

Incidence of Peripartum Cardiomyopathy and Maternal Outcomes: A Five-Year Review of Patients Treated at A Tertiary Teaching Hospital in Tanzania

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Abstract**Background**

Peripartum cardiomyopathy (PPCM) is a rare heart disease which affects previously healthy women toward the end of pregnancy or within five months following delivery. The incidence of PPCM shows wide regional variations and has been rising, probably due to increased risk factors and the incidence in Tanzania is unclear. The aim of this study was to determine the temporal trends in incidence and maternal outcomes among PPCM patients attended at the largest tertiary hospital in Tanzania -Muhimbili National Hospital.

Methods

A descriptive retrospective case review study was done at Muhimbili National Hospital (MNH). A five-year review (July 2013-June 2018) of 129 case notes from the patients with PPCM was conducted. Trends of incidence of PPCM and maternal outcomes (maternal death, pulmonary edema, thromboembolism and stroke, cardiogenic shock and length of hospital stay) following PPCM were analysed. The Pearson's coefficient test was used to determine the temporal trends in incidence of Peripartum cardiomyopathy over the study period. P-value of less than 0.05 was considered statistically significant.

Result

The overall incidence of Peripartum cardiomyopathy for five years was 3.0 per 1000 live births (1 in 333). There was observed increase in incidence rate from 1.4 in the first year to 4.8 in the fifth year of study which was statistically significant with P trend <0.0001. The most common complications observed in women with Peripartum cardiomyopathy in the overall cohort was pulmonary edema 31%, maternal death 7.8%, thromboembolism/stroke 4.7 % and cardiogenic shock 4.7 %. The average hospital stay was 9 days.

Conclusion

There was an overall increase in the incidence of Postpartum cardiomyopathy at Muhimbili National Hospital in the five-year period. The most common complications were pulmonary edema and maternal death.

Key words: *Incidence of peripartum cardiomyopathy, Maternal outcome.*

Background

Peripartum cardiomyopathy (PPCM) according to the Working Group on PPCM of the Heart Failure Association (HFA) of the European Society of Cardiology (ESC) is defined as the development of cardiomyopathy during the last month of pregnancy or within five months of delivery in the absence of preexisting heart disease, no identifiable cause of heart disease, with evidence of left ventricular systolic dysfunction (Ejection fraction less than 45%) demonstrated by echocardiography (1). PPCM is not uncommon condition with its incidence varying worldwide. In the United States it is estimated to be on the increase from 1 in 4,000 pregnancies to 1:1000 from national inpatient database (2,3). Africans and African American women have an increased risk of developing PPCM such as in Haiti where it is 1 in 400 deliveries (4) while in Nigeria it is 1 in 100 pregnancies (1,5) as compared to Caucasians in Denmark and Germany 1:1500 and 1 in 15,000 respectively (6,7). There is paucity of data in Tanzania on incidence as in Eastern and Southern Africa with only South Africa reporting incidence at 1: 1000 in 2005 (8).

The etiology of PPCM remains unknown. Different mechanisms have been proposed including viral myocarditis, abnormal immune response, hemodynamic response to pregnancy, hormonal abnormalities, malnutrition and genetic mutations. Also, elevated plasma levels of tumor necrosis factor- α , Fas-Apo-1, interleukin-6, and C-reactive protein, suggest an inflammatory component to development of the disease have been demonstrated (1,9,10). In review done by Sliwa *et al* on epidemiology and aetiology of PPCM in Africa similar potential mechanisms on developing heart failure and PPCM were demonstrated (11).

The several risk factors that predispose women to PPCM are increased maternal age, multiparity, preeclampsia, gestational hypertension, African descent and multiple gestations (12–14). Some other studies done in Haiti and South Africa have not shown advanced age influence development of PPCM (4,8). It is not clear if this phenomenon applies to other countries such as Tanzania. Low social economic status, poor nutritional status and geographical distributions especially in tropical and subtropical climates could explain the difference in terms of advanced age and increased parity (8,15).

PPCM is associated with adverse maternal outcomes. These include cardiogenic shock, arrhythmias, thromboembolism and stroke, cardiopulmonary arrest, pulmonary edema, pericardial effusion, need for intensive care and death (16). Higher rates of stillbirth, cesarean section, and longer length of hospital stay are other maternal outcomes associated with PPCM (2,18). Adverse maternal outcomes including failure to recover ventricular function and mortality after treatment have been reported to affect American women of African descent as compared to Caucasian women (19,20). The disparity on the outcomes is not clear, it could

be due to genetic or socio-economic issues. It is unclear if same pattern could be observed in Tanzania women.

It is therefore important to study the trend on incidence and outcome of PPCM in Tanzania. The aim of this study was to determine the trend and outcome of women who had PPCM in the largest tertiary hospital in Tanzania.

Materials and methods

This was a retrospective case review study from August to November 2018 among patients admitted with PPCM at Muhimbili National Hospital (MNH), the largest referral hospital in Tanzania and teaching hospital for Muhimbili University of Health and Allied Sciences (MUHAS). It is located in Dar es Salaam, a commercial city in Tanzania with a population of 5.4 million. The hospital receives referral patients from the three municipal referral hospitals in Dar es Salaam and from nearby Coast regional hospitals, predominantly but also receive referred patients from all regions of the country for specialized care. The hospital's maternity block houses five antenatal wards where women with any maternal complications are admitted for care. Additionally, there is one labour ward for obstetric patients admitted in labour.

Within MNH there is a specialized cardiac institute, Jakaya Kikwete Cardiac Institute (JKCI) with expertise on managing cardiac patients. All patients with heart failure admitted at MNH and suspected to have PPCM are reviewed by cardiologists from JKCI and evaluated with Echocardiogram and offered further management.

Study population

It comprised all patients admitted in maternity blocks at MNH during the study period from July 2013 to June 2018.

Study Sample

Patients admitted in maternity wards at MNH with diagnosis of Peripartum Cardiomyopathy. Inclusion criteria: i). All patients who developed heart failure in the last month of pregnancy or within 5 weeks postpartum attended at MNH (5 weeks postpartum was used because majority of women do not return after five weeks). ii). No other cause of heart failure with reduced EF can be found. iii). Patients with echocardiographic findings of LVEF < 45 %. Patients with pre-existing heart disease like valvular heart disease, congenital heart conditions were excluded from the study.

Data collection procedure and variables

All patients file numbers (hospital identification numbers) with admission or discharge diagnosis of PPCM during the study period were noted down from the admission books and hospital discharge database. The patient files were then traced from the medical records department. Files of the patients who met the inclusion criteria were included for review using a semi structured checklist. Data collected was reviewed for completeness before being entered into an electronic version software for analysis (SPSS version 23)

The variables considered included; age, marital status, education level, occupation; obstetric characteristics; gestational age at time of admission, parity, presence or absence of preeclampsia, multiple gestation; echocardiographic features; ejection fraction and length of hospital stay as documented in the case notes. Maternal Adverse events included; maternal death, presence of pulmonary edema, thromboembolism, cardiogenic shock, stroke.

Data was entered and analyzed with Statistical Package for Social Sciences (SPSS Inc, Chicago, IL USA) version 23. Categorical variables were summarized using frequency and proportion. Continuous variables were summarized using means and standard deviation. The Chi-square for trends was used to determine the temporal trends in incidence of PPCM over the study period. P-value of less than 0.05 in the years reviewed was considered statistically significant.

Ethical considerations

The ethical approval was obtained from Senate Research and Publication Committee of Muhimbili University of Health and Allied Sciences (MUHAS) and permission to conduct the study was obtained from Executive Directors of MNH and JKCI. No consent was needed because data was obtained retrospectively. A request for a waiver of informed consent was made by the MUHAS Institutional Review Board (IRB). The researchers kept the names and information under lock and key confidentiality.

Results

During the study period there were a total of 67,285 admissions, 42,985 live births and 339 women aged 14 to 50 years had a clinical diagnosis of PPCM whereby only 129 patients met the criteria of PPCM as per our diagnosis criteria. These data provided an overall PPCM incidence rate of 3.0 per 1000 live birth (Figure 1, Table 1).

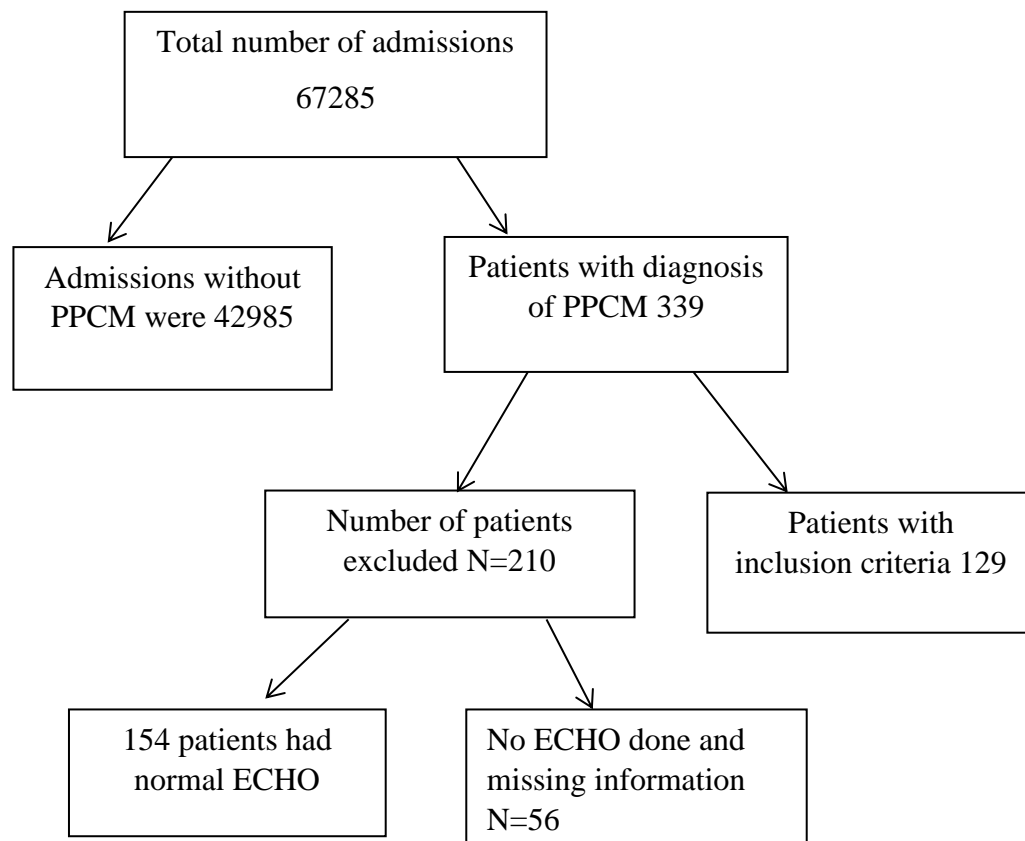


Figure1. Flow chart showing number of admissions, live birth and cases between July 2013 to June 2018

Table 1: Baseline demographic characteristics of patients with PPCM

Variable	Frequency n=129	Percentage
Age		
<20	12	9.3
20-34	84	65.1
>34	33	25.6
Parity		
Primigravida	5	3.9
<Para 5	110	85.3
≥Para 5	14	10.8
Marital Status		
Single	6	4.7
Living together	123	95.3
Education		
No formal education	1	0.8
Primary	108	83.7
Secondary	17	13.2
College	3	2.3

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Occupation		
Employed	26	20.2
Not employed	103	79.8
Nature of Referral		
Not referred	12	9.3
Referred from other H. F.	117	90.7

Mean age of overall cohort was 28.7 ± 6.7 years with 65.1% of women in the age group of 20 to 34 years being more common. Majority had parity of less than five. Most of the patients 90.7% were referred from other health facilities (Table 2).

Table 2: Temporal trends in PPCM incidence rates per 1000

	N=129	Overall incidence	Jul2013- Jun2014	Jul2014- Jun 2015	Jul2015- Jun 2016	Jul2016- Jun 2017	Jul2017- Jun2018	P Trend
Overall	129	3.0	1.4	1.9	2.9	3.7	4.8	<0.0001
Age, mean (SD)								
<20	12	7.2	2.1	4.4	6.7	8.4	9.5	<0.0001
20 to 34	84	2.4	1.0	1.4	3.1	3.1	3.9	
>34	33	5.0	3.1	3.7	1.5	4.5	9.7	
Pregnancy associated HTN								
Yes	53	38.0	16.4	34.0	51.9	63.1	35.6	0.3049
No	76	1.8	0.8	1.0	1.7	2.2	3.5	
Multiple pregnancy								
Yes	26	46.7	31.5	48.8	80.0	61.0	36.6	0.585
No	103	2.4	0.9	1.5	2.3	3.0	4.4	

The overall cohort incidence rate was 3.0 per 1,000 live births. There was increased incidence rate from 1.4 per 1,000 live births in (July 2013 – June 2014) to 4.8 per 1,000 live birth (July 2017 – June 2018) (Figure 2), which is statistically significant with P trend <0.0001.

Significant (P value <0.0001) increase in trend was also observed in women who were less than 20 years (Figure 3). Women with pregnancy associated hypertension had high incidence rate compared to women without pregnancy associated hypertension and the trend was not significant. Women with multiple pregnancies were also noted to have high incidence rate compared to singleton but the trend was not statistically significant.

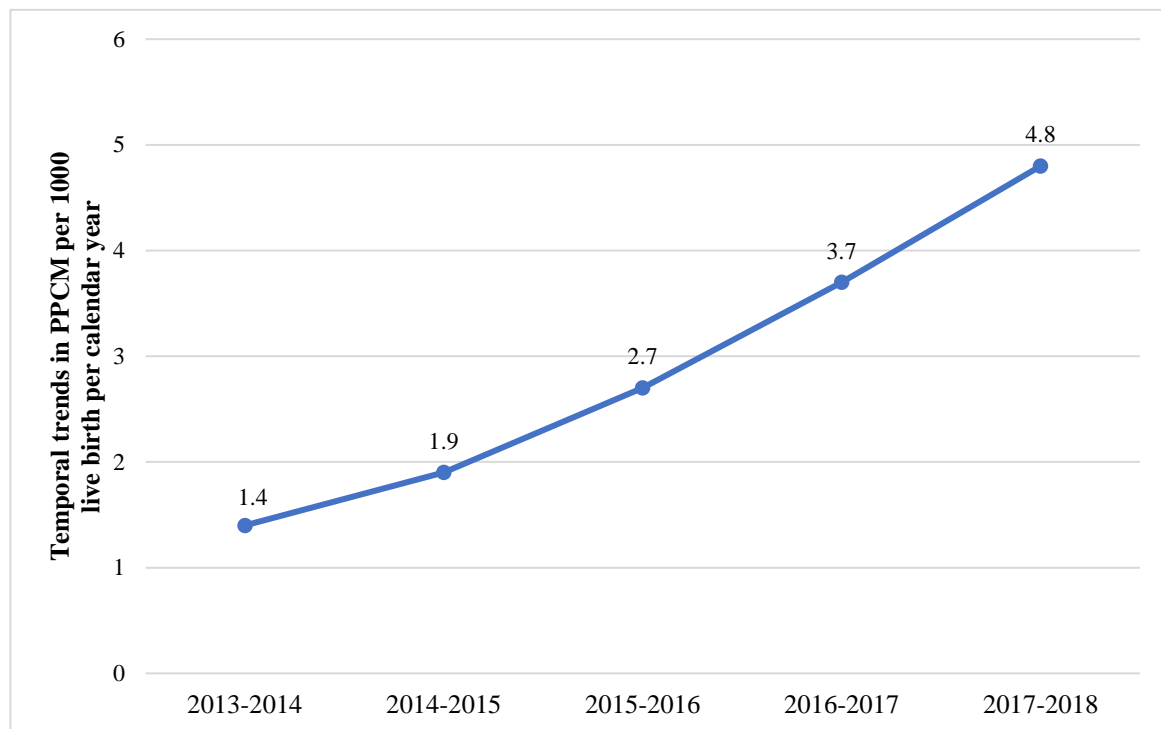


Figure 2. Temporal trends in PPCM per 1000 live birth per calendar year

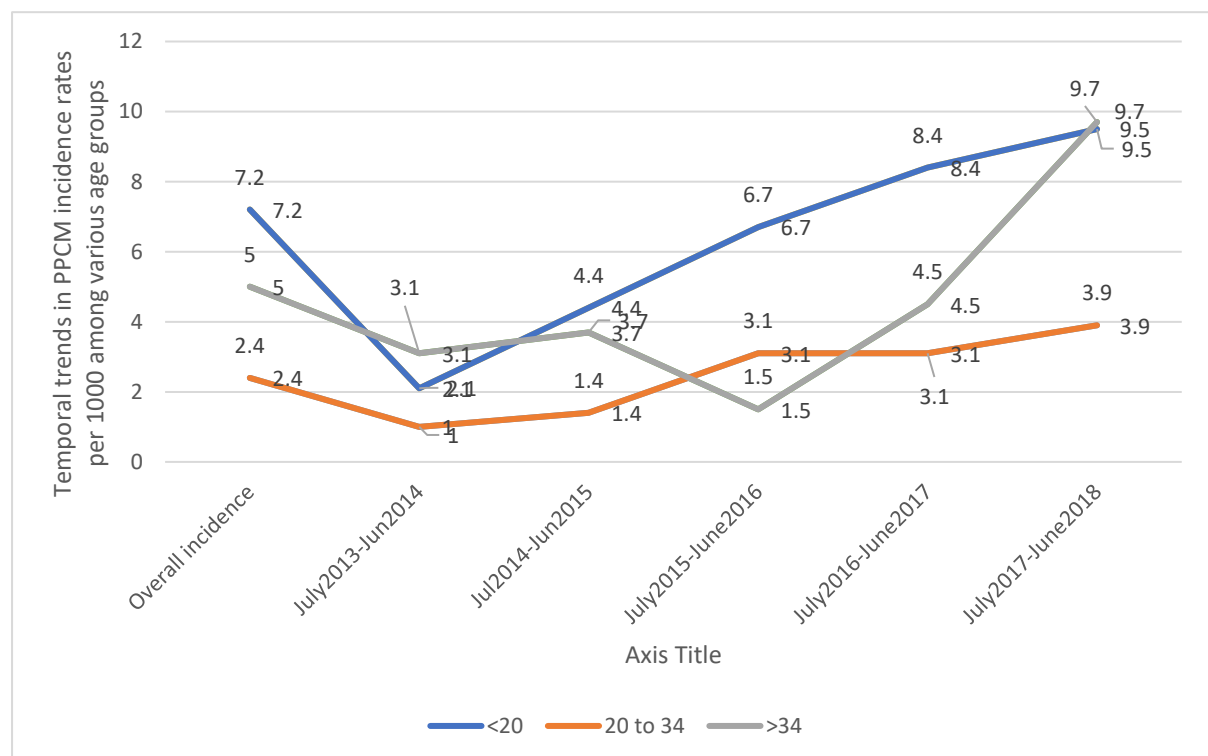


Figure 3. Temporal trends in PPCM incidence rates per 1000 among various age groups

Table 3: Primary outcomes of PPCM from July 2013 to June 2018

Outcome	Overall	Jul2013- Jun 2014	Jul2014- Jun 2015	Jul2015- Jun 2016	Jul2016- Jun 2017	Jul2017- Jun 2018	P value
Death							
Yes	10(7.8%)	0(0.0%)	0(0%)	1(3.8%)	4(12.5%)	5(11.6%)	0.046
No	119 (92.2%)	11(100%)	17 (100%)	25 (96.2%)	28 (87.5%)	38 (88.4%)	
Pulmonary edema							
Yes	40(31%)	3 (27.3%)	5 (29.4%)	6 (23.1%)	6(18.8%)	20 (47.5%)	0.124
No	89(69%)	8(72.7%)	12(70.6%)	20(76.9%)	26(81.2%)	23(53.3%)	
Cardiogenic shock							
Yes	6(4.7%)	0(0%)	0(0%)	1(3.8%)	1(3.1%)	4(9.3%)	0.086
No	123(95.3%)	11(100%)	17 (100%)	25(96.2%)	31(96.9%)	39(90.7%)	
Thromboembolism and stroke							
Yes	6(4.7%)	1(9.1%)	1(5.9%)	1(3.8%)	2(6.3%)	1(2.3%)	0.390
No	123(95.3%)	10(90.9%)	16(94.1%)	25(96.2%)	30(93.7%)	42(97.7%)	
Length of hospital stay							
<5 Days	27(20.9%)	3(27.3%)	2(11.8%)	6(23.1%)	5(15.6%)	11(25.6%)	0.681
>5 Days	102(79.1%)	8(72.7%)	15(88.2%)	20(76.9%)	27(84.4%)	32(74.4%)	

Maternal major adverse events (MAE) included death, thromboembolism/ stroke, PE, cardiogenic shock and length of hospital say. The number of maternal deaths due to PPCM increased during the study period with statistically significant trend. There was no significant trend in other adverse outcomes (Table 3).

Discussion

In this hospital-based study, we report the overall incidence as well as temporal trends in incidence and outcomes of PPCM using a review of case notes of patients at MNH. The overall PPCM incidence rate over the five years period was 3.0 per 1000 live birth (1 in 333 live births) with increased significant trend over the study period. Overall cohort maternal major adverse events occurred in nearly 50% of patients with PPCM. The most common complication observed in women with PPCM in overall cohort was pulmonary edema (31%) followed by in hospital mortality which occurred in 7.8%.

The overall incidence of peripartum cardiomyopathy observed in our study aligns with findings from other research, which report rates between 1 in 300 to 1 in 4000 deliveries(3,17,18,21). It is possible the actual incidence of PPCM has increased over the time may be related to

increase in established risk factors for PPCM. But also, improvement in the clinical diagnostic capability of the institution (MNH), with the establishment of a designated maternity ICU where timely diagnostic evaluations are being done. These factors could have influenced our study results through increased detection of PPCM cases, potentially capturing instances that might have been missed in the past. In this study 41% of study cohort had hypertensive disorder in pregnancy. Preeclampsia has antiangiogenic properties and in later gestation placenta secretes substances such as endothelial growth factor inhibitors thus may explain why PPCM is common in preeclampsia and multiple pregnancy (22).

Majority, 90.7% of the study population were referred patients from other health facilities to MNH for further management. MNH has a specialized cardiac institute (JKCI) which is fully equipped with necessary human resource and equipment for diagnosis and management of patients with heart conditions. Thus, availability of such services resulted in increase in the number of patients referred to MNH.

This study is consistent with the findings in Haiti where the incidence is 1 in 300 live births (3) and lower than Zari-Nigeria where the incidence was 1 in 100 live births (23). Furthermore it differs very much from similar studies done in SA where the incidence rate is 1 in 1000 live birth, in USA where the incidence rate is nearly 1 in 4000 live birth and in Japan is 1 in 20000 (17,24). This highlights the massive addition in demand to health care this condition brings to the already overwhelmingly high maternal morbidities in existence.

The temporal increase in PPCM incidence rate was seen in all women aged > 20 years with a mean age at presentation being 28.7 ± 6.7 years. A similar pattern was observed in Asia, USA and Europe (25). Particular attention should be taken to this age group which is compounded by increased risk for hypertensive disorders of pregnancy, a high index of suspicion and diagnostic acumen is needed to detect early and manage it (26). Furthermore, the increased burden of PPCM can have effect on subsequent pregnancies. Women with PPCM and whose Ejection Fraction (EF) do not return to normal are at higher risk of recurrence of PPCM in subsequent pregnancy, developing heart failure, worsening clinical conditions, increasing the need for heart transplant and even death (27,28). Counselling and regular monitoring of the heart function by echocardiogram is important before the woman decides to get pregnant again.

In this study maternal major adverse events (MAE) occurred in almost half of the women with PPCM. The proportion of MAE doubled from the first year to the fifth year. These findings are similar to studies done in Asia (29), however higher compared with other studies done in the USA and Europe (13). This difference observed could be due to improved medical diagnostic ability at MNH resulting in improved survival of these patients to allow revelation other MAEs.

The most common complication in women with PPCM is pulmonary edema. The proportion of patients with pulmonary edema in the fifth year increased by almost twice compared to those in the first year. Comparable findings were reflected in Singapore and India (30,31). Other adverse outcomes of interest which occurred were thromboembolism and stroke documented in 4.7% of all patients. This brings about the need to recognize and ensure multidisciplinary team management of these patients and management of the expected complications.

In patient mortality in overall cohort in women with PPCM was 7.8% and there was observed 11.6% increase over the 5 years study period (29). This elevated mortality rate could be attributed to the fact that the majority of our patients were referrals, often arriving at our tertiary hospital in critical condition. As a referral center, we tend to receive patients with more severe cases of PPCM. The findings of this study is nearly similar to study done in USA (17) but lower than those done in Asian countries and in Nigeria (18,23) reflecting a need for maternity units to be equipped properly and be able to manage these complications..

Study Limitations

This study was limited to patients who were admitted during pregnancy and within five weeks and PPCM can develop up to five months post-delivery. Outcomes of the patients were studied only during hospitalization and the long-term survival of PPCM is yet to be determined. Being retrospective study using administrative data some files had missing information and were excluded.

It is possible we may have underestimated the incidence rate as all patients who had no ECHO done were excluded from the study and some patients had ECHO done after starting anti-failure which might lead to improvement of cardiac functions. However, the findings are valid and highlight a highly fatal maternal condition that requires integrated effort.

Conclusion

This study demonstrates that the overall rate of peripartum cardiomyopathy has increased during the last five years. The most common complications were pulmonary edema and maternal death. Since symptoms of PPCM are similar to common symptoms of late pregnancy high index of suspicious is needed especially to those who have risk factors. Careful assessment of risk factors in pregnant women could help early diagnosis and treatment which in turn will prevent maternal major adverse events. Women presenting with heart failure during peripartum period should be evaluated for PPCM using ECHO to confirm diagnosis.

Abbreviations

AIDS	Acquired Immunodeficiency Syndrome
HF	Heart Failure
HIV	Human Immunodeficiency Virus
MAE	Maternal Major Adverse Events
MNH	Muhimbili National Hospital
PPCM	Peripartum Cardiomyopathy
TE	Thromboembolism
EF	Ejection Fraction
JKCI	Jakaya Kikwete Cardiac Institute
LVEF	Left ventricular ejection fraction

Declarations

Availability of data and materials

The dataset used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

The ethical approval for this study was obtained from Senate Research and Publication Committee the Institutional Review Board of the Muhimbili University of Health and Allied Sciences (MUHAS). Permission to conduct the study was granted by the Executive Directors of the Muhimbili National Hospital and Jakaya Kikwete Heart Institute.

Consent for Publication

Not applicable

Competing interests

The authors have no competing interest to declare.

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Authors' Contribution

ST, FA, PW, BB, AK, CK designed the study. ST and FA collected the data. ST and FA conducted data analysis. ST wrote the first draft of the manuscript. All authors read the draft and contributed to the interpretation of the results. All authors read and approved the final manuscript for submission.

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