ESC HEART FAILURE
ESC Heart Failure 2020; **7**: 236–244
Published online 28 January 2020 in Wiley Online Library (wileyonlinelibrary.com) **DOI:** 10.1002/ehf2.12562

ORIGINAL RESEARCH ARTICLE

Incidence, clinical characteristics, and risk factors of peripartum cardiomyopathy in Nigeria: results from the PEACE Registry

K.M. Karaye[1,2,3]*, N.A. Ishaq[2], H. Sa'idu[1], S.A. Balarabe[4], M.A. Talle[5], M.S. Isa[6], U.G. Adamu[7], H. Umar[8], H.I. Okolie[9], M.N. Shehu[10,11], I.Y. Mohammed[12,13], B. Sanni[2], O.S. Ogah[14], I. Oboirien[15], E.M. Umuerri[16], A.C. Mankwe[17], V.Y. Shidali[18], P. Njoku[19], S. Dodiyi-Manuel[20], T.T. Shogade[21], T. Olunuga[22], D. Ojji[23], V. Josephs[22], A.C. Mbakwem[24], J. Tukur[25,26], S.A. Isezuo[8] on behalf of PEACE Registry Investigators

[1]*Department of Medicine, Bayero University, Kano, Nigeria;* [2]*Department of Medicine, Aminu Kano Teaching Hospital, Kano, Nigeria;* [3]*Department of Public Health and Clinical Medicine, Umea University, Umea, Sweden;* [4]*Department of Medicine, Muhammad Abdullahi Wase Specialist Hospital, Kano, Nigeria;* [5]*Department of Medicine, University of Maiduguri Teaching Hospital/University of Maiduguri, Maiduguri, Nigeria;* [6]*Department of Medicine, Ahmadu Bello University Teaching Hospital, Zaria, Nigeria;* [7]*Department of Medicine, Federal Medical Centre Bida, Bida, Nigeria;* [8]*Department of Medicine, Usman Dan-Fodio University Teaching Hospital, Sokoto, Nigeria;* [9]*Department of Medicine, Federal Teaching Hospital Gombe, Gombe, Nigeria;* [10]*Department of Medicine, General Ahmadi Kurfi Specialist Hospital, Katsina, Nigeria;* [11]*Department of Medicine, Federal Medical Centre, Katsina, Nigeria;* [12]*Department of Chemical Pathology, Bayero University, Kano, Nigeria;* [13]*Department of Chemical Pathology, Aminu Kano Teaching Hospital, Kano, Nigeria;* [14]*Department of Medicine, University College Hospital, Ibadan, Nigeria;* [15]*Department of Medicine, Dalhatu Araf Specialist Hospital, Lafia, Nigeria;* [16]*Department of Medicine, Delta State University Teaching Hospital, Oghara, Nigeria;* [17]*Department of Medicine, Federal Medical Centre Yenagoa, Yenagoa, Nigeria;* [18]*Department of Medicine, Federal Medical Centre Makurdi, Makurdi, Nigeria;* [19]*Department of Medicine, University of Nigeria Teaching Hospital, Enugu, Nigeria;* [20]*Department of Medicine, University of Port Harcourt Teaching Hospital, Port Harcourt, Nigeria;* [21]*Department of Medicine, University of Uyo Teaching Hospital, Uyo, Nigeria;* [22]*Department of Medicine, University of Benin Teaching Hospital, Benin City, Nigeria;* [23]*Department of Medicine, University of Abuja Teaching Hospital, Gwagwalada, Nigeria;* [24]*Department of Medicine, University of Lagos Teaching Hospital, Lagos, Nigeria;* [25]*Department of Obstetrics and Gynaecology, Bayero University, Kano, Nigeria;* [26]*Department of Obstetrics and Gynaecology, Aminu Kano Teaching Hospital, Kano, Nigeria*

Abstract

Aims The aim of this study was to describe the incidence, clinical characteristics and risk factors of peripartum cardiomyopathy (PPCM) in Nigeria.

Methods and Results The study was conducted in 22 hospitals in Nigeria, and PPCM patients were consecutively recruited between June 2017 and March 2018. To determine factors associated with PPCM, the patients were compared with apparently healthy women who recently delivered, as controls. Four hundred six patients were compared with 99 controls. The incidence and disease burden (based on the rate of consecutive recruitment of subjects) varied widely between the six geographical zones of Nigeria. From the North–West zone, 72.3% of the patients was recruited, where an incidence as high as 1 per 96 live births was obtained in a centre, while the disease was uncommon (7.6% of all recruited patients) in the South. Majority of the patients (76.6%) and controls (74.8%) ($p = 0.694$) were of Hausa–Fulani ethnic group. Atrial fibrillation, intracardiac thrombus, stroke, and right ventricular systolic dysfunction were found in 1.7%, 6.4%, 2.2%, and 54.9% of the patients, respectively. Lack of formal education (odds ratio [OR] 3.08, 95% confidence interval [1.71, 5.53]; $P < 0.001$), unemployment (OR: 3.28 [2.05, 5.24]; $P < 0.001$), underweight (OR: 13.43 [4.17, 43.21]; $P < 0.001$) and history of pre-eclampsia (OR: 9.01 [2.18, 37.75]; $P = 0.002$) emerged as independent PPCM risk factors using regression models. Customary hot baths (OR: 1.24 [0.80, 1.93]; $P = 0.344$), pap enriched with dried lake salt (OR: 1.20 [0.74, 1.94]; $P = 0.451$), and Hausa–Fulani ethnicity (OR: 1.11 [0.67, 1.84]; $P = 0.698$) did not achieve significance as PPCM risk factors.

Conclusions In Nigeria, the burden of PPCM was greatest in the North–West zone, which has the highest known incidence. PPCM was predicted by sociodemographic factors and pre-eclampsia, which should be considered in its control at population level. Postpartum customary birth practices and Hausa–Fulani ethnicity were not associated with PPCM in Nigeria.

Keywords Peripartum cardiomyopathy; Incidence; Risk factors; PEACE Registry

Received: 23 July 2019; Revised: 25 October 2019; Accepted: 29 October 2019
**Correspondence to: Kamilu M. Karaye, Department of Medicine, Aminu Kano Teaching Hospital, PO Box 4445, Kano, Nigeria. Tel: +2348037042171, Email: kkaraye@yahoo.co.uk*

Introduction

Peripartum cardiomyopathy (PPCM) is an important cause of heart failure (HF) with reduced ejection fraction (EF) that exclusively affects women without preexisting heart disease towards the end of pregnancy or in the first few months after delivery.[1] It is a global disease with epidemiology that varies widely.[1] The true incidence and prevalence of PPCM in Africa is unknown, largely because of paucity of population-based studies. However, single-centre hospital-based studies have suggested that PPCM is highly prevalent in Northern Nigeria with significant morbidity and mortality.[2,3] An incidence rate as high as 1:102 deliveries and prevalence as high as 4.2% of all patients referred for echocardiography, representing 52.4% of all cardiomyopathies, have been reported.[2,3] Similar studies elsewhere in Africa reported lower incidence rates of 1 in 1000 live births in South Africa and 1 in 3800 deliveries in Burkina Faso.[4,5]

Peripartum cardiomyopathy has been associated with several risk factors over the years, but there is significant inconsistency between studies.[1,6–8] The suggested risk factors include African origin, increased maternal age, multiparity, pre-eclampsia, twin pregnancy, obesity, poor socioeconomic status/malnutrition, certain customary birth practices in northern Nigeria, and selenium deficiency.[1,6–8] The customary birth practices of the Hausa and Fulani ethnic groups, believed to improve the health of new mothers, included regular twice daily hot baths ('Wankan Jego' in Hausa language), regular ingestion of pap enriched with dry lake salt ('Kunun Kanwa' in Hausa language), and lying on heated mud beds (made of baked mud, heated with firewood from beneath), starting from shortly after giving birth and continuing for about 3 months.[6]

In a previous study in Nigeria, we found low serum selenium and rural residency as independent risk factors for PPCM, while the more frequently reported risk factors did not achieve statistical significance.[8] To study the disease further, we set up the *Peripartum Cardiomyopathy in Nigeria* (PEACE) Registry, which is a national study that aimed to describe the burden and demographic, social and clinical characteristics, ventricular remodelling, and survival of PPCM in Nigeria (ClinicalTrials.gov Identifier: NCT03081949).[9]

In this paper, we aimed to describe the incidence, clinical characteristics, and risk factors of PPCM in Nigeria.

Methods

The study protocol for PEACE Registry has already been published, and some interim results have been presented as abstracts at scientific meetings.[9]

Peripartum Cardiomyopathy in Nigeria Registry is a longitudinal study that was carried out in 22 centres spread across Nigeria (*Figure 1*). Cardiologists in Nigeria were invited to participate as investigators through the email platform and conferences of the Nigerian Cardiac Society. All PPCM patients presenting to the study centres between June 2017 and March 2018 were consecutively recruited after satisfying the inclusion criteria. New PPCM patients were included if they were symptomatic at presentation to the study centre or within the previous 4 weeks if they had been commenced on treatment at a previous hospital. Patients being followed up at the participating centres before the commencement of the study, who had left ventricular (LV) ejection fraction (LVEF) $<45\%$, were recruited regardless of the presence of symptoms.[9]

The incidence of PPCM at each centre was determined by recording the total number of all new PPCM cases and expressing it as a fraction of all live births during the study period.

To determine the factors associated with PPCM, we compared the baseline characteristics of the patients with those of apparently healthy women who had delivered within the previous 6–8 weeks as controls. To be included as controls, subjects had to also be apparently healthy and below the age of 40 years. Centres were encouraged to recruit at least five subjects as controls from their postnatal clinics. The evaluation of the controls was funded by the Registry.

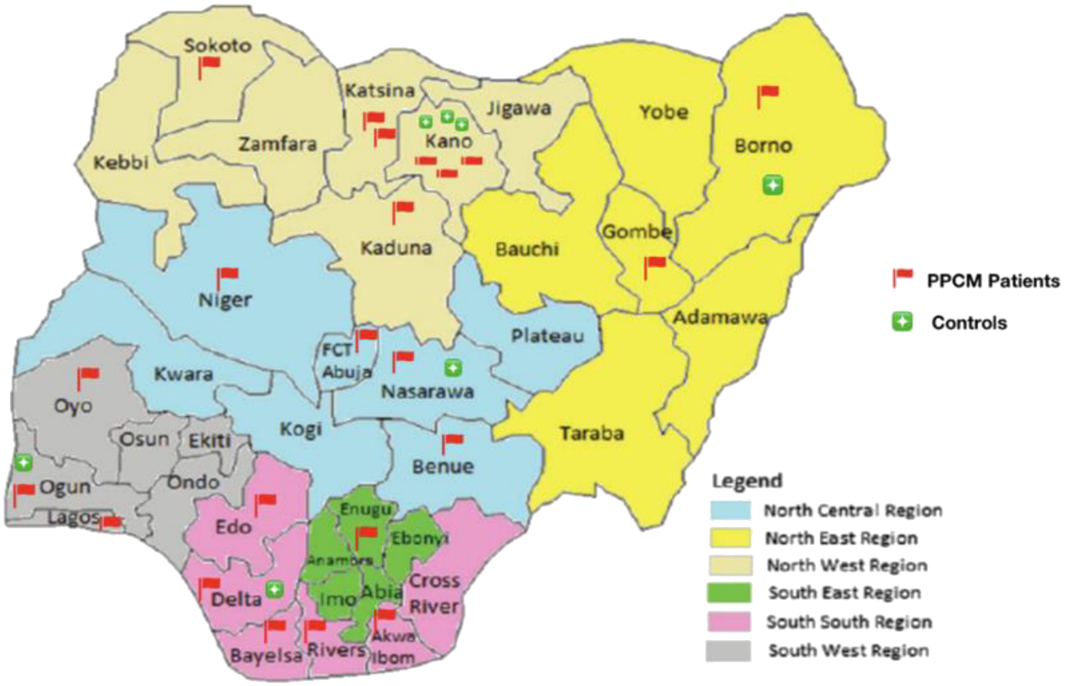
Subjects were enrolled into the study after obtaining written informed consent. Ethical approval for the study was obtained from the Ethical Research Committees of all the participating centres before the commencement of the study. The study conformed to the ethical guidelines of the Declaration of Helsinki on the principles for medical research involving human subjects.[10]

A pretested questionnaire was used to collect demographic, clinical, and laboratory data of the subjects. Electrocardiography and echocardiography were carried out on each subject using standard criteria and methods, as previously described.[11,12]

Peripartum cardiomyopathy was defined as an idiopathic cardiomyopathy presenting with HF secondary to LV systolic dysfunction (SD) towards the end of pregnancy or in the months following delivery, where no other cause of HF is found (a diagnosis of exclusion). The LV may not be dilated but the LVEF is nearly always reduced below 45%.[1] For the purpose of this study, younger age was defined as <20 years, older maternal age as >30 years, underweight as body mass index (BMI) <18.5 kg/m^2, obesity as BMI ≥ 30 kg/m^2, systemic hypertension as systolic blood pressure (BP) ≥ 140 mmHg and/or diastolic BP ≥ 90 mmHg, hypotension as systolic BP <100 mmHg in sitting position and broad QRS as duration ≥ 110 ms.

Right ventricular (RV) basal diameter and the long axis amplitude of motion (tricuspid annular plane systolic excursion, TAPSE) were also measured for each subject.[11] TAPSE was measured from end-systolic to end-diastolic points during

Figure 1 Map of Nigeria displaying the distribution of *Peripartum Cardiomyopathy* in Nigeria Registry study sites. Legend: Map of Nigeria with the red flags and green stars indicating the sites that recruited peripartum cardiomyopathy patients and controls respectively, in the various geopolitical zones and states.



held end expiration. Care was taken to align the M-mode beam along the direction of tricuspid annulus motion, with the minimum angle in between. RVSD was defined as the presence of TAPSE <16 mm.[11]

Data analysis

Continuous variables were explored for the presence of skewness. Proportions, medians with interquartile ranges (IQRs) and means with standard deviations were used to summarize the subjects' characteristics, as appropriate. Chi-square, Fisher's exact probability, Student's *t* and Mann–Whitney tests were used to compare categorical and continuous variables, as appropriate. Univariate analyses and multivariate regression models were developed to explore the relationship between PPCM and variables of interest, and values were expressed as odds ratios (ORs) and 95% confidence intervals (CIs). Two-sided *P*-value <0.05 was used as minimum level of statistical significance. The statistical analysis was carried out using SPSS version 17.0 software.

Results

A total of 406 patients were recruited from 22 centres in Nigeria and compared with 99 controls recruited from seven of the centres, between June 2017 and March 2018 (*Figure 1*). Of the 22 participating centres, 13 were in the northern zones and 9 were in the South. Three centres in Kano (North–West zone) and one each in Borno (North–East zone), Lafia (North–Central zone), Oghara (South–South zone), and Abeokuta (South–West zone) recruited the controls (*Figure 1*).

The patients had a mean age of 28.6 ± 7.2 years and median parity of 3 (IQR = 1–6) while the controls had a mean age of 29.6 ± 5.5 years ($P = 0.186$) and median parity of 4 (IQR = 2–6) ($P = 0.525$).

Incidence of peripartum cardiomyopathy

A total of 509 newly diagnosed and previously diagnosed PPCM patients were screened at the study centres within the recruitment period, but we excluded 103 of them because of inadequate echocardiography data (30 patients) or LVEF $\geq$45% (73 patients). Of the six geographical zones in Nigeria (*Figure 1*), the highest recruitment of 296 (72.9%) patients was from North–West zone followed by the North–East ($n = 54$, 13.3%), North–Central ($n = 25$, 6.2%), South–West ($n = 16$, 3.9%), South–South ($n = 13$, 3.2%), and South–East ($n = 2$, 0.5%) zones. Therefore, a total of 375 (92.4%) and 31 (7.6%) patients were recruited from the northern and southern zones, respectively. This translated into an incidence rate of 1 PPCM case per 96

live births at Murtala Muhammad Specialist Hospital, Kano, making it the highest recruiting centre. The incidence rates at some of the other centres include 1:109 in Zaria (Kaduna State), 1:117 at Aminu Kano Teaching Hospital (another Kano centre), 1:177 in Maiduguri (Borno State), 1:340 in Gombe, 1:900 in Lafia (Nasarawa State), 1: 1170 in Abeokuta (Ogun State), 1:1350 in Yenagoa (Bayelsa State), and 1:2700 in Makurdi (Benue State) (*Figure 2*).

Of the 99 subjects in the control group, 82 (82.8%) were recruited from the North–West zone and the remaining 17 (17.2%) from the other zones (*Figure 1*).

Demographic characteristics of subjects

The baseline demographic characteristics of the patients and controls were presented and compared in *Table 1*. It shows that in comparison with controls, the patients had higher proportion with younger age, no formal education, and unemployment, while the controls had higher proportion with multiparity.

Although the patients belonged to 29 different ethnic groups, 311 (76.6%) of them were of Hausa–Fulani ethnicity, 5.4% were Kanuris, and the Nupes and Yorubas each represented 3.9% of the cohort.

Clinical characteristics of subjects

The baseline clinical characteristics of the patients and controls were presented and compared in *Table 1*. It shows that the patients had higher prevalence of history of pre-eclampsia in at least one of their previous pregnancies, underweight, hypotension, and broad QRS duration than the controls. They also had higher mean heart rate and larger sizes of left atrium (LA) and LV and lower LVEF than the controls. The postpartum customary hot baths were being practiced by $<50\%$ of both groups and that of the salt-enriched pap by about one-thirds of each group ($P > 0.05$). Furthermore, patients had greater mean RV basal dimension, lower mean TAPSE, and higher frequency of RV systolic dysfunction than the controls.

All the controls and 89 (21.9%) PPCM patients were asymptomatic at recruitment. However, 154 (37.9%) patients with PPCM were assessed to be in New York Heart Association (NYHA) functional Class II, 71 (17.5%) were in NYHA Class III, and 65 (16.0%) were in NYHA Class IV at enrolment. Evidence of fluid retention was evident, with pedal oedema found in 181 (44.6%), raised jugular venous pressure in 162 (39.9%), ascites in 177 (43.6%), and hepatomegaly in 183 (45.1%) patients. In addition, 30 (7.4%) patients had pneumonia, 5 (1.2%) had urinary tract infection, 9 (2.2%) had stroke,

Figure 2 Map of Nigeria displaying the incidence rate of peripartum cardiomyopathy by states. Legend: Map of Nigeria displaying the incidence of peripartum cardiomyopathy by states in five geographic zones.

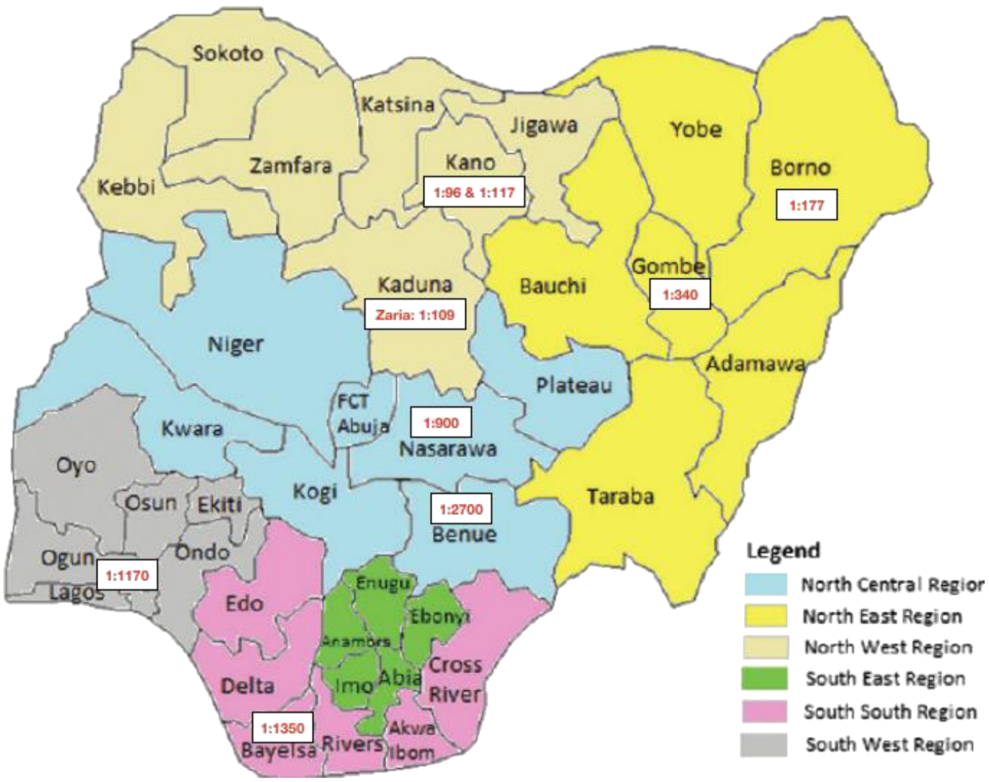


Table 1 Baseline characteristics of subjects

Variables	PPCM $N = 406$	Controls $N = 99$	*P*-value
Demographic characteristics			
Age (years)	28.6 ± 7.2	29.6 ± 5.5	0.186
Age ≥ 30 years	140(34.5%)	41(41.4%)	0.201
Age < 20 years	29(7.1%)	1(1.0%)	0.017*
Parity, median (IQR)	3(1–6)	4(2–6)	0.525
Multiparity	289(71.2%)	81(81.8%)	0. 032*
Twin pregnancy	59(14.5%)	18(18.2%)	0.353
No formal education	144(35.5)	15(15.2%)	<0.001*
Unemployment	329(81.0%)	56(56.6%)	<0.001*
Hausa/Fulani ethnicity	311(76.6%)	74(74.8)	0.694
Clinical characteristics			
Customary hot birth practice	202(49.8%)	44(44.4%)	0.371
Customary salt-enriched pap	135(33.3%)	29(29.3%)	0.475
Pre-eclampsia	64(15.8%)	2(2.0%)	<0.001*
Family history of PPHF	24(5.9%)	1(1.0%)	0.065
Alcohol	5(1.2%)	0	0.587
Cigarettes	4(1.0%)	0	0.722
BMI (kg/m^2)	20.1 ± 6.3	25.4 ± 4.6	<0.001*
Obesity	15(3.7%)	7(7.1%)	0.166
Underweight	120(29.6%)	0	<0.001*
Heart rate (bpm)	103 ± 18	88 ± 14	<0.001*
Systolic BP (mmHg)	108 ± 17	118 ± 16	<0.001*
Diastolic BP (mmHg)	75 ± 14	76 ± 11	0.667
Hypertension	66(16.3%)	13(13.1%)	0.538
Hypotension	88(21.7%)	2(2.0%)	<0.001*
Electrocardiogram			
Atrial fibrillation	7(1.7%)	0	0.403
Other arrhythmias	2(0.5%)	0	0.847
QRS duration (ms)	100.1 ± 26.3	86.9 ± 15.4	<0.001*
QRS duration ≥110 ms	89(21.9%)	9(9.1%)	0.001*
Echocardiogram			
Left atrium (mm)	43.5 ± 6.1	34.8 ± 4.9	<0.001*
LVEDD (mm)	62.5 ± 7.0	47.1 ± 6.8	<0.001*
LVEF (%)	30.7 ± 7.8	61.2 ± 8.3	<0.001*
RV basal dimension (mm)	43.2 ± 8.5	30.8 ± 6.6	<0.001*
TAPSE (mm)	15.1 ± 5.8	21.7 ± 3.7	<0.001*
RVSD	223(54.9%)	4(4.0%)	<0.001*
Laboratory results			
Serum sodium (mmol/L)	134.6 ± 15.3	138.6 ± 6.0	0.017*
Serum creatinine (μmol/L)	86.2 ± 36.8	59.7 ± 12.9	<0.001*
Hemoglobin (g/dL)	14.5 ± 8.6	13.0 ± 1.5	0.403

BMI, body mass index; LVEDD, left ventricular end-diastolic dimension; LVEF, left ventricular ejection fraction; PPHF, postpartum heart failure; RV, right ventricle; RVSD, right ventricle systolic dysfunction; TAPSE, tricuspid annular plane systolic excursion.
**P*-value is statistically significant.

1 (0.3%) each had deep vein thrombosis and renal failure, and 26 (6.4%) had cardiac mural thrombus.

Regarding medications at enrolment, 364 (89.7%) patients were on loop diuretics, 367 (90.4%) were on spironolactone, 207 (51.0%) on either angiotensin converting enzyme inhibitors or angiotensin II receptor blockers, 99 (24.4%) on beta blockers, 289 (71.2%) on digoxin, 27 (6.7%) on warfarin, 3 (0.7%) on hydralazine-isosorbide nitrate combination and 78 (19.2%) on either aspirin or clopidogrel.

Factors associated with peripartum cardiomyopathy

Several variables of interest were tested for significant association with PPCM using univariate analyses and multivariate binary regression models (*Tables 2* and *3*). In the univariate analyses, five variables (age < 20 years, lack of formal education, unemployment, pre-eclampsia, and underweight) increased the odds for PPCM while two others (multiparity and twin pregnancy) decreased it. When these were included in the multivariate binary regression model, lack of formal education, underweight, unemployment status, and pre-eclampsia emerged as independent risk factors of PPCM.

Discussion

In this study, a total of 406 well-characterized PPCM patients were consecutively recruited from 22 centres across Nigeria

Table 2 Univariate analysis

Risk factors	Odds ratio	95% Confidence intervals	*P*-value
Older maternal age (≥30 years)	0.745	0.475, 1.167	0.198
Younger age (<20 years)	7.54	1.01, 56.03	0.048*
Multiparity	0.55	0.32, 0.96	0.034*
No formal education	3.08	1.71, 5.53	<0.001*
Unemployment	3.28	2.05, 5.24	<0.001*
Obesity	0.50	0.20, 1.27	0.147
Hypertension	1.28	0.68, 2.44	0.444
Customary hot birth practice	1.24	0.80, 1.93	0.344
Customary salt-enriched pap	1.20	0.74, 1.94	0.451
Pre-eclampsi	9.01	2.18, 37.75	0.002*
Hausa-Fulani ethnicity	1.11	0.67, 1.84	0.698
Twin pregnancy	0.55	0.32, 0.96	0.034*
Underweight	13.43	4.17, 43.21	<0.001*

**P*-vlaue is statistically significant.

within 3–9 months, making it the largest ever PPCM study in Africa and one of the largest in the world. The incidence of PPCM, clinical profiles of the patients, and factors associated with the disease in Nigeria were described.

The incidence of PPCM in the highest recruiting centre in the city of Kano was (1:96 live births) similar to the rate in Zaria (1:104), both in the North and West, but 14 times higher than what was obtained in the South–South zone (1:1350) and 28 times higher than the incidence in the eastern part of the North–Central zone.[6] Thus, 92.4% of the patients were recruited from the northern regions, predominantly from the North–West zone (72.9%), which is mainly inhabited by the Hausa–Fulani ethnic group. The incidence in Kano and Zaria were similar to the 1:102 live births previously reported from another North–Western Nigerian City of Sokoto, while the 1:1350 and 1:2700 live births recorded in the South–South and North–Central zones respectively were comparable with the rates reported from South Africa (1:1000 live births) and Burkina Faso (1:3,800 live births).[2,4,5]

Our study has described the clinical profile of PPCM patients in Nigeria. We showed that one-thirds of the patients had mild HF symptoms and a similar proportion had moderate–severe symptoms at presentation, but comorbid conditions were uncommon. Of these, 7.4% had pneumonia, which was the most frequent, and 6.4% had intracardiac thrombus at enrolment while 2.2% presented with a stroke. In a smaller sample of 11 admitted PPCM inpatients, we previously reported that six had mural thrombi and four of them presented with a stroke.[13] Ntusi *et al*. also reported that in a cohort of 30 PPCM patients in South Africa, five had intracardiac thrombus, and two had stroke at presentation.[14] PPCM has thus emerged as an important cause of cardio-embolic events in young women.

In this study, three sociodemographic variables (lack of formal education, unemployment status, and underweight) and pre-eclampsia emerged as the independent risk factors. Underweight and pre-eclampsia had the strongest association with PPCM, increasing its odds by 12- and 10-fold, respectively. Pre-eclampsia has been strongly associated with PPCM, with a prevalence that is more than four times the rate expected in the general population.[15] This observation is irrespective of race or geography and suggests that PPCM and pre-eclampsia may share a common underlying pathophysiologic mechanism.[15,16] However, Hausa–Fulani ethnicity (OR: 1.11 [0.67, 1.84]) per se was not a risk factor for PPCM, suggesting that the high incidence of the disease was mainly driven by sociodemographic and perhaps environmental factors.

For reasons that are not yet clear, we got a high frequency of history of twins, including the index and previous pregnancies, among both patients (14.5%) and controls (18.2%) (P = 0.353) in this study. Similarly, a previous study in Kano (Northern Nigeria) found a high prevalence of twin pregnancy of 21.1 per 1000 live births.[17] However, this estimate was only for the index pregnancy and not for all previous pregnancies, as was the case in our study.[17] Our results also showed that RV disease was significantly more common in patients than controls, with significantly higher mean RV basal dimension and prevalence of RVSD (54.9% vs. 4.0%). It is noteworthy that we were among the first to describe RVSD using TAPSE in PPCM, reporting a similar prevalence of 54.6 % and showing that PPCM is indeed a biventricular disease.[18] The treatment pattern of the patients at baseline showed more frequent use of loop diuretics (89.7%), spironolactone (90.4%), and digoxin (71.2%) than the use of some important disease-modifying treatments such as angiotensin converting enzyme inhibitors/angiotensin II receptor blockers (51%) or beta blockers (24.4%). Hydrallazine-isosorbide nitrate use was very low (0.7%), and none was prescribed with bromocriptine, sacubitril–valsartan combination, ivabradine, or any

Table 3 Multivariate binary logistic regression analysis

Risk factor	Odds ratio	95% Confidence intervals	*P*-value
No formal education	2.29	1.22, 4.29	0.010*
Underweight	11.95	3.65, 39.14	<0.001*
Unemployment	2.90	1.71, 4.90	<0.001*
Pre-eclampsia	10.00	2.33, 43.00	0.002*
Twin pregnancy	1.18	0.60, 2.32	0.631
Younger age	4.01	0.51, 31.78	0.189
Multiparity	0.648	0.35, 1.20	0.167

**P*-vlaue is statistically significant.

intracardiac device at baseline. However, 6.7% were on warfarin given that 6.4% of them had intracardiac thrombi. PPCM is a disease with relatively good LV and RV reverse remodelling, which are associated with improved survival, and the disease-modifying drugs are central to these characteristics.[1,3,14,19,20]

Overall, our data suggest that PPCM is predominantly an affliction of the poor and undernourished, with 35.5%, 81%, and 29.6% of the patients having no formal education, being unemployed, and underweight, respectively. In agreement, we had previously reported that 46.2% of PPCM patients (14% of controls, $P < 0.001$) lived in rural areas with poor social amenities.[8] Isezuo *et al*. also reported that 93.8% of PPCM patients in Sokoto were in the lower socioeconomic class.[2] Similarly, Davidson and Parry observed four decades ago in Zaria that significantly more PPCF than other patients lived in rural areas with poorly kept homes, and only 4% had formal education.[21] In a large study of 91 724 consecutively recruited healthy pregnant women in 42 tertiary level hospitals in Nigeria, Adamu *et al*. found an incidence of pre-eclampsia of 4 cases per 100 live births and prevalence of unemployment of 51.3% and of formal education of 30.8%.[22] Therefore, the socioeconomic profile of PPCM patients is relatively worse than that of average healthy pregnant women in Northern Nigeria. Socioeconomic deprivation is a powerful independent predictor of HF development and adverse outcomes in general.[23] However, the precise mechanisms accounting for this risk remain elusive.

Peripartum cardiomyopathy is most likely the endpoint of numerous different pathophysiological processes and 'chains of complex events', which may or may not be modifiable. The numerous processes leading to PPCM could involve socioeconomic factors leading to selenium deficiency and other nutritional factors, deleterious effects of abnormal prolactin fragment, and genetic susceptibility.[1,6–8,24] In a sub-study of the Investigations of Pregnancy-Associated Cardiomyopathy study, the guanine nucleotidebinding proteins β-3 subunit (GNB3) TT genotype was shown to be more prevalent in Black women with PPCM and associated with poorer outcomes.[24] We recently reported that selenium deficiency was evident in 76.9% of PPCM patients and related to rural residency (OR = 2.773). The selenium deficiency theory of PPCM is being further explored by the PEACE Registry and will hopefully be reported in the last quarter of 2019 (ClinicalTrials.gov Identifier: NCT03081949).[9] However, the assessments for the GNB3 TT genotype and other potential biomarkers are beyond the scope of our work at present but could be explored in our future studies.

The earliest studies of postpartum cardiac failure in northern Nigeria implicated certain local Hausa–Fulani customary birth practices in the aetiopathogenesis of a form of high-output HF, PPCF.[6,25] Davidson et al reported 45 years ago that only 1% of Hausa PPCF patients did not take the postpartum hot baths, 3% did not use the hot beds, and 6% took no 'Kunun Kanwa' at all. They concluded that 'the postpartum customs of Hausa women in Zaria were important in the pathogenesis of PPCF, although they may not be wholly responsible for the syndrome, to which the Hausa people seem to be particularly at risk'.[6] Our results (and previous study) have now shown that although PPCM is still very common, the custom of using the 'hot beds' has been abandoned, while the 'Wankan Jego' and 'Kunun Kanwa' are now going out of fashion, only being practiced by 49.8% of patients (and 44.4% of controls, $P = 0.371$) and 33.3% of patients (and 29.3% of controls, $P = 0.475$) respectively, and they were not associated with PPCM.[8] We therefore recommend that the significance of these customary birth practices in the pathogenesis of PPCM in Nigeria be downplayed.[8]

It is unlikely that PPCM is related to maternal age in Nigeria because the prevalence of age below 20 years in our study (7.1%) did not achieve statistical significance as a risk factor ($P = 0.189$) in multivariate analysis and was less than what was found (17.5%) among 91 724 consecutively recruited healthy pregnant women in 42 tertiary level hospitals in Nigeria.[22]

Limitations

First, we acknowledge that the South–East geographical zone was under-represented in the registry mainly because participation by investigators was voluntary. Second, PEACE Registry was not primarily planned as a biomarker or genetic study; hence, some of the desirable biomarkers such as B-type natriuretic peptide were not measured. However, serum selenium and glutathione peroxidase will be measured in one of the registry's sub-study (ClinicalTrials.gov Identifier: NCT03081949). Third, because of the unfortunate paucity of funding, we could not recruit equal number of controls as patients, although we tried to maintain a regional patient: control ratio of 4:1 to adjust for the potential effects of ethnicity on the results.

Conclusions

In Nigeria, the burden of PPCM seems to be greater in the North–West zone where an incidence as high as 1:96 live births was documented. PPCM was predicted by three sociodemographic factors and history of pre-eclampsia. Thus, it seems that in Nigeria, the disease is predominantly an affliction of the poor and undernourished. This should be considered in its control at population level, but more specific, yet to be described risk factors are likely relevant in its pathogenesis and varied distribution in Nigeria.

Postpartum customary birth practices and Hausa–Fulani ethnicity were not associated with PPCM in Nigeria.

Conflict of interest

None declared.

Acknowledgements

The authors acknowledge and are grateful to Professors Salim Yusuf, Karen Sliwa, and Abdulrazaq Habib for their comments and suggestions on this manuscript.

Funding

This work was supported by Dantata Group of Companies, Nigeria; Ammasco International Ltd, Kano, Nigeria; and Fortune Oil Mills Nigeria Ltd, Kano, Nigeria.

References

1. Sliwa K, Hilfiker-Kleiner D, Petrie MC, Mebazaa A, Pieske B, Buchmann E, Regitz-Zagrosek V, Schaufelberger M, Tavazzi L, van Veldhuisen DJ, Watkins H, Shah AJ, Seferovic PM, Elkayam U, Pankuweit S, Papp Z, Mouquet F, McMurray JJ. Heart Failure Association of the European Society of Cardiology Working Group on Peripartum Cardiomyopathy. Current state of knowledge on aetiology, diagnosis, management, and therapy of peripartum cardiomyopathy: a position statement from the Heart Failure Association of the European Society of Cardiology Working Group on peripartum cardiomyopathy. *Eur J Heart Fail* 2010; **12**: 767–778.
2. Isezuo SA, Abubakar SA. Epidemiologic profile of peripartum cardiomyopathy in a tertiary care hospital. *Ethn Dis* 2007; **17**: 228–333.
3. Karaye KM, Lindmark K, Henein MY. One-year survival in Nigerians with peripartum cardiomyopathy. *Heart Views* 2016; **17**: 55–61.
4. Desai D, Moodley J, Naidoo D. Peripartum cardiomyopathy: experiences at King Edward VIII Hospital, Durban, South Africa and a review of the literature. *Trop Doct* 1995; **25**: 118–123.
5. Yaméogo NV, Samadoulougou AK, Kagambèga LJ, Kologo KJ, Millogo GRC, Thiam A, Guenancia C, Zansonré P. Maternal and fetal prognosis of subsequent pregnancy in black African women with peripartum cardiomyopathy. *BMC Cardiovasc Disord* 2018; **18**: 119.
6. Davidson NM, Trevitt L, Parry EH. Perpartum cardiac failure. An explanation the observed geographic distribution in Nigeria. *Bull World Health Organ* 1974; **51**: 203–208.
7. Cenac A, Simonoff M, Moretto P, Djibo A. A low plasma selenium is a risk factor for peripartum cardiomyopathy. A comparative study in Sahelian Africa. *Int J Cardiol* 1992; **36**: 57–59.
8. Karaye KM, Yahaya IA, Lindmark K, Henein MY. Serum selenium and ceruloplasmin in Nigerians with peripartum cardiomyopathy. *Int J Mol Sci* 2015; **16**: 7644–7654.
9. Karaye KM, Mohammed IY, Ogah OS, Basil N, Okeahialam BN. Rationale and design for the peripartum cardiomyopathy in Nigeria (PEACE) Registry. *International Cardiovascular Forum Journal* 2017; **12**: 12–17.
10. World Medical Association Declaration of Helsinki. Ethical principles for medical research involving human subjects. *J Postgrad Med* 2002; **48**: 206–208.
11. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, Flachskampf FA, Foster E, Goldstein SA, Kuznetsova T, Lancellotti P, Muraru D, Picard MH, Rietzschel ER, Rudski L, Spencer KT, Tsang W, Voigt JU. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Am Soc Echocardiogr* 2015; **28**: 1–39.
12. Kadish AH, Buxton AE, Kennedy HL, Knight BP, Mason JW, Schuger CD, Tracy CM, Boone AW, Elnicki M, Hirshfeld JW Jr, Lorell BH, Rodgers GP, Tracy CM, Weitz HH. ACC/AHA clinical competence statement on electrocardiography and ambulatory electrocardiography: a report of the American College of Cardiology/American Heart Association/American College of Physicians – American Society of Internal Medicine Task Force on Clinical Competence (ACC/AHA Committee to develop a clinical competence statement on electrocardiography and ambulatory electrocardiography). *J Am Coll Cardiol* 2001; **38**: 2091–2100.
13. Karaye KM, Sani MU. Factors associated with poor prognosis among patients admitted with heart failure in a Nigerian tertiary medical centre: a cross-sectional study. *BMC Cardiovasc Disord* 2008; **8**: 16.
14. Ntusi NBA, Badri M, Gumedze F, Sliwa K, Mayosi BM. Pregnancy-associated heart failure: A comparison of clinical presentation and outcome between hypertensive heart failure of pregnancy and idiopathic peripartum cardiomyopathy. *PLoS ONE* 2015; **10**: e0133466.
15. Bello N, Rendon IS, Arany Z. The relationship between pre-eclampsia and peripartum cardiomyopathy: a systematic review and meta-analysis. *J Am Coll Cardiol* 2013; **62**: 1715–1723.
16. Patten IS, Rana S, Shahul S, Rowe GC, Jang C, Liu L, Hacker MR, Rhee JS, Mitchell J, Mahmood F, Hess P, Farrell C, Koulisis N, Khankin EV, Burke SD, Tudorache I, Bauersachs J, del Monte F, Hilfiker-Kleiner D, Karumanchi SA, Arany Z. Cardiac angiogenic imbalance leads to peripartum cardiomyopathy. *Nature* 2012; **485**: 333–338.
17. Galadanci HS, Ashimi AO, Iliyasu Z. Prevalence and outcome of multiple pregnancies in Aminu Kano Teaching Hospital. *Niger J Basic Clin Sci* 2004; **1**: 18–21.
18. Karaye KM. Right ventricular systolic function in peripartum and dilated cardiomyopathies. *Eur J Echocardiogr* 2011; **12**: 372–374.
19. Kamiya CA, Kitakaze M, Ishibashi-Ueda H, Nakatani S, Murohara T, Tomoike H, Ikeda T. Different characteristics of peripartum cardiomyopathy between patients complicated with and without hypertensive disorders. Results from the Japanese Nationwide survey of peripartum cardiomyopathy. *Circ J* 2011; **75**: 1975–1981.
20. Karaye KM, Lindmark K, Henein MY. Right ventricular systolic dysfunction and remodelling in Nigerians with peripartum cardiomyopathy: a longitudinal study. *BMC Cardiovasc Disord* 2016; **16**: 27.
21. Davidson NM, Parry EH. Peri-partum cardiac failure. *Q J Med* 1978; **47**: 431–461.
22. Adamu AN, Okusanya BO, Tukur J, Ashimi AO, Oguntayo OA, Tunau KA, Ekele BA, Oladapo OT. Maternal near-miss and death among women with

hypertensive disorders in pregnancy: a secondary analysis of the Nigeria Near-miss and Maternal Death Survey. *BJOG* 2019; **126**: 12–18.
23. Dokainish H, Teo K, Zhut J, Roy A, AlHabib KF, ElSayed A, Palileo-Villaneuva L, Lopez-Jaramillo P, Karaye K, Yusoff K, Orlandini A, Sliwa K, Mondo C, Lanas F, Prabhakaran D, Badr A, Elmaghawry M, Damasceno A, Tibazarwa K, Belley-Cote E, Balasubramanian K, Yacoub MH, Huffman MD, Harkness K, Grinvalds A, McKelvie R, Yusuf S, On behalf of the INTER-CHF Investigators. Heart Failure in Africa, Asia, the Middle East and South America: The INTER-CHF study. *Int J Cardiol* 2016; **204**: 133–141.
24. Sheppard R, Hsich E, Damp J, Elkayam U, Kealey A, Ramani G, Zucker M, Alexis JD, Horne BD, Hanley-Yanez K, Pisarcik J, Halder I, Fett JD, McNamara DM, IPAC Investigators. GNB3 C825T polymorphism and myocardial recovery in peripartum cardiomyopathy: results of the multicenter investigations of pregnancy-associated cardiomyopathy study. *Circ Heart Fail* 2016; **9**: e002683.
25. Fillmore SJ, Parry EH. The evolution of peripartal heart failure in Zaria. *Circulation* 1977; **56**: 1058–1061.

Appendix 1. Additional list of PEACE Registry investigators by centres

Aminu Kano Teaching Hospital, Kano: Karaye KM, Ishaq NA, Mohammed IY, Sanni B, Mohammed BL, Abubakar HA, Tukur J. *Murtala Mohammed Specialist Hospital, Kano*: Sa'idu H, Kabir A, Armayau I. *Mohammed Abdullahi Wase Specialist Hospital, Kano*: Balarabe SA. *Ahmadu Bello University Teaching Hospital Zaria*: Isa MS, Awwal MA. *Federal Medical Centre Abeokuta*: Olunuga T, Adebayo S, Durodola A, Adesina J, Ajani A, Oladeji O. *University of Uyo Teaching Hospital*: Shogade TT, Essien IO, Umoh IO, Inyang-Etoh EC, Andy JJ. *University of Benin Teaching Hospital*: Josephs VA, Obasohan AO, Ogbemudia A, Aghimien OD, Iyawe L, Aghimien EC. *Usman Dan-Fodio University Teaching Hospital Sokoto*: Umar H, Zagga UM, Isezuo S. *General Ahmadi Kurfi Specialist Hospital & Federal Medical Centre, Katsina*: Shehu MN, Sadeeq I. *Dalhatu Araf Specialist Hospital, Lafia*: Oboirien I, Patrick A. *University of Nigeria Teaching Hospital, Enugu*: Njoku P, Onwubere BJC.