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The Hidden Phase: Recognizing Late-Onset Peripartum Cardiomyopathy in Ethnic Sub-Saharan African Populations

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ABSTRACT

Background: *Peripartum cardiomyopathy (PPCM) is a, life-threatening heart muscle disease affecting women during late pregnancy and postpartum. Traditionally, PPCM diagnosis has been limited to symptom onset within 5 months after childbirth. However, this long-established timeframe is debated as potentially too restrictive, and detailed reports on late-onset PPCM, are scarce.*

Methods: *This prospective study in Sokoto, Nigeria, consecutively recruited 10 patients over 48 months who presented with heart failure symptoms beyond the conventional 5-month postpartum diagnostic timeframe (window) but still met the European Society of Cardiology (ESC) diagnostic criteria for PPCM.*

Results: *The cohort comprised predominantly young women (90%), mean age 30.5 ± 6.5 years), most of whom were multiparous (80%), well-educated (90%), of middle socioeconomic status (80%), and unemployed (100%). All had adequate antenatal care, hospital delivery, and were actively breastfeeding at symptom onset. The mean duration from delivery to symptom onset was 13 ± 2.1 months and the mean duration of symptoms prior to hospital presentation was 3.2 ± 3.74 weeks. Patients typically presented with left-sided heart failure (80%) and in NYHA class II (70%). On auscultation mitral regurgitant murmur was detected in (50%). Echocardiography frequently showed 4-chamber dilatation (50%), mild to moderate LV systolic dysfunction (60% mild, 40% moderate). Left ventricular (LV) structural pathological remodelling (abnormal LV geometry (100%) and abnormal LV mass index (100%). and 4, 2 & 3 chamber dilation (100%). Significant mitral regurgitation was also common (50% moderate, 20% severe). Most common electrocardiographic findings included sinus tachycardia (100%) and prolonged QTc (70%) and T wave inversion (50%). All patients had cardiomegaly and cardiogenic pulmonary edema on chest X-ray.*

Conclusion: *The findings from this small cohort in Nigeria highlight the clinical presentation and characteristics of late-onset PPCM occurring significantly beyond the traditional 5-month postpartum window. These data support the need for considering PPCM in women presenting with heart failure symptoms later in the postpartum period, even outside historically defined timeframes, provided they meet established ESC working diagnostic criteria.*

Keywords
Peripartum Cardiomyopathy, Late-Onset PPCM, Sub-Saharan Africa, Cardiovascular Disease.

Abbreviations
PPCM: Peripartum Cardiomyopathy, HF: Heart Failure, ESC: European Society of Cardiology, LV: Left Ventricle, DLEP: Dried Lake-salt Enriched Pap.

Introduction
Peripartum cardiomyopathy (PPCM) is a serious global health concern affecting pregnant women during and after childbirth, with a particularly high incidence in Northwestern Nigeria [1]. The prevalence and outcomes of PPCM vary across different ethnic and geographical regions [2,3]. Clinically, PPCM manifests as heart failure (HF) during the last month of pregnancy, or within five months postpartum, or beyond [4-6]. PPCM increases the risk of cardiovascular complications, including venous and systemic thromboembolism, atrial and ventricular arrhythmias, and sudden cardiac death [7,8].

Our understanding of PPCM has evolved considerably over the past five decades, but the underlying causes remain unclear. Similarly, the definition and diagnostic criteria for PPCM have been refined over time, most recently by the Heart Failure Association (HFA) of the European Society of Cardiology (ESC) Working Group on PPCM [6]. Despite these advancements, the optimal timeframe for PPCM diagnosis continues to be debated. The traditional diagnostic criteria may be too restrictive, as suggested by some studies [6,9]. The recent ESC working group criteria are more inclusive but do not specify a definitive postpartum timeframe for diagnosis [6].

Elkayam et al. [9], challenged the conventional timeframe, reporting that nearly 20% of PPCM patients experienced heart failure symptoms before the last month of pregnancy. Importantly, they found no significant differences in clinical outcomes or demographics between those diagnosed early and those diagnosed according to the traditional criteria. This finding suggests that earlier diagnosis may improve patient outcomes [9].

The variability in clinical presentation, including the potential for earlier symptom onset, and the occurrence of late-onset symptoms, underscores the need for clinicians to maintain a high level of suspicion for PPCM throughout late pregnancy, the postpartum period, and beyond [9]. These observations suggest a broader understanding of the diagnostic timeframe for PPCM is needed, advocating for a more comprehensive approach that considers late presentations. This could lead to earlier recognition and more timely management of PPCM.

However, a deeper understanding of PPCM cases presenting beyond the traditional five-month postpartum window remains limited. This knowledge gap is critical because it affects the timeliness of diagnosis, management, and patient outcomes. The long-established definition of PPCM restricts diagnosis to the last month of pregnancy and the first five months after delivery. However, emerging evidence indicates that symptoms can appear much later, suggesting that the current criteria may miss cases of PPCM with delayed onset [10]. Some studies have shown that women may experience heart failure symptoms well beyond the traditional diagnostic window, complicating timely recognition of PPCM in clinical practice [11]. Furthermore, the clinical presentation of PPCM can vary significantly, with some patients exhibiting arrhythmias rather than typical heart failure symptoms. This atypical presentation can lead to delayed diagnosis or misdiagnosis, particularly when symptoms manifest beyond the long-established diagnostic timeframe [4,5,11], highlighting the importance of considering arrhythmic and late-onset PPCM.

Significant gaps exist in our understanding of the pathophysiology, risk factors, and outcomes associated with late-onset PPCM. The literature contains few documented case reports and series, which do not provide a robust understanding of this condition [10,11]. Because most previous research on PPCM has focused on early presentations [10,11], there is a need for larger, multi-center studies on late-onset PPCM to establish clearer diagnostic criteria and guidelines for medical and interventional treatment of these patients [10].

Failure to recognize late-onset PPCM can lead to mismanagement and poorer outcomes for women who develop symptoms beyond the traditional timeframe. This underscores the importance of educating clinicians about the possibility of late-onset PPCM presentation and the need for ongoing monitoring of postpartum cardiac structure and function [11]. Multidisciplinary approaches and comprehensive diagnostic evaluations are strongly recommended to ensure that women with late-onset PPCM symptoms are promptly identified and receive appropriate care [10,11]. In summary, the existing literature reveals a significant lack of knowledge regarding late-onset PPCM, particularly beyond the traditional 5-months diagnostic window. Addressing this gap is crucial for improving the diagnosis, management, and outcomes for affected women.

Both early and late-onset PPCM can significantly impact maternal cardiovascular (CV) health if not diagnosed and managed promptly. Recognizing these distinct entities of PPCM is important for several reasons: (1) To prevent long-term cardiac structural and electrical remodelling, leading to left and right ventricular dysfunction [12]; (2) To reduce maternal CV-related mortality risk [13]; and (3) To prevent misdiagnosis of late-onset PPCM, which may result in worse outcomes and longer recovery times, particularly in Black women [12]. The potential benefits of early identification of late-onset PPCM include: (1) Improved recovery of left ventricular ejection fraction (LVEF), with patients diagnosed early having significantly higher recovery rates compared to those diagnosed later [12]; (2) Higher baseline LVEF in women diagnosed early, which is a strong predictor of recovery [12]; (3) The importance of early postpartum follow-up

for at-risk women, especially those with hypertensive disorders of pregnancy (HDP), to facilitate timely diagnosis and treatment [12]; and (4) Mitigation of disparities in PPCM outcomes among different racial and socioeconomic groups through addressing the timing of diagnosis and ensuring equitable access to care [12]. In conclusion, early presentation and diagnosis of PPCM play a critical role in improving outcomes, and increased awareness and monitoring of at-risk populations can lead to better management of this life-threatening condition.

Both early and late-onset peripartum cardiomyopathy (PPCM) can pose significant risks to both mothers and infants. For mothers, these risks include: (1) An increased risk of severe complications, rapid deterioration in cardiac function, recurrent hospitalization, and death [14,15]; (2) Long-term health consequences due to persistent left ventricular dysfunction, with increased cardiovascular morbidity in future pregnancies [15]; (3) A significant risk of recurrence in subsequent pregnancies [15]; and (4) Psychological distress, with significant implications for future pregnancies and overall maternal health [15]. For infants, the risks include: (1) A higher risk of adverse outcomes, preterm birth, low birth weight, and long-term developmental issues [15]; (2) Neonatal intensive care unit admission [14,15]; and (3) Increased perinatal mortality [14,15]. In summary, distinct entities of PPCM significantly impacts both maternal and infant health, leading to increased risks of morbidity and mortality. Early recognition and management of this conditions are crucial for improving outcomes for both mothers and their infants.

Finally, our research study aims to: (1) Investigate and validate the occurrence of late-onset PPCM beyond the traditional diagnostic timeframe of 5 months, focusing on its frequency and clinical presentation; (2) Address existing knowledge gaps regarding late-onset PPCM in this specific population, ultimately contributing to improved diagnosis, management, and outcomes for affected mothers; (3) Increase awareness of late-onset PPCM among clinicians and lactating mothers; (4) Foster multi-center collaborative research on late-onset PPCM; and (6) Potentially prompt a revision of the traditional diagnostic criteria timeframe. Our current study will carefully analyse the sociodemographic, clinical, echocardiographic, electrocardiographic, chest radiographic findings of late-onset PPCM and may shed significant light on these profiles, and the overall understanding of late-onset PPCM.

Methods

This study was carried out in accordance with the principles and guidelines for human research outlined in the Helsinki Declaration [16]. Ethical approval was granted by the relevant institutional ethics review committees, with the following reference numbers: Usmanu Danfodiyo university Teaching Hospital, sokoto (NHREC/UDUTH-HREC/11/1/2021), Specialist Hospital Sokoto (SHS/SUB/133/Vol.1/4/1/2021), and Medi-Stop Clinical Diagnostic (MCD/SUB/012/Vol.11/101/2021). Informed consent was obtained from all participants, adhering to the guidelines stipulated in the Helsinki Declaration [16].

This cross-sectional study was conducted in 3 health facilities within Sokoto state. Nigeria and 10 consecutive peripartum women age (15 years and older) were recruited over 48 month period who presented with heart failure syndrome beyond long-established diagnostic criterion for PPCM timeframe of (5moth) Hibbard and Demakis et al. [4,5], after childbirth, and still met the European Society of Cardiology (ESC) Working Group diagnostic criteria for Peripartum Cardiomyopathy, as idiopathic cardiomyopathy leading to heart failure due to left ventricular (LV) systolic dysfunction occurring late in pregnancy or within months after delivery, with no other heart failure causes identified. It is a diagnosis of exclusion. While the left ventricle may not show dilation, the ejection fraction typically falls below 45% [6]. We collected sociodemographic, anthropometric, clinical, imaging and laboratory data through a structured questionnaire. Additionally, we inquired about culturally specific pregnancy practices, such as traditional hot baths and the consumption of dried lake-salt enriched pap (DLEP), known as 'Kunun kanwa' in the Hausa dialect [1].

At the time of clinical presentation, each patient's New York Heart Association (NYHA) functional class was determined and a detailed clinical history was obtained from each patient, including symptoms suggestive of left-sided and right-sided heart failure and a family history of similar illnesses. Past medical history of hypertension, diabetes, sickle cell anemia, substance abuse and each patient underwent a meticulous physical examination,

Blood Pressure Measurements

Blood pressure was measured on participants after a 10-minute rest using a mercury sphygmomanometer [17]. Three readings were averaged to determine brachial systolic and diastolic BP at Korotkoff sounds 1 and 5 in a sitting position. Hypertension was defined as systolic BP (SBP) of 140 mmHg or higher and/or a diastolic BP (DBP) of 90 mmHg or higher, on three separate occasions or antihypertensive medication use in patient with established hypertension. Participants with BP <140/90 mmHg were classified as normotensive.

The Anthropometric Measurements

Standard procedures were employed to measure body weight (in kg) using a calibrated weighing scale, with participants standing in light clothing.

Height (m): Height was measured with a stadiometer (Seca 213, UK), ensuring participants stood barefoot with their heels, back, and occiput against the scale, while looking straight ahead.

Body Mass Index (BMI): BMI was calculated by dividing weight (kg) by the square of height (m^2) [18].

Body Surface Area (BSA): BSA was estimated in square meters (m^2) using the Mosteller formula [19].

Echocardiography

Echocardiographic examinations were conducted on all PPCM patients using a Sonascape SSI-5000 system with a 1-6 MHz transducer, following American Society of Echocardiography (ASE) guidelines [20,21]. Assessments included 2D-guided M-mode imaging and Doppler studies. Left ventricular mass (LVM) was calculated using the Devereux modified cubed formula [22], and indexed to body surface area (BSA) [19], to obtain LV mass index (LVMI). Left ventricular hypertrophy (LVH) was defined using gender-specific thresholds [20,23].

Relative wall thickness (RWT) was calculated as 2 × PWTD (posterior wall thickness, diastolic) / LVEDD (left ventricular end-diastolic dimension) [20], and along with LVMI, used to classify LV geometry [20]. Left ventricular end-diastolic volume (LVEDV) and end-systolic volume (LVESV) were calculated [24], and indexed to BSA [19]. Left ventricular ejection fraction (LVEF) was assessed using the Teichholz formula [24]. Right ventricular internal diameter (RVIDd) and right atrial internal dimension (RAID) were measured and indexed to BSA [19,20]. Regional and global wall motion abnormalities were also evaluated.

Left ventricular diastolic function was assessed using Doppler echocardiography (E/A ratio, DT, IVRT) and graded [23]. Valvular regurgitation severity was semi-quantitatively assessed using color flow Doppler and jet area measurement as recommended by the ASE [21,23]. Other findings, such as clots, trabeculations, valve abnormalities, pericardial effusion, septal defects, and pulmonary arterial pressure, were also documented.

Electrocardiography (ECG)

A standard 12-lead electrocardiogram (ECG) was performed on each patient, including a long rhythm strip in lead II, following the recommendations of the American Heart Association (AHA) [25], and standard lead and instrument specifications. All patient's relevant ECG parameters and findings were documented.

Chest Radiograph

A posteroanterior chest radiograph was performed on all participants to evaluate cardiac silhouette, cardiothoracic ratio (CTR) for cardiomegaly, lung parenchyma abnormalities, aortic arch enlargement, alveolar/interstitial edema, upper lobe diversion, prominent vascular markings, bat-wing appearance, pleural effusion.

Other Investigations

Haemoglobin (Hb) levels, fasting blood sugar (FBS), fasting lipid profile (FLP), and serum Chest X-ray PA, levels of urea, electrolytes, and creatinine (E/U/Cr) were measured using validated commercial laboratory facilities.

Inclusion Criteria

The study included peripartum women of age (15 years and older) who visited three health facilities with a clinical diagnosis of heart failure syndrome who presented with heart failure syndrome beyond long-established diagnostic criterion for PPCM timeframe of 5 months Hibbard and Demakis et al. [4,5], after childbirth and still met the European Society of Cardiology (ESC) Working Group diagnostic criteria for Peripartum Cardiomyopathy [6],

Exclusion Criteria

Postpartum women under the age of 15 and those with established PPCM but within long established diagnostic criteria time frame for PPCM by Hibbard and Demakis et al. [4,5] were excluded from the study. Additionally, those with comorbidities such as diabetes, hyperthyroidism, sickle cell anemia (SCA), or Human Immunodeficiency Virus (HIV) infection and substantial alcohol consumption were also excluded.

Statistical Analysis

Data analysis was performed using Statistical Package for Social Sciences (SPSS) software, version 16.0 for Windows (SPSS Inc., Chicago, IL, USA). Descriptive statistics were used to analyze both continuous and categorical variables. Mean and standard deviation were calculated for quantitative variables, while qualitative variables were expressed as frequencies, proportions, or percentages and presented in tables or bar graphs.

Results

Socio-Demographic Characteristics and Anthropometric Measures of late onset PPCM

The mean age of the study population was 30.5 ± 6.5 (ranging from 21-45years). Most of the patients were multiparous, well-educated but unemployed and are of middle socioeconomic status residing in urban area. All the patients were actively breast feeding when symptoms of HF started. Three of patients had past history of gestational hypertension. None of the participants reported smoking and/or use of alcohol. The mean height and BMI of the participants were within normal limits (>1.50m and >23kg/m^2); (see Table 1).

Clinical History and Physical Examination Findings late onset PPCM patients

The mean duration of symptoms onset after delivery was 13 ± 2.1 months (ranging from 8-15 months) while the mean duration of symptoms prior to hospital health facilities presentation was 3.2 ± 3.74 weeks (ranging from 1-12 weeks). They presented in NYHA class II (70%), III (10%) and IV (20%), S_3 gallop was observed (100%) in all the patients while raised JVP was seen in (20%) of the patients at presentation. Most patients presented with left-sided heart failure (80%). Clinically only (40%) had mitral regurgitant murmur while co-occurring mitral and tricuspid regurgitant murmur was observed in one patient. One patient had complication cardio-embolic stroke with documented left ventricular apical thrombus on echocardiogram; (see Table 2).

Echocardiographic Profile of late onset PPCM Patients

All the patients had LVEF < 45% with (60%) of the patients having mild LV systolic dysfunction and (40%) having moderate LV systolic dysfunction (see Figure 1). LV diastolic function was

indeterminate in (70%) of the patients due to merged trans-mitral E/A velocity spectra probably as a result of significant MR and tachycardia while normal in (30%) of the patients. All the patients had abnormal LVEDVI (100%) and LVESVI (100%). Moderate to severe LVMI was observed in all the patients; (see Figure 2). LV geometry was abnormal in all patients; (see Figure 3). Mild MR was observed in (30%) moderate in (50%) and severe in (20%) of the patients. Mild tricuspid regurgitation was observed in (50%), moderate in (30%) and severe in 20 (%) of the patients. While mild aortic regurgitation was observed in (30%) of the patients. Other relevant echocardiographic parameters were stated below; (see Table 3).

Table 1: Show sociodemographic characteristics and anthropometric measures of the late onset PPCM patients.

Parameters	**Frequency (%)**
Marital Status (n=10)	
Married	10 (100)
Educational Status (n=10)	
Quranic education	1 (10)
Secondary education	2 (20)
Tertiary education	7 (70)
Occupation (n=10)	
Unemployed	10 (100)
Tribe (n=10)	
Hausa/Fulani	10 (100)
Place of Residence	
Urban	9 (90)
Rural	1 (10)
Socioeconomic status	
Middle socioeconomic status	8 (80)
Low socioeconomic status	2 (20)
Antenatal Care Attendance (n=10)	
Adequate	10 (100)
Parity	
Primipara **1**	2 (20)
Multipara **2-5**	6 (60)
Grand multipara **>5**	2 (20)
Child delivery	
Hospital	10 (100)
Twin gestation	1 (10)
Actively breast feeding	10 (100)
Previous history of gestational hypertension	3 (30)
Traditional customary practice	
Hot water bath only	3 (30)
Both hot water bath and intake dried lake-salt enriched pap (DLEP), known as 'Kunun kanwa' in the Hausa dialect	7 (70)
Anthropometric measures	**Mean ± SD**
Weight(kg) ± SD	63 ± 2.6
Height(M) ± SD	1.62 ± 0.04
Body Mass Index (BMI) kg/m^2 ± SD	24 ± 0.92

Table 2: Show relevant clinical history and physical examination findings of late onset PPCM patients

Clinical Parameters	**Mean ± SD**
Pulse Rate ± SD /minute	110 ± 34.1
Systolic blood pressure (SBP) ± SD mmHg	105 ± 12.2
Diastolic blood pressure (DBP) ± SD mmHg	70 ± 9.7
	Frequency (%)
Jugular venous pressure (JVP)	
Normal	8 (80)
Raised	2 (20)
Apex beat (AB)	
Displaced	10 (100)
Third heart sound (n=10)	
S3 gallop (n=10)	10 (100)
Loud P2 (n=10)	
Present	10 (100)
Murmurs (n=10)	
Mitral pansystolic murmur (PSM)	4 (40)
Mitral and Tricuspid pansystolic murmur (PSM)	1 (10)
No murmurs	5 (50)
Bi-basal crepitation (n=10)	
Present	10 (100)
Pattern ventricular heart failure; at presentation (n=10)	
Left ventricular heart failure (LVHF)	8 (80)
Biventricular heart failure (BVHF)	2(20)
Point of clinical evaluation (n=10)	
Out-patient	8(80)
In-patient	2(20)

Table 3: Show echocardiographic findings of late onset PPCM patients

Variables	**Mean ± SD**
Left atrial internal dimension (LAID) ± SD (mm)	44 ± 2.4
Right atrial internal dimension (RAID) ± SD (mm)	43 ± 6.4
Left Ventricular end-diastolic diameter (LVEDd) ± SD (mm)	56.0 ± 18.5
Left Ventricular end-systolic diameter (LVESd) ± SD (mm)	51.7 ± 5.0
Right ventricular internal dimension (RVID1) A4CHV ± SD (mm)	43 ± 8.7
Fractional shortening FS	17. ± 1.9
Mean pulmonary arterial pressure (MPAP) ± SD (mm)	36 ± 8.6
	Frequency (%)
Left ventricular End-Diastolic Volume Index (ml/m^2)	
Normal 29-61ml/m^2	0 (0)
Abnormal > 61 ml/m^2	10 (100)
Left ventricular End-Systolic Volume Index (ml/m^2)	
Normal 8-27 ml/m^2	0 (0)
Abnormal > 27 ml/m^2	10 (100)
Left ventricular global hypokinesia	10 (100)
Tricuspid annular plane systolic excursion (TAPSE) (n=10)	
Normal RV systolic function TAPSE >17mm	(40)
RV systolic dysfunction TAPSE < 17mm	6 (60)
Pattern of heart chambers dilatation (n=10)	
4-Chamber dilatation	5 (50)
2-Chamber dilatation (LV, LA)	4 (40)
3-Chamber dilatation (LA, RV, & RA)	1 (10)
Left ventricular apical thrombus	1 (10)

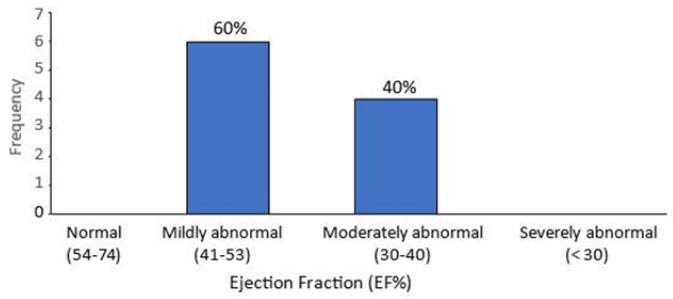

Figure 1: Show Severity of LV systolic dysfunction using ejection fraction (EF%) of the late-onset PPCM patients.

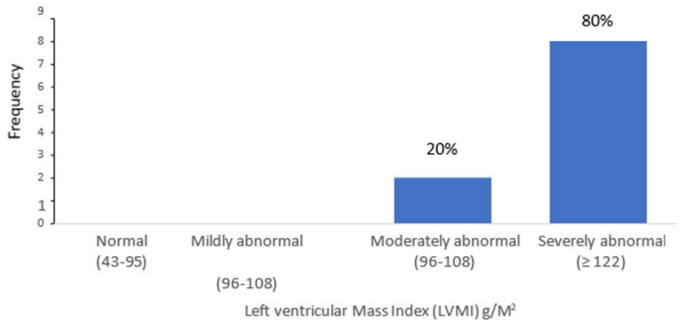

Figure 2: Show severity of left ventricular hypertrophy using LVMI (g/m^2) by linear method in late-onset PPCM patients.

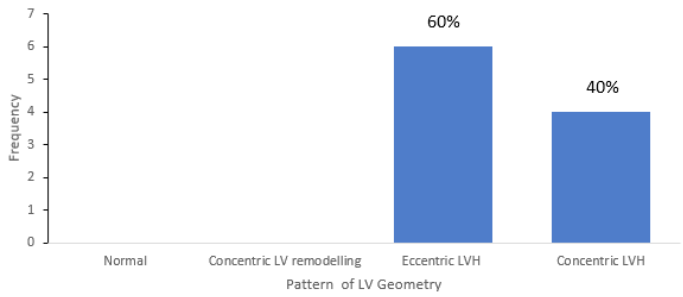

Figure 3: Show pattern of LV geometry in late-onset PPCM patients.

Electrocardiographic Features of late-onset PPCM patients

The mean HR was (114 ± 10.17 bpm), PR interval was 129 ± 51.8 ms and mean QRS duration was (97 ± 16.8 ms). Normal global QRS amplitude was observed in all (100%) the patients with QRS voltage ratio ≤ 3 in (80%) of the patients. The most common ECG abnormalities detected were sinus tachycardia (100%), prolonged QTc (70%) and T wave inversion (50%) in the study population. ST depression in V3-V6 was observed in (30%) of the patients. Extremely rare ECG abnormalities observed in the study population include LVH (10%), LAE (20%), and LBBB (10%) and atrial tachycardia in (10%); (see Table 4).

Roentgenographic Features of late-onset PPCM patients

The chest radiograph shows varying degree of cardiomegaly with cardiothoracic ratio (CTR) between (0.51 to 0.68) in all the patients. All the patients had radiological evidence of cardiogenic pulmonary edema of upward blood diversion and hilar prominent vascular markings at presentation; (see Table 5).

Table 4: Show electrocardiographic findings of late onset PPCM patients

Parameters	Frequency (%)
Sinus tachycardia (HR > 100/minute)	10 (100)
Corrected QT (QTc) ms (n=10)	
Female	
Normal QTc (≤ 460ms)	3(30)
Prolonged QTc (>460ms)	7(70)
QRS Axis (n=10)	
Normal	6(60)
LAD	2(20)
RAD	2 (20)
QRS amplitude mm (n=10)	
Normal global QRS voltages	10 (100)
QRS voltage ratio RV6/ maximum R in lead I, II, III (lead with maximum R)	
RV6/ I, II, III ratio ≤ 3	8 (80)
RV6/I, II, III ratio > 3	2(20)
ST depression	3 (30)
T wave inversion	5 (50)
LVH	1 (10)
LBBB	1 (10)
Atrial tachycardia	1 (10)

Table 5: Show roentgenographic (Chest Xray) features of the late onset PPCM patients.

Parameters	Frequency (%)
Cardio-thoracic ratio (CTR): (n=10)	
0.42-0.5	0 (0)
0.51-0.6	2 (20)
0.61-7	8 (80)
Upward blood diversion in the upper lung fields (Cephalization of pulmonary vessels) and prominent hilar vascular markings (n=10)	10 (100)

In the treatment pattern of this study population the most frequent anti-failure drugs used were loops diuretics (Frusemide and torsemide), angiotensin converting enzyme inhibitors (ACEIs), beta blockers (BBs), spironolactone and less frequently used were uperio and warfarin (see Figure 4).

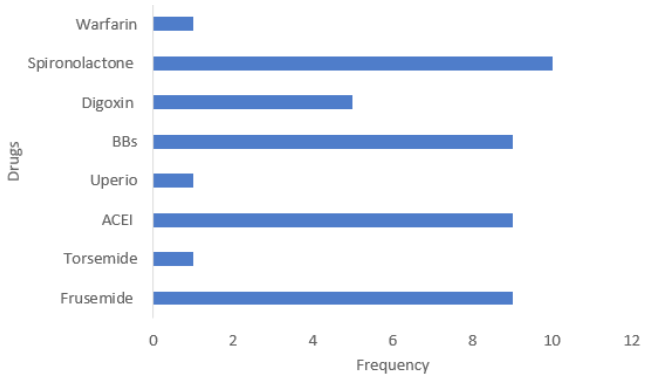

Figure 4: Show treatment pattern administered to late-onset PPCM patients.

Discussion

This study highlights the presentation of late-onset PPCM within the context of heart disease in Sub-Saharan Africa. Key observations show that affected patients were primarily young (thirties), multiparous women from the Hausa/Fulani ethnic group with a middle socioeconomic status, residing in urban areas. Despite receiving adequate antenatal care and hospital deliveries, heart failure symptoms emerged during breastfeeding, averaging 13 months postpartum, with a short three-week delay before seeking care. Most presented with left-sided heart failure and significant left ventricular remodeling. Common ECG findings included sinus tachycardia and prolonged QT intervals, while chest X-rays showed cardiomegaly and pulmonary edema. These findings define a distinct profile for late-onset PPCM in this region, crucial for timely diagnosis and management.

This study offers compelling insights into the characteristics and clinical presentation of late-onset PPCM within a specific population in Northwestern Nigeria. The research focused on a cohort of predominantly young, multiparous women in their thirties from the Hausa/Fulani ethnic group, the largest in a region marked by high poverty rates [1,26]. A significant finding was the apparent restriction of PPCM to this specific ethnic group, lending further weight to the notion of ethnic and geographical variations in the occurrence of this condition [2,3]. The observed association between multiparity and PPCM in this group aligns with existing literature [1,27].

A particularly noteworthy and unexpected observation was the prevalence of late-onset PPCM among Hausa/Fulani patients who presented a unique profile: middle socioeconomic status, well-educated, but not formally employed, with adequate antenatal care, a normal body mass index (BMI), and residing predominantly in the urban center of Sokoto. This contrasts sharply with the findings of Karaye et al. [1], who reported that PPCM patients were typically of low socioeconomic status, uneducated, underweight, and largely from rural areas of Northwestern Nigeria [1,27]. In this study we propose that these more favourable maternal socioeconomic indicators encompassing health, nutritional, and educational status, along with potentially different immunologic responses might have contributed to the delayed onset of PPCM presenting as late-onset PPCM in this study population. It's important to note that while a significant portion of the participants engaged in traditional puerperal practices previously linked to PPCM, more recent research has challenged this etiopathogenetic connection [1].

The study also highlighted the common issue of delayed presentation to healthcare facilities among patients, often experiencing symptoms for weeks or even months before seeking medical attention. This delay is largely attributed to a lack of disease awareness within the predominantly uneducated population and the financial barriers imposed by Nigeria's healthcare system, which often requires out-of-pocket payments [28]. Interestingly, despite the relatively higher socioeconomic status and education levels of the late-onset PPCM group in this study, their average time from symptom onset to hospital presentation was three weeks, suggesting that even in this more privileged cohort, delays persist and underscore the critical need for enhanced disease awareness.

Gestational hypertension is recognized as a significant risk factor associated with the development of peripartum cardiomyopathy, suggesting a potential overlap in their pathophysiological mechanisms [1]. In this study 30% of the patient had past history of gestation hypertension.

Clinically, all participants exhibited a left-sided third heart sound gallop (S3 gallop) upon presentation, a hallmark sign of left ventricular dysfunction consistent with left-sided heart failure. Additionally, half of the study population presented with a functional mitral regurgitant murmur, likely resulting from structural pathological remodelling leading to the enlargement of the atrial and ventricular chambers and the mitral annulus. One patient experienced a cardioembolic stroke and was found to have a left ventricular apical thrombus on echocardiogram, a finding consistent with previous PPCM studies [1,29]. Potential predisposing factors for this thrombus in the late-onset PPCM patient included postpartum hormonal shifts [30,31], left ventricular dilatation and systolic dysfunction, global hypokinesia, although the patient did not have atrial arrhythmias like atrial fibrillation. This case suggests that late-onset PPCM may also be a significant risk factor for stroke.

Echoing findings by Giovanni Peretto et al. [11], this study also identified an arrhythmic presentation of PPCM. One patient with late-onset PPCM presented with recurrent palpitations and shortness of breath. Cardiac examination revealed a displaced apex beat and a mitral pansystolic murmur, while the electrocardiogram (ECG) showed atrial tachycardia, and echocardiographic findings were consistent with PPCM. This case highlights the diverse clinical manifestations of late-onset PPCM.

The study also delves into the potential role of prolactin in the pathogenesis of PPCM. It is increasingly understood that the proteolytic cleavage of circulating prolactin into a 16 kDa fragment, which exhibits anti-angiogenic and pro-apoptotic properties, may contribute to myocardial dysfunction [32]. Given that all the late-onset PPCM patients in this study experienced the onset of heart failure symptoms while actively breastfeeding, the researchers propose a possible link between this pathologic prolactin-induced myocardial dysfunction and the development of late-onset PPCM.

The observation of significant left ventricular (LV) dilatation in late-onset PPCM patients aligns with findings from Karaye et al. and the European Society of Cardiology (ESC) working group diagnostic criteria for PPCM [1,6]. All participants had a left ventricular ejection fraction (LVEF) below 45%, consistent with diagnostic criteria proposed by Hibbard, Demakis, and the ESC [4-6]. The majority of patients exhibited mild to moderate LV systolic dysfunction, while right ventricular (RV) systolic dysfunction was also prevalent, a finding consistent with Karaye et al. [1]. Notably, spectral Doppler evaluations indicated indeterminate

LV diastolic dysfunction in three-quarters of the patients, likely influenced by significant mitral regurgitation and tachycardia. The study also found abnormal LVEDVI and LVESVI, reliable indicators of global systolic function, corroborating Karaye et al.'s findings [1]. Furthermore, similar to early-onset PPCM and dilated cardiomyopathy, all patients with late-onset PPCM showed LV global hypokinesia, a significant observation across this spectrum of cardiomyopathies [33]. These cardiomyopathies, regardless of their cause or type, are often associated with significant structural pathological remodelling of the heart [34], involving complex molecular, cellular, and interstitial changes following injury [34], that affect the heart's shape, size, geometry, mass, and function [34], often leading to adverse outcomes such as ventricular dysfunction and malignant arrhythmias.

Echocardiography stands as the primary non-invasive tool for assessing this structural pathological remodelling, including left ventricular hypertrophy (LVH), changes in ventricular size, and LV geometry [34]. LVH, defined by an abnormal left ventricular mass index (LVMI) and geometric patterns [35], is a critical indicator for diagnosing cardiovascular disease with significant clinical implications [36,37]. In late-onset PPCM, similar to other structural heart diseases, LVH is likely influenced by genetic factors, age of onset, initial cause, neurohormonal activation, and variations in hemodynamic mechanisms, along with LV systolic and diastolic dysfunctions [38]. This study observed significant LV structural pathological remodelling (LVH and abnormal patterns of LV geometry in the majority of late-onset PPCM patients, a finding also reported by Karaye et al. [1]. This suggests that such structural pathological remodeling could serve as strong independent predictors of disease progression, morbidity, and mortality [39], in late-onset PPCM if not addressed with appropriate treatment.

Color Doppler echocardiography in this study revealed varying degrees of regurgitation in the mitral and tricuspid valves, consistent with the findings of Karaye et al. [1].

Peripartum cardiomyopathy (PPCM) often presents with a range of electrocardiogram (ECG) changes that can mimic other cardiac conditions [40,41]. In resource-constrained settings, ECG, being more readily available, accessible, and cost-effective than echocardiography, plays a vital role as a first-line screening tool for identifying ECG "red flags" associated with sudden cardiac death in PPCM and other forms of dilated cardiomyopathy [42]. The most common ECG abnormalities observed in this study's late-onset PPCM cohort were sinus tachycardia, T wave inversion, and prolonged QT intervals, sharing similarities with PPCM studies by Karaye and Umar et al [1,40]. While echocardiographic findings in late-onset PPCM and idiopathic dilated cardiomyopathy (DCM) may appear similar, the ECG findings differed in some aspects. The study found a QRS voltage ratio of ≤ 3 in the majority of late-onset PPCM patients, contrasting with the typical ratio of ≥ 3 in DCM, which is often attributed to substantial myocardial loss, fat infiltration, LV dilatation, and significant LV myocardial fibrosis [40-45]. Although serious atrial and ventricular arrhythmias were uncommon in late-onset PPCM in this study, the notable high prevalence of prolonged QTc intervals raises concern for an increased risk of torsades de pointes and subsequent ventricular fibrillation, potentially leading to sudden cardiac death. In summary, the study highlights that while severe ECG abnormalities may be rare in late-onset PPCM, the presence of prolonged QT intervals poses a significant risk for life-threatening ventricular arrhythmias.

While echocardiography remains the gold standard for diagnosing PPCM and assessing left ventricular function, radiographic findings such as cardiomegaly and pulmonary congestion on chest X-ray in postpartum women can raise clinical suspicion for PPCM [46]. The presence of varying degrees of cardiomegaly and radiographic evidence of cardiogenic pulmonary edema on chest X-ray, in conjunction with clinical signs and symptoms of heart failure, necessitates prompt and comprehensive cardiac evaluation to establish a PPCM diagnosis and guide timely management, which is crucial for improving maternal outcomes [46]. In this study, all late-onset PPCM patients exhibited cardiomegaly with a cardiothoracic ratio (CTR) between 0.51 and 0.68 and radiologic evidence of cardiogenic pulmonary edema. This finding may be attributed to significant structural pathological myocardial remodelling, abnormal LVESVI and LVEDVI, and the observed pulmonary arterial hypertension in the study population, aligning with findings by [1,27], and carrying significant implications for late-onset PPCM.

The strategic clinical implications of this study warrant careful consideration: (1) Late-onset PPCM appears to be more prevalent in multiparous women of middle socioeconomic status, who are well-educated, reside in urban areas, and have better nutrition and normal weight. These factors may explain the delayed onset of PPCM beyond the traditional diagnostic timeframe established by Hibbard and Demakis [4,5]. (2) Late-onset PPCM is characterized by significant LV structural pathological remodelling (LVH and abnormal patterns of LV geometry). This pathological structural remodelling is substantial in late-onset PPCM and may predict progressive LV dysfunction if not promptly identified and managed appropriately. (3) Prolonged QT intervals are highly prevalent among late-onset PPCM patients, potentially leading to life-threatening cardiac arrhythmias and sudden cardiac death. (4) There is a need to reconsider the long-established diagnostic criteria for PPCM by Hibbard and Demakis [4,5] to better encompass late-onset presentations. (5) It is crucial to raise awareness among clinicians regarding late-onset PPCM and to implement routine follow-up screenings for postpartum women at risk to improve clinical outcomes.

The treatment regimen administered to this study population showed a more frequent use of loop diuretics, ACE inhibitors, beta-blockers, and spironolactone, with less frequent use of medications like Uperio and warfarin. This treatment pattern mirrors that reported in the study by Karaye et al. [1].

Conclusions

Recognizing late-onset PPCM as a distinct and prevalent entity, especially among educated women of middle socioeconomic status in Sub-Saharan Africa, is paramount. The significant LV remodeling, prolonged QTc, and abnormal chest radiographs underscore the potential for progressive ventricular dysfunction and poorer outcomes. This study ignites an urgent call for increased awareness and targeted research. By shifting our focus to this underrecognized form of PPCM and validating these findings through larger, multi-center studies, we can pave the way for earlier diagnosis, tailored treatments, and ultimately, brighter futures for affected mothers in the region.

Limitations of the Study

Due to limited facilities, genetic studies, tissue Doppler imaging, and patient follow-up studies were not carried out.

Significance of this Study Findings for Clinical Practice Include:

(1) To raise awareness among clinicians of late-onset PPCM (2) To call for implementing routine follow-up screenings for postpartum women at risk of late onset PPCM can facilitate early diagnosis (3) The need for revising long-established diagnostic criteria for PPCM (4) Effective management of late-onset PPCM should involve a cardio-obstetrics team (5) The need for establishing clear guidelines for postpartum cardiovascular follow-up assessments/ function throughout postpartum and lactation period can aid in early detection of late onset PPCM (6) Educating postpartum women about the red flags symptoms and signs of late-onset PPCM can empower them to seek timely diagnosis and treatment; (7) Educating postpartum women on the risks of recurrence in subsequent pregnancies are essential. In summary findings from this study may be used to develop educational materials for mothers about late-onset PPCM.

Implications of this Study are as Follows;

(1) There is lack of comprehensive data on late-onset PPCM, and more studies are needed to establish prevalence rates, clinical characteristics, and long-term outcomes. This study is vital for developing guidelines and educational materials for healthcare providers and patients; (2) Late-onset PPCM may be underdiagnosed or misdiagnosed if long-established diagnostics criteria is to be applied; (3) Understanding the late-onset presentation of PPCM is crucial, as it can lead to significant morbidity and mortality. (4) Research can help identify patterns and risk factors, improving early detection and treatment strategies, ultimately enhancing maternal health outcomes; (5) Understanding the implications of late-onset PPCM on future pregnancies is essential. Research can provide insights into the risks of recurrence and inform counselling for affected women regarding family planning and management during subsequent pregnancies.

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