not be conducted in maternities.

Conclusion

Clinicians must expose themselves to a wide variety of cases, interpret adequately patient's history and examinations findings as well as investigation results, maintain the requisite knowledge base, and utilize subtle hints that improve patient outcome.

Conflicting Interest Nil

Authors' contributions

NLC managed the patient in the ward, and researched on the management of this rare condition, OE carried out the electrocardiographic and echocardiographic tests, UK drafted the manuscript, the design of the study, conceived of the study, and participated in the design and coordination and helped to draft the manuscript. All authors approved the final manuscript.

REFERENCES

1. Markos S, Firdawoke SN, Gagamo ED, Workeneh MZ. Unusual Case of Right-Side Infective Endocarditis in a 40-Year-Old Woman with Postpartum Endometritis: A Case Report. *Int Med Case Rep J.* 2024 Apr 3;17:275-279.
2. Divyashree K, Singh H, Dahiya N, Suri V, Bhalla A. An Unusual Case of Post-partum Native Tricuspid Valve Infective Endocarditis. *Oman Med J.* 2023 Sep 28;38(5):e555.
3. Fava AM, Xu B. Tricuspid valve endocarditis: Cardiovascular imaging evaluation and management. *World J Clin Cases.* 2021 Oct 26;9(30):8974-8984.
4. Dural İE, Gökaslan S, Yalım Z, Aksu U, Yılmaz ÖF, Ersoy İ, et al. Postpartum infective endocarditis with *Enterococcus faecalis* after vaginal delivery. *Anatol J Cardiol.* 2021 Dec;25(12):920-921

5. Nair R, Kumar S, Mani R. Peripartum native valve endocarditis without underlying risk factors. *Indian J Thorac Cardiovasc Surg.* 2021 Sep;37(5):565-568.
6. Wiradnyana AAGP, Darmayasa IM, Saspriyana KY. The Characteristics of Pregnant Women with Cardiac Disease in Prof. Dr. I.G.N.G. Ngoerah Hospital, Denpasar. *J Obstet Gynaecol Pract POGS* 2025;3(1):8–21.

Case Report

ACCIDENTAL FORMALIN INGESTION IN A CHILD: A RARE CASE REPORT

Okonkwo CJ^{1*}, Udah CA², Onyeagwara NC³

¹Department of Otorhinolaryngology Head and Neck Surgery, Federal Teaching Hospital Owerri, Owerri, Imo State, Nigeria.

²Department of Paediatrics, Federal Teaching Hospital Owerri, Owerri, Imo State, Nigeria.

³Department of Otorhinolaryngology Head and Neck Surgery, University of Benin Teaching Hospital Benin, Benin City, Edo State, Nigeria.

***Corresponding author:** Dr. Okonkwo C.J.; 08032919793; drokonkwocjm@fthowerri.gov.ng.

Abstract

Background: Formalin is a solution of formaldehyde gas dissolved in water, along with a small quantity of methanol to ensure its stability. It is the form in which formaldehyde is commonly used in various applications, including as a disinfectant and tissue fixative. In our region, occurrences of accidental ingestion by children are rare. This rarity is due to the fact that formalin is not commonly found in households. Additionally, it has a strong, unpleasant taste and a distinctive, irritating smell. Ingesting formalin can cause immediate harmful effects on a child's health.

Case presentation: This report examines a case involving a four-year-old male who was brought to our facility after accidentally ingesting formalin, marking the first recorded incident in a child in our facility.

Conclusion: Formalin ingestion is lethal, necessitating stringent storage and handling procedures. Timely hospital evaluation and appropriate supportive care may mitigate complications.

Keywords: Accidental, Ingestion, Formalin, Corrosive.

Cite this article: Okonkwo, CJ, Udah CA, Onyeagwara NC. Accidental formalin ingestion in a child: a rare case report. Niger Delta J Med Med Res. 2025;4(2):66–69.

INTRODUCTION

Formalin is an aqueous solution of formaldehyde consisting of 37-40% formaldehyde, and 10-15% methanol. [1,2] Formaldehyde is a colourless, water soluble gas characterised by its strong odour, which can be absorbed through various surfaces of the human body. [1,2,3] Owing to its special chemical properties, as well as its far-reaching use in both the medical field and various other industrial sectors, formalin plays an important role in the global economy. [3,4] In medicine, it is commonly used as a tissue fixative for histopathological specimens, a disinfective agent and the component of embalming fluid. [5] Furthermore, it is used as an algicide and parasiticide in fish industries, fumigant in poultry farms and as a

preserving agent in detergents and cosmetic products like shampoos, soaps and nail polish. [3,4] Despite official regulations, its illegal use in non-medical sectors has become a popular practice in some countries, with some studies reporting a high concentration of formaldehyde in these products. [3,4]

Formalin is a known carcinogen in humans, and its risks should not be underestimated. It can be absorbed through all surfaces of the human body. [7,8] The fatal oral dose for humans is estimated to range between 60 to 90 milliliters (ml), making exposure particularly dangerous. [7] Once formaldehyde enters the body, it is metabolized by aldehyde dehydrogenase found in the liver and red

blood cells, rapidly converting it into formic acid. [7,8] This critical process is essential, as formic acid is eventually broken down to carbon dioxide and water. [8] However, this oxidative enzymatic reaction depends on the availability of folate. [8] The production of formic acid can lead to severe metabolic acidosis, emphasizing the urgent need for awareness and precautions regarding formaldehyde exposure. [7,8]

The immediate deleterious effect seen following ingestion of formalin may be seen in the gastrointestinal tract and other organs of the body. [7,9] The most severe damage is observed in the stomach because its contact with the stomach lasts longer than that with other parts of the gastrointestinal tract. [8,9] Complications that could arise include shock, respiratory insufficiency, gastric ulceration, gastric perforation, peritonitis and death. [7,8,9] Gastric stricture is one of the most common late complications. [8,9]

Importantly, ingesting formalin is quite rare because of its strong, unpleasant odour and taste as well as its intense irritant and corrosive properties. [5,7] However, its colourless appearance can lead to confusion in domestic settings, where it might be mistaken for water, normal saline, local anaesthetics and spirit in healthcare facilities. [5,10]

This report describes a rare and unfortunate case of accidental ingestion of formalin in a 4-year-old male child and its successful management.

CASE PRESENTATION

A four-year-old boy was brought to our hospital after he accidentally swallowed formalin just 20 minutes before arriving. He found a clear plastic bottle of what looked like water in their vehicle after school and attempted to drink from it. However, the bottle was actually filled with formalin, a substance utilised by his parents in the soap-making process.

While we could not determine the exact amount of formalin ingested, it was a small quantity-less than a mouthful. After consuming the liquid, he experienced burning and minor bleeding from his gums and vomited immediately when given palm oil. He was quickly rushed to the emergency Paediatric unit at Federal Teaching Hospital Owerri in Imo State for critical care.

Upon arrival, he was conscious and alert, not pale. His vital signs were stable: temperature at 37.3°C, pulse rate of 126 beats per minute, respiratory rate of 38 breaths per minute and oxygen saturation at 98% on room air. He was placed on a nil per oral (NPO) status until further assessment. He received intravenous (IV) fluids (5% dextrose saline) and IV medications including amoxicillin-clavulanic acid and IV paracetamol. His vital signs were closely monitored and the Ear, Nose and Throat team along with the Paediatric Gastroenterologist unit were promptly consulted for expert evaluation.

An examination revealed signs of mucositis, which is inflammation of the mucous membranes in the mouth and throat. All other examinations showed normal results. A diagnosis of mucositis secondary to accidental formalin ingestion was made. Treatment included IV omeprazole and IV dexamethasone, along with a restriction to 200 ml of clear fluids. Blood tests indicated metabolic acidosis, with an initial bicarbonate level of 11 mmol/l, mild hypokalemia 3.1 mmol/l, and other values within normal limits. The metabolic acidosis was corrected with bicarbonate, and the follow-up tests showed an improved bicarbonate level of 20 mmol/l. His complete blood count was normal.

After 24 hours in our care, a plan for an upper gastrointestinal endoscopy was made by the Gastroenterologist, but it could not proceed due to unavailable equipment. His treatment was supplemented with vitamin C syrup and Riboflavin.

By the fifth day, the boy had no pain when swallowing and was able to tolerate semi-solid foods like pap. Two days later, x-rays of his neck, chest and abdomen showed normal findings. A follow-up examination of his mouth and throat demonstrated that the swelling was resolving, leading to his discharge with a prescription for oral medications. At a follow-up appointment two weeks later, he was thriving. The mucositis had completely healed, and he could swallow without any discomfort, highlighting the success of the treatment and care provided. A barium swallow was requested for further assessment, but the patient has not yet undergone the procedure.

DISCUSSION

Accidental formalin ingestion is one of the most preventable causes of morbidity and mortality in children. [5,9] About 80% of paediatric poisoning is commonly

seen in children 1 to 5 years of age [5]; our patient is 4 years of age. This could be due to their hyperactivity, inquisitiveness and tendency to mouthing objects. [5] While accidental ingestion of formalin is observed in children, suicide and/or homicidal attempts are mostly observed in adults. [2,11] However, only few documented cases of formalin poisoning have been reported. [9] The patient is male, and although no sex predilection is documented, the condition may be more prevalent in males due to the inherently hyperactive behavior often observed in boys relative to girls. [12]

The most common accidentally ingested household chemicals are cleaning agents, kerosene, and pesticides. [5] Formalin poisoning is rare in children, as it is readily unavailable at home. [5,9] It also has an alarming pungent odour and taste which alerts one before fatal ingestion or inhalation. [5,7,8] This may be the reason why our patient vomited after consumption.

Furthermore, owing to its colourless and crystal-clear nature, it can be easily mistaken for water in a domestic setting, as seen in our index case. [5,7,8] In our case, thirst was the urge, while careless disposition of the bottle made it available for the patient.

The fatal dose of formalin ranges from 50 to 100 ml. [2,5] However, studies have reported multi-organ failure and shock following ingestion of about 20 ml of formalin. [7,9] In our index case, the quantity of formalin ingested could not be ascertained. However, he developed oral cavity and oropharyngeal mucositis and metabolic acidosis which was treated before discharge home.

The level of serum formic acid could not be ascertained in our index case because of the lack of chromatography and spectrometry in our facility. [3,4]

Prompt diagnosis with aggressive supportive treatment remains the mainstay of management to prevent complications. [11,13] Continuous water irrigation for immediate decontamination of the exposed parts of the body is recommended. [5,7] About 120-240 ml of water or milk is preferable. [7] Our index patient received 200 ml of water.

The role of activated charcoal has been suggested but inconclusive, and the use of antidotes and gastric lavage is

not recommended. [5,7] Supportive treatment with water irrigation, intravenous fluids, and correction of metabolic acidosis have shown to be the mainstays of management in this and other cases. [5,8] Bronchodilators and vasopressors may be used in some cases. [5,8,9] Further recommendations include the infusion of N-acetyl cystine and the use of haemodialysis to halt the formation of formic acid and its removal from the blood, respectively. [5,11]

This report highlights the importance of regularizing the sales and storage of formalin. It should be stored in places inaccessible to children using a special proof container with proper labelling of warning signs. Again, the role of palm oil is not documented and may lead to clogging of the airways and reflux, which may exacerbate symptoms.

Conclusion

Formalin ingestion poses potential life-threatening complications depending on the dose ingested and time of presentation to the hospital. Adequate supportive treatment is the mainstay of treatment. Proper labelling, storage and restricted sale of formalin may prevent unwanted hazards caused by accidental ingestion of formalin in children.

COMPETING INTEREST

The authors have declared that there is no competing interest.

AUTHORS INFORMATION

1. Dr. Chinedu Joseph Okonkwo. Consultant Otorhinolaryngologist Head and Neck Surgeon. Otorhinolaryngology, Head and Neck Surgery Department, Federal Teaching Hospital Owerri, Imo State, Nigeria.
2. Dr. Chidinma Adaobi Udah. Consultant Paediatric Gastroenterologist. Department of Paediatrics, Federal Teaching Hospital Owerri, Imo State, Nigeria.
3. Dr. Ngozi Carol Onyeagwara. Professor and consultant Otorhinolaryngologist Head and Neck Surgeon. Otorhinolaryngology, Head and Neck Surgery Department, University of Benin Teaching Hospital, Benin City, Edo State, Nigeria.

REFERENCES

1. SurangamaChakraborty, Veeresh MR. Formalin, a Rare Suicidal Poison-a case report. *IOSR Journal of Dental and Medical Sciences*. 2015; 14(4):24-26. doi: 10.9790/0853-14472426.
2. Hungund C, Mohanram A, Pai V, Rani S. Fatal Formalin Poisoning: A Case Report. *Spring & Summer*. 2011;5: 468-469.
3. Echerfaoui F, Orche AE, Bourakadi KE, Benomar A, Adade CA, laouni A et al. Determination of free formaldehyde in cosmetics products through derivatization with 2,4-DNPH using an optimized and validated HPLC-PDA method. *Acta Chromatographica*. 2024. 1-10. doi:10.1556/1326.2024.01244.
4. Ambadekar SR, Nikam DB. Accurate Quantification of Formaldehyde in selected Cosmetics by Fast Liquid Chromatography. 2020;9(4):1722-1738. doi: 10.20959/wjpr2024-17223.
5. Sahu SS, Naveen A, Mohanty MK, Kundu A. Accidental formalin poisoning in a child with acute fatal manifestations: A rare case report. *J Family Med Prim Care*. 2022; 11(6): 3293-3297.
6. Catalani S, Donato F, Madeo E, Apostoli P, De Palma G, Pira E, et al. Occupational exposure to formaldehyde and risk of non-Hodgkin lymphoma: A meta-analysis. *BMC Cancer*. 2019; 19:1245. doi:10.1186/s12888-019-6445-z.
7. Pandey CK, Agarwal A, Baronia A, Singh N. Toxicity of ingested formalin and its management. *Human & Experimental Toxicology*. 2000;19: 360-366.
8. Yanagawa Y, Kaneko N, Hatanaka K, Sakamoto T, Okada Y, Yoshinitsu S. A case of attempted suicide from ingestion of formalin. *Clinical Toxicology*. 2007;45: 72-76.
9. Beeregowda YC, Srihari A, Pradan SK, Susheela P, Manjunatha YC. Homicidal acute formalin poisoning in an infant from a rural sericulture family presenting with multisystem failure. *Pediatr Emer Care*. 2013; 29: 653-655.
10. Dandriyal R, Giri KY, Alam S, Singh AP. Accidental intraoral formalin injection: a rare case report. *Clinics and practice*. 2014;4:686.
11. Raut SM, Haridas SV, Kachare RV, Pawar VG, Dode PS. Fatal Formalin Poisoning: A rare case report. *International Journ of Forensic Medicine and Toxicological Sciences*. 2018;3(4):100-102. doi: 10.18231/2456-9615.2018.0021.
12. Okonkwo CJ, Onyeagwara NC. An audit of Paediatric nasal foreign bodies in Federal Teaching Hospital Owerri, Imo State, Nigeria. *Niger Delta J Med Med Res*. 2024;3(2):73-78.
Baskin D, Urganci N, Abbasoglu L, Alkim C, Yalcin M, Karadag C et al. A standardized protocol for the acute management of corrosive ingestion in children. *Pediatr Surg Int*. 2004;20:824-828.

Original Article

PERCEPTION OF CAESAREAN DELIVERY BY PATIENTS AND THEIR CARE-GIVERS IN THE ULTRA-SHORT STAY VERSUS THE TRADITIONAL POST-OPERATIVE MANAGEMENT PROTOCOL, FOLLOWING UNCOMPLICATED CAESAREAN DELIVERY: A RANDOMIZED CONTROLLED TRIAL

Oyeyemi N^{1*}, Onwudiegwu U², Pughikumo DT³, Oyeyemi AS^{4,5}

¹Department of Obstetrics & Gynaecology, Federal Medical Centre, Yenagoa, Bayelsa State, Nigeria.

²Institute of Medical Education, Bayelsa Medical University, Yenagoa, Bayelsa State, Nigeria.

³Department of Physiology, College of Health Sciences, Niger Delta University, Wilberforce Island, Bayelsa State, Nigeria.

⁴Department of Community Medicine, Faculty of Clinical Sciences, Niger Delta University, Wilberforce Island, Bayelsa State, Nigeria.

⁵Department of Community Medicine, Niger Delta University Teaching Hospital, Okolobiri, Bayelsa State, Nigeria.

*Corresponding author: Dr. Nuvie Oyeyemi; +2348035488675; nuviyemi@yahoo.com

Abstract

Background: Caesarean delivery is the most common major surgical procedure currently done in Obstetrics worldwide and is presently a relatively safe procedure, though there still remains a cultural aversion for it in developing countries like Nigeria. There is therefore a need to examine post-operative management protocols that can reduce length of hospital stay and their effects on the perception of Caesarean delivery by the patients and their significant others/care-givers, following uncomplicated Caesarean delivery.

Objective: To determine and compare the perception of caesarean delivery by patients and their care-givers; between the ultra-short stay and traditional post-operative management protocols, following uncomplicated Caesarean delivery.

Materials and Methods: This was a randomized controlled trial done in 3 centres in Bayelsa state, South-South, Nigeria. The Federal Medical Centre, Yenagoa, the Niger Delta University Teaching Hospital, Okolobiri, and the Diète-Koki Memorial Hospital, Opolo. One hundred and seventy-nine women who have just had uncomplicated caesarean delivery were randomized into the ultra-short stay (90) and traditional groups (89). The women in the ultra-short stay group were given minty chewing gums (menthos) to chew for 2 hours, within the first 6 hours after surgery. They started ambulating and oral intake initiated from 6 hours post-operative (regular diet commenced at 12 hours); and urethral catheter discontinued 6-12 hours post-operative.

Results: There was a significantly more positive perception of caesarean delivery in women who had the ultra-short stay post-operative management protocol ($\chi^2=19.51$, $p<0.001$), and their significant others/care-givers ($\chi^2=21.78$, $p<0.001$), than women who had the traditional protocol.

Conclusion: There is a better perception of caesarean delivery in women who are managed using the ultra-short stay, and their care-givers, than in the traditional post-operative management protocols; following uncomplicated Caesarean delivery.

Keywords: Patients, Perception, Care-givers, Significant others, Uncomplicated Caesarean delivery, Yenagoa.

Cite this article: Oyeyemi N, Onwudiegwu U, Pughikumo DL, Oyeyemi AS. Perception of Caesarean delivery by patients and their care-givers in the ultra-short stay versus the traditional post-operative management protocol, following uncomplicated caesarean delivery. a randomized controlled trial. Niger Delta J Med Med Res. 2025;4(2):70–78.

INTRODUCTION

Caesarean delivery is the most common major surgical procedure currently done in Obstetrics worldwide, and is presently a relatively safe procedure, though there still remain a cultural aversion for it; with myths and misconceptions about it, especially in developing countries like Nigeria. [1,2] These misconceptions include the exaggerated assumption of a mandatory prolonged duration of hospital stay following Caesarean delivery, and an extended period of incapacitation following the procedure; among others. There is therefore a need to examine post-operative management protocols that can reduce length of hospital stay and their effects on the perception of Caesarean delivery by the patients and their significant others/care-givers, following uncomplicated Caesarean delivery, and possibly make the operation more acceptable when indicated. [1,2] The socioeconomic implication of the length of hospital stay following uncomplicated Caesarean delivery is also very important. [1,3] Most studies have not detected an increased rate of morbidity associated with early discharge following Caesarean delivery.[4,5,6] Therefore, protocols that reduce duration of hospital stay following Caesarean delivery, will probably also improve patients' perception of Caesarean delivery, and the perception of their care-givers/significant others. This may also help in refuting the misconception about a compulsory prolonged hospital stay after every Caesarean delivery and therefore make the operation more acceptable, when indicated; especially in sub-Saharan Africa where there is still some aversion for it.[1]

In some societies, in Nigeria, vaginal delivery is perceived as 'normal delivery' and it is what is generally accepted, conversely, Caesarean delivery is considered 'abnormal' delivery. [7] Therefore many women are not open to the option of Caesarean delivery, when indicated. [7,8] Many have to get their husband's blessings/consent and perhaps his relatives, before consenting to Caesarean delivery. [7] Also endorsement from religious leaders (who know little or nothing about the indications for Caesarean delivery) is considered mandatory by some. [7,8] Caesarean delivery may be perceived by most men as a curse and punishment

to the woman and family and may be seen as a 'death warrant'. [9-11] A survey done in Nigeria revealed that in Bayelsa state, the norm was for relatives and society to decide how a woman should give birth in her community. [7] Many of the women would rather go to a traditional birth attendant (TBA) so that they are seen as the biblical '*Hebrew women*'. These TBAs are typically called 'massagers. Most of the women would rather have faith that they would have a vaginal delivery by praying and using 'anointing oil' given to them by their religious leaders. [7]

The women also expressed the misgiving that some hospitals, especially private hospitals, would recommend Caesarean delivery because it was their means of making money. [7] Many women in Bayelsa also expressed the opinion that for them and most women in their communities, Caesarean delivery was for those who were not 'strong enough'. They would rather listen to their significant others (mothers, mothers-in-law, husbands, pastors, pastors' wives), about the mode of delivery, even if the doctor recommends Caesarean delivery as the best and safest option for them. [7] It was concluded that the dominant factors that influenced the women's choices were religion, their significant others and cost.[7] On the other hand, increasing numbers of women worldwide are opting for an elective Caesarean delivery without medical indications and there is a decrease in the rate of vaginal birth after Caesarean delivery.[12,13] All these makes it important to review the length of hospital stay following Caesarean delivery, in order to clarify the misgivings, and also to reduce the inconveniences involved.

Specific Objectives:

1. To determine patients' perception of Caesarean delivery following uncomplicated Caesarean delivery, after the ultra-short stay and the traditional post-operative management protocol.
2. To compare patient perception of Caesarean delivery in the ultra-short stay versus the traditional hospital-stay, after uncomplicated Caesarean section
3. To determine patients' significant others/care-givers' perception of Caesarean delivery in both the ultra-

short stay and traditional hospital-stay protocol, following uncomplicated Caesarean delivery.

4. To compare the significant others/care-givers' perception of Caesarean delivery, in the ultra-short stay versus the traditional hospital stay protocol following uncomplicated Caesarean delivery.

MATERIALS AND METHODS

This was a multicentre randomized controlled trial, of the parallel design with allocation ratio of 1:1[14], carried out from April 2024 to April 2025, among booked antenatal patients in the Federal Medical Centre, Yenagoa (FMC-Y); the Niger Delta University Teaching Hospital (NDUTH), Okolobiri; the Diète-Koki Memorial Hospital (DKMH), Opolo; all in Bayelsa state, South-south Nigeria. Patients who just had uncomplicated Caesarean delivery for various indications, and are in the recovery room, fully awake. Women excluded were those outside the reproductive age group which is 15-49 years,[15] those who had any medical condition that required management by other specialities post-delivery that may warrant prolonged hospital stay, and Immunosuppressed or HIV positive women with features of the Acquired Immune Deficiency Syndrome (AIDS); women who had prolonged labour or prolonged rupture of membranes.

A total of 180 eligible consenting patients were consecutively recruited into the study. Randomization was done using computer generated random numbers (unstratified balanced allocation from WinPepi)[16] and random allocation concealment done using sealed opaque envelopes numbered from 1 to 60 for each centre. In this way, recruited patients were randomised into either of two groups representing the arms of the study: group A (traditional protocol) and group B (ultra-short stay protocol). An independent observer picked the envelopes consecutively at the time the eligible patient got to the recovery room after an uncomplicated Caesarean delivery, A total of 90 women were allocated into the ultra-short stay group and 89 (one of the women inadvertently allocated here in one of the centres had a iatrogenic bladder injury intra-operatively, so she was subsequently excluded reducing the participants to 89) into the traditional group. The sealed envelope picked was placed within the patients' case notes. All the surgeries were

performed by Consultants and Senior Registrars in the Department of Obstetrics and Gynaecology of the respective hospitals.

At recruitment in the recovery room, the women in the ultra-short stay group were given minty (menthos) chewing gums to chew for at least 2 hours and the appropriate sections of the proforma and interviewer-administered questionnaire (containing patient biodata and intra-operative information) were filled. The protocol (specific interventions) for the ultra-short stay protocol was placed at the nursing station on the ward for attention of the nursing staff. Those for the traditional protocol (group A) were managed according to normal unit protocol.

All patients in group A were commenced on graded oral sips at 24 hours post-operative and regular diet 12 hours later; ambulated within 24 hours (sitting out of bed from 12 hours and walking around ward from 24 hours) post-operative and had urethral catheter (with strict urinary output monitoring) discontinued 24 hours after surgery. Intravenous fluids dextrose water alternating with normal saline was given at 1 litre 8-hourly for at least the first 24 hours after surgery and until oral intake was well established. Analgesics, intramuscular pentazocine at 30 mg 6-hourly, suppository diclofenac 100 mg 12-hourly for 72 hours and intramuscular paracetamol 600-900 mg 8-hourly administered for the first 24 hours after surgery. Antibiotics, usually intravenous ceftriaxone, gentamicin and metronidazole at 1g 12-hourly, 80 mg 8-hourly and 500 mg 8-hourly respectively were also given for the first 48 to 72 hours. Antibiotics were converted to the oral equivalents when the intravenous regimen had been completed and analgesics to oral paracetamol 1g 8-hourly, and diclofenac 50-100 mg 12-hourly respectively. Wound was inspected and exposed on the fifth post-operative day and patient subsequently discharged home.

All patients in group B commenced graded oral fluids at six hours post-operative, gradually graded to semi-solids, then intravenous fluids were discontinued; and regular diet was commenced at 12 hours post-operative. They sat out of bed from 6 hours post-operative and walked around the ward from 12 hours post-operative. Urethral catheter was discontinued 6-12 hours after surgery. Analgesics,

intramuscular pentazocine at 30 mg 6-hourly, suppository diclofenac 100 mg 12-hourly until discharge and intramuscular paracetamol 600-900 mg 8-hourly was administered for the first 24 hours after surgery. Antibiotics, intravenous ceftriaxone, gentamicin and metronidazole, at 1g 12-hourly, 80 mg 8-hourly and 500 mg 8-hourly respectively were also converted to the oral equivalents at discharge and the analgesics changed to oral paracetamol 1g 8-hourly and diclofenac 50-100 mg 12-hourly respectively. Wound was inspected and exposed on the second post-operative day (36-48 hours post-operative) and patient subsequently discharged home on the same day without schedule for home visits, but with customer care lines to call if necessary.

The wound was cleaned with methylated spirit in both groups, and patients were instructed to clean wound with methylated spirit twice to thrice daily at home until the 2 weeks postnatal visit. The proforma and interviewer-administered questionnaires on patients' and care-giver's perception was filled at this visit, or through phone calls for those who missed their visits.

Data analysis was done using the IBM SPSS statistical software version 25. Data was presented in text and tables. Analysis included use of descriptive statistics such as mean, proportion and standard deviation to summarize the quantitative variables. Association between categorical variables was tested using Chi-square and differences in group means were assessed using t-test. A confidence level of 95% was used with the level of significance set at a p-value of <0.05.

RESULTS

There were 179 women who had uncomplicated Caesarean delivery, who were randomized into 90 women for the ultra-short stay post-operative management protocol and 89 for the traditional protocol. Eight women dropped out of the protocols, two in the traditional group (one had severe post-partum haemorrhage, acute kidney injury and had prolonged hospital stay; the other had voiding difficulties at removal of urethral catheter which resulted in prolonged hospital stay). Six women in the

ultra-short stay protocol group, dropped out of the protocol; reasons ranging from post-operative blood transfusions, signs of wound sepsis at wound exposure, to post-partum pregnancy-induced hypertension, all extending hospital stay.

Most of the participants were married women (93.3% in each group respectively) between the ages of 19 and 45 years. The 2 groups were comparable in age, parity, marital status, religion, tribe, except educational status where there were slightly more educated women in the ultra-short stay than the traditional protocol group ($X^2 = 7.82$, P-value = 0.020). Indications for Caesarean delivery, estimated gestational age at delivery and intra-operative variables had no statistically significant difference in these characteristics between the 2 groups, except cadre of surgeon, where more consultants did the surgeries in the ultra-short stay protocol group. The Surgeons were consultants in 84.4% and 62.9% ; senior registrars in 37.1% and 15.6% of the participants in the ultra-short stay and traditional groups respectively ($X^2 = 10.71$, p-value = 0.001).

The significant others reported were their husbands, mothers and sisters. The mothers were their biological mothers, mother-in-law, or any other mother figure often referred to as mother (like their pastor's wife). The sisters were either biological sisters (younger or older), female cousin or sister-in-law (husband's sister or brother's wife). These were the individuals with them at delivery, in the recovery room, on the lying-in ward, and through the post-partum period and the puerperium. The patient perception was categorised as positive, negative and indifferent. Perception was rated positive if they thought Caesarean delivery was a good option for delivery, rated negative if they perceived it as a bad and unfavourable option, and indifferent if they thought of it as "just there" or neither good nor bad.

The perception of the participants of Caesarean delivery as well as that of their significant others/care-givers were significantly more positive in the ultra-short stay than the traditional protocol, with both the intention-to-treat and per-protocol analysis

CONSORT FLOW CHART

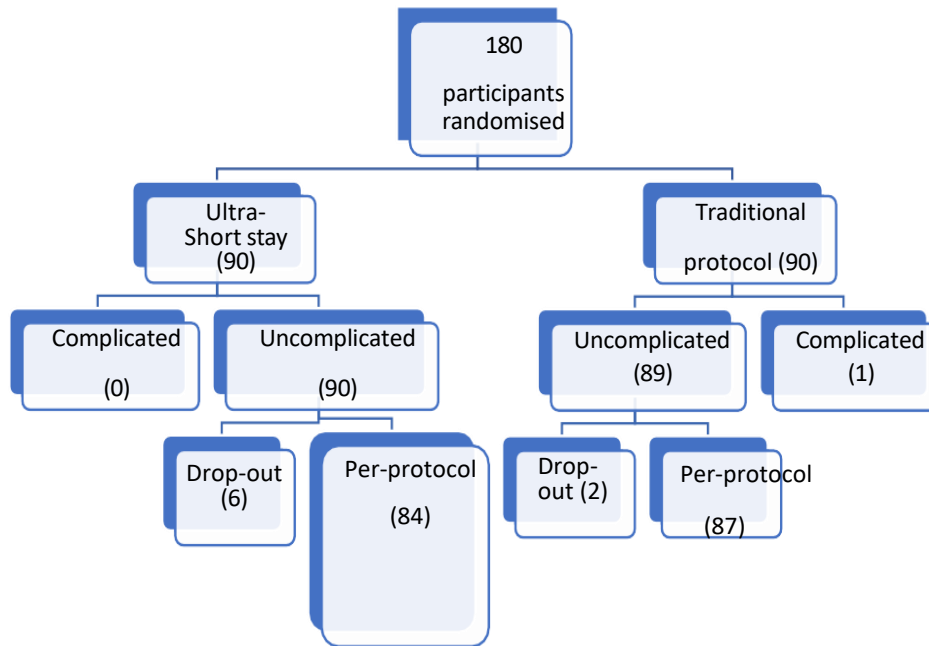


Figure 1: Flow diagram showing randomization to analysis

Table I: Perception of caesarean section by participants and significant others – intention-to-treat analysis.

Variables	Traditional (n = 89)	Ultra-short (n = 90)	t/χ ²	P - value
Perception by participants (C - section)				
Positive	53 (59.6%)	79 (87.8%)	18.51	< 0.001*
Negative	11 (12.4%)	4 (4.4%)		
Indifference	25 (28.1%)	7 (7.8%)		
Perception by significant others (C - section)				
Positive	29 (32.6%)	59 (65.6%)	21.78	< 0.001
Negative	17 (19.1%)	14 (15.6%)		
Indifference	43 (48.3%)	17 (18.9%)		
Significant others				
Husband	13 (12.8%)	11 (12.2%)	1.21	0.545
Mother	65 (73.0%)	61 (67.8%)		
Sister	11 (12.4%)	18 (20.0%)		

*Fisher’s exact P - value, t-test applies to numerical variables while chi-squared test (χ²) applies to categorical variables. P - value < 0.05 is statistically significant.

The perception of the participants of Caesarean delivery as well as that of their significant others was significantly more positive in the ultra-short stay than the traditional protocol. The significant others/care-givers of the patients

were predominantly mothers or mother figures and this distribution was comparable in both groups. These results were comparable to those obtained in the per-protocol analysis,

Table II: Perception of caesarean section by participants and significant others, per-protocol

Variables	Traditional (n = 87)	Ultra-short (n = 84)	t / χ^2	P – value
Perception by participants (C - section)				
Positive	52 (59.8%)	77 (91.7%)	23.47	< 0.001*
Negative	10 (11.5%)	2 (2.4%)		
Indifference	25 (28.7%)	5 (6.0%)		
Perception by significant others (C - section)				
Positive	29 (33.3%)	55 (65.5%)	18.79	< 0.001
Negative	17 (19.5%)	12 (14.3%)		
Indifference	43 (47.1%)	17 (20.2%)		
Significant others				
Husband	13 (14.9%)	10 (11.9%)	1.54	0.462
Mother	64 (73.6%)	59 (70.2%)		
Sister	10 (11.5%)	15 (17.9%)		

*Fisher’s exact P - value, t - test applies to numerical variables while chi-squared test (χ^2) applies to categorical variables. P - value < 0.05 is statistically significant.

Table III: Bivariate analysis of possible sociodemographic predictors of participant’s perception of Caesarean delivery, after combining the groups.

Participant’s perception of Caesarean delivery (n = 179)					
Variable	Positive	Negative	Indifference	χ^2	P value
Age					
≤ 24	10 (7.6%)	0 (0.0%)	2 (6.3%)	5.70	0.457
25 – 29	36 (27.3%)	3 (20.0%)	5 (15.6%)		
30 – 34	47 (35.6%)	9 (60.0%)	5 (15.6%)		
≥ 35	39 (29.5%)	3 (20.0%)	11 (34.4%)		
Marital					
Single	5 (3.8%)	3 (20.0%)	2 (6.3%)	7.39	0.117
Married	125 (94.7%)	12(80%)	30 (93.8%)		
Widowed	2 (1.5%)	0 (0.0%)	0 (0.0%)		
Education					
No formal	2 (1.5%)	0 (0.0%)	0 (0.0%)	16.11	0.003
Secondary	32 (24.2%)	11(73.3%)	10(31.3%)		
Tertiary	98 (74.2%)	4 (26.7%)	22(68.8%)		
Religion					
Christianity	132 (100%)	13(86.7%)	31 (96.9%)	15.03	0.001
Islam	0 (0.0%)	2 (13.3%)	1 (3.1%)		
Tribe					
Yoruba	3 (2.3%)	1 (6.7%)	1 (3.1%)	9.14	0.331
Ibo	23 (17.4%)	3 (20.0%)	8 (25.0%)		
Hausa	4 (3.0%)	2 (13.3%)	0 (0.0%)		
Ijaw	84 (63.6%)	7 (46.7%)	21 (65.6%)		
Other	18 (13.6%)	2 (13.3%)	2 (6.3%)		

*Fisher’s exact P-value. P – value of < 0.05 is statistically significant.

Bivariate analysis of possible sociodemographic predictors of perception of Caesarean delivery by participants with the two groups combined showed statistical significance in both level of education and religion. A significantly higher proportion of participants who had tertiary level of education had a positive perception of caesarean delivery. Furthermore, a significantly higher proportion of the Christians had a

positive perception of Caesarean delivery. Though very few Muslims participated in the study (only 3), none of them had a positive perception of Caesarean delivery. Parity was also not a statistically significant predictor of patient's perception of Caesarean delivery ($X^2 = 6.04$, P -value = 0.196).

DISCUSSION

The study determined and compared the patient perception and the perception of their significant others/care-givers of Caesarean delivery in the ultra-short-stay versus the traditional post-operative management protocol in women who had uncomplicated Caesarean delivery in Bayelsa State, South-south Nigeria. Patients' and care-givers' perception of Caesarean delivery was categorized as positive if they were favourably disposed to Caesarean delivery, negative if they were ill-disposed to Caesarean delivery, and indifferent if they were non-committal in their opinions of Caesarean delivery. The difference in indications for Caesarean delivery between the two groups was not statistically significant ($X^2 = 6.89$, P -value = 0.331). More consultants performed the surgeries in the ultra-short stay group than in the traditional group (84.4% and 62.9% respectively). This was statistically significant ($X^2 = 10.71$, P -value = 0.001). The predominant type of anaesthesia used was the subarachnoid block (97.8% for the traditional and 94.4% for the ultra-short stay), the difference between the 2 groups was not statistically significant ($X^2 = 1.35$, P -value = 0.509). This regional anaesthetic technique (subarachnoid block) has been found to be the safest and most appropriate type of anaesthesia for this procedure, as it encourages early post-operative ambulation thereby minimizing the risk of venous thrombosis. [17]

Studies have also shown that regional anaesthesia for Caesarean delivery seemed to be associated with shorter duration of hospital stay than general anaesthesia.[17] Regional anaesthesia also affords the patient the opportunity to be awake through the delivery process and she is able to witness the delivery of her baby and hear its first cry, this is likely to enhance a positive perception of this mode of delivery. Though the study did not show type of anaesthesia used as an intra-operative predictor of patients' perception of Caesarean delivery ($X^2 = 3.17$, P -

value = 0.530). The care-givers too may also have a more positive perception of Caesarean delivery when their patient is wheeled into the recovery room fully awake and able to converse with them. Most of the participants had Pfannenstiel incisions (96.6% in the traditional group and 97.8% in the ultra-short stay), and the difference in the 2 groups was not statistically significant ($X^2 = 2.35$, P -value = 0.309). The cosmetic effect/benefit of the transverse suprapubic incision (Pfannenstiel and Joel-Cohen incisions) is often fascinating to the patient and her care-givers especially when it is her first Caesarean delivery, this may likely enhance their perception of Caesarean delivery. Though this study too did not show type of skin incision as an intra-operative predictor of patients' perception of Caesarean delivery ($X^2 = 1.83$, P -value = 0.767).

Studies have also shown that early hospital discharge after Caesarean delivery results in reduced healthcare costs and enables patients to go home early with their babies.[18] This may help in promoting a positive perception of Caesarean delivery in both the patients and their care-givers. A previous study found that early discharge following uncomplicated Caesarean delivery was more cost-effective than a traditional hospital stay, considering community costs, and highly cost-effective with respect to only health system costs.[2,20] However, early discharge should not stop the need in the lying-in ward during the immediate post-Caesarean delivery period, to counsel women on breastfeeding, family planning, newborn care, and care of the surgical wound.[2,18] All these will ultimately help to enhance a positive perception of Caesarean delivery.

Conclusion

The ultra-short hospital stay post-operative management protocol produced significantly more positive patient perception of Caesarean delivery than the traditional protocol. The care-givers of patients also had a significantly more positive perception of Caesarean delivery, in the ultra-short stay than the traditional protocol. Therefore, enhanced recovery and early discharge after Caesarean delivery causes a better perception of the procedure in both the patients and their care-givers.

Financial Support and Sponsorship

Nil

Conflict of interest

There are no conflicts of interest

REFERENCES

1. Oyeyemi N, Oyeneyin L, Oluwole A, Oyeyemi A, Afolabi B. Post-operative management in uncomplicated caesarean delivery: A randomised trial of short-stay versus traditional protocol at the Lagos University Teaching Hospital, Nigeria. *Niger Postgrad Med J*, 2019. Jan-Mar;26(1):31-37.
2. Oyeyemi N, Afolabi BB, Oyeneyin OL, Oyeyemi AS. Are patients more satisfied with the short-stay than the traditional protocol following uncomplicated caesarean delivery? A clinical trial in the Lagos University Teaching Hospital (LUTH), Nigeria. *Niger Delta J Med Med Res*. 2024;3(3):113–119.
3. The CAESAR study collaborative group. Caesarean section surgical techniques: a randomised factorial trial (CAESAR). *BJOG* 2010;117:1366–1376.
4. Ghaffari P, Vanda R, Aramesh S. Hospital discharge on the first compared with the second day after a planned cesarean delivery had equivalent maternal postpartum outcomes: a randomized single-blind controlled clinical trial. *BMC Pregnancy Childbirth* 2021;466 (21).
5. Gialdini C, Chamillard M, Diaz V. Evidence-based surgical procedures to optimize caesarean outcomes: an overview of systematic reviews. *EClinicalMedicine*, 2024:102632
6. Kruse AR, Lauszus FF, Forman A, Kesmodel US, Rugaard MB, Knudsen RK, et al. Effect of early discharge after planned cesarean section on recovery and parental sense of security. A randomized clinical trial. *Acta Obstet Gynecol Scand*. 2021 May; 100(5):955-963.
7. Nigeria Health Watch. Caesarean Sections in Nigeria – Thoughts, Belief Systems and Perceptions 2020. [Internet] [Cited 2025 Aug 24]. Available from articles.nigeriahealthwatch.com
8. Abazie O, Abdul-Kareem AY. Pregnant Women's Knowledge and Perceptions of Caesarean section in Lagos State, Nigeria. *African Journal of Midwifery and Women's Health* 2019;13(3):1-11.
9. Elom NA, Nwimo IO, Ilo CI. Belief towards Caesarean Section: A community-based study of male partners in Ebonyi State, Nigeria. *SAGE Open Medicare* 2023;11.
10. Adeoye-Sunday I, Kalu CA. Pregnant Nigerian Women's view of Caesarean Section. *Niger J Clin Pract*. 2011;14:276-279.
11. Faremi IA, Ibitoye O, Olatubi DP. Attitude of Pregnant Women in South Western Nigeria towards Caesarean Section as a method of birth. *Inter J Reprod. Contraceptive Obstet Gyne*. 2014; 3:704-714.
12. Cotzias CS, Paterson-Brown S, Fisk NM. Obstetricians say yes to maternal request for elective Caesarean section: a survey of current opinion. *European Journal of Obstetrics, Gynaecology and Reproductive Biology* 2001;97:15–16.
13. Hamilton BE, Martin JA, Ventura SJ. Births: Preliminary Data for 2007. National Vital Statistics Reports. Hyattsville, Md, National Center for Health Statistics, 2009;57(12)
14. Abrahamson JH, Abrahamson ZH (eds). *Clinical Trials. Research Methods in Community Medicine* 6th ed. John Wiley and Sons Ltd, 2008: 325-344.
15. Handbook on Reproductive Health indicators, United Nations. New York, 2001. Introduction, p13. [Internet] [Cited 2025 Aug 24]. Available from <http://www.unescap.org/esid/psis/publications/handbookhealth/handbook.pdf>
16. Abrahamson: JH. WINPEPI updated: computer programs for epidemiologists and their teaching potential. *Epidemiologic Perspectives & Innovations* 2011;8:1 doi:10.1186/1742-5573-8-1s

17. Fassoulaki A, Petropoulos G, Staikou C, Siafaka I, Sarantopoulos C. General versus neuraxial anaesthesia for Caesarean section: impact on the duration of hospital stay. *J Obstet Gynecol.* 2009 Jan; 29(1):25-30.
18. Centres for Disease Control. Trends in Length of Stay for Hospital Deliveries – United States, 1970-1992. *MMWR Weekly.* 1995; 44(17):335-7.

