FREQUENCY OF RESPONSIBLE FACTORS FOR PERIPARTUM CARDIOMYOPATHY IN PATIENT PRESENTING TO GYNEA DEPARTMENT READING HOSPITAL PESHAWAR

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ABSTRACT
Background: When there is no other known cause of heart failure, peripartum cardiomyopathy (PPCM) is an idiopathic cardiomyopathy that manifests as heart failure due to left ventricular (LV) systolic malfunction around the end of pregnancy or in the months after delivery.
Objective: To determine the frequency of responsible factors for peripartum cardiomyopathy in patient presenting to Gynae department of Lady Reading Hospital, Peshawar.
Material and Methods: This descriptive cross-sectional study was conducted in the Department of Obstetrics and Gynecology at Lady Reading Hospital, Peshawar, over a duration of six months from January 27, 2020, to July 27, 2020. Clinical examination and routine investigation like echo was performed for the confirmation of PPCM. Echo test was performed in the cardiology department under the supervision of expert cardiologist having at least five years of experience. All the data were analyzed in SPSS version 16.
Results: A total of 247 patients were observed with mean age was 33 years with SD± 12.84. 66% patients had gestational age 37-38 weeks and 34% patients had gestational age 39-40 weeks. 18% patients were primi para and 82% patients were multi para. More over responsible factors for peripartum cardiomyopathy were pregnancy induced hypertension 67(27%), Preeclampsia 109(44%) and Type 2 diabetes mellitus was 30(12%).
Conclusion: Our study concludes that responsible factors for peripartum cardiomyopathy were pregnancy induced hypertension 27%, Preeclampsia 44%, and Type 2 diabetes mellitus was 12%.

Keywords: responsible factors, peripartum cardiomyopathy

INTRODUCTION

Peripartum cardiomyopathy (PPCM) is an idiopathic cardiomyopathy that appears as left ventricular (LV) systolic dysfunction in the latter stages of pregnancy or in the postpartum period when no other cause of heart failure is found[1].

Even though their hearts may not be dilated, patients with PPCM nearly always have ejection fractions (EF) that are less than 45%[1].

The primary symptoms of peripartum cardiomyopathy, such as shortness of breath, fatigue, fluid retention, and excessive weight gain, can often be mistaken for normal discomforts of pregnancy, leading to misse d opportunities for timely diagnosis and treatment[2]. Cardiovascular disease, including peripartum cardiomyopathy, is the leading cause of death among women in California, underscoring the need for increased awareness and proactive[2].

Physiological changes during pregnancy, including cardiovascular, hematological, neurohormonal, and metabolic alterations, can predispose women to adverse cardiac events like myocardial infarction. These changes must be recognized and carefully monitored by a multidisciplinary team to identify and manage any complications that may arise. Furthermore, comorbidities like peripartum depression can pose additional barriers to engagement with healthcare, further complicating the management of peripartum cardiomyopathy [2].

Globally accurate data on the incidence or prevalence of PPCM are not accessible due to the absence of population-based registries. The PPCM rate in the United States is 10.3 (95% CI 10.2 to 10.4) per 10,000 live births, or one in 968 live births, according to Kolte et al. (2014).5. However, from 8.5 per 10,000 live births (1 in 1181 live births) in 2004 to 11.8 per 10,000 live births (1 in 849 live births) in 2011, the PPCM incidence rate increased significantly over the cohort[3].

Factors contributing to the development of peripartum cardiomyopathy may include preexisting medical conditions, such as hypertension, diabetes, or obesity, as well as lifestyle factors like poor diet and physical inactivity. The implementation of current guidelines for cardiovascular risk factor screening and treatment in women, particularly those with a history of adverse pregnancy outcomes, is crucial for early identification and management of these risk factors[2].

The maternal major adverse events and still birth occurred more frequently in patients with PPCM during delivery[4].There is about 15.8% mortality within 1 year of delivery in patients with PPCM[5].This mortality further increase in subsequent pregnancies[3].

The factors associated in which the occurrence of PPCM is more include, advanced maternal age (36.7 incidences in aged 40 to 54 years [95% CI 35.4 to 37.9] per 10 000 live births)[3], African-American race (47.5% of woman are of black race)[3], chronic hypertension (267.5 [95% CI 262.3 to 272.7] per 10 000 live births)[3], preeclampsia(22% of PPCM patients [95% CI: 16% to 28%], 4 times of general populations)[6], multiple gestations (PPCM patient are 9% in twin pregnancy [95% CI: 7% to 11%])[6], pregnancy induced hypertention (22.9% of patient were having PIH)[7], Type 2 diabetes (8.6%)[7]. A recent meta-analysis of 22 studies covering 979 cases of PPCM showed the prevalence of preeclampsia of 22% which is >4 times of the 3% to 5% general population prevalence[6].

Age has a significant correlation with the occurrence of PPCM. While the condition can affect women at any age, in a comparison of women over 40 and under 20, >50% of occurrences occur in women over 30, with an odds ratio of 10. [3]. According to Kolte et al. (2014), black women have accounted for almost 40% of instances in national surveys conducted in the United States. Multigestational status

instances often present with PPCM. The average rate of twin gestations in PPCM cases across 16 studies in the meta-analysis was 9% [6].

Also the PPCM have been reported with in triplet pregnancy[817]. The recurrence of the PPCM in the subsequent pregnancy have been shown to be higher in rate and with increased mortlality[9].

In Pakistan, a study has been showed the higher incidence of PPCM in patients with type 2 diabetes (8.6%) and with pregnancy induced hypertension(22.9%)[7].Some studies do not agree with the all risks factors stated above. For example, in contrast to higher incidence of PPCM in multigestation, PIH and Eclampsia (as above)[7], another study in the US concluded that the incidence of PPCM is higher in single gestation pregnancy (6.2% in multiple gestation and 10.5% in singleton pregnancy) with no effect of pregnancy induced hypertension (10.1 [95% CI 9.5 to 10.6] in PIH and 10.4 [95% CI 10.3 to 10.5] per 10 000 live births in without PIH)[35].However complete data regarding this in other part of the world (including Pakistan) is scanty and should need to be confirm and well evaluated in further studies as different study show difference in risk factors[3,4,9].

This study has been conducted to determine the risk factors of peripartum cardiomyopathy. As no such study has been conducted in our population for the last five years so this study will provide us the latest and updated information regarding frequency of risk factors for peripartum cardiomyopathy in patient presenting to Gynea department Lady Reading Hospital Peshawar. Moreover, the results of this study will be shared with other health professionals and will be used for other research work.

MATERIAL AND METHODS
The study was conducted at the Department of Obstetrics and Gynecology, Lady Reading Hospital, Peshawar, over a six-month period from January 27, 2020, to July 27, 2020. It was a descriptive cross-sectional design with a sample size of 247, determined based on a 8.6% prevalence of type 2 diabetes mellitus in peripartum cardiomyopathy (PPCM) cases, a 95% confidence interval, and a 3.5% margin of error, according to the WHO formula for sample size calculation. Consecutive non-probability sampling was employed. Inclusion criteria consisted of all diagnosed cases of PPCM (as per the operational definition), patients aged 18-40 years, and those with a gestational age greater than 32 weeks on LMP or less than 5 months post-delivery. Exclusion criteria included patients with recognized causes of cardiomyopathy such as tachycardia-induced heart disease, coronary heart disease, heart valve disease, alcoholic cardiomyopathy, and pre-existing hypertension, as well as those with congenital heart diseases.

Data Collection Procedure
This study was conducted after approval from hospital ethic committee. All the patients fulfilling the inclusion criteria were enrolled in the study through Obstetrics and Gynecology,Department. Written informed consent was taken from all included patients after explaining all the benefits and risks.

Clinical examination and routine investigation like echo was performed for the confirmation of PPCM. Echo test was performed in the cardiology department under the supervision of expert cardiologist having at least five years of experience. Responsible factors like pregnancy induced hypertension (PIH), Preeclampsia, Type 2 diabetes mellitus was evaluated as per operational definition.

All the above mentioned information like age, gestational age, parity, obesity, past history of PPCM was recorded in a pre design proforma. Exclusion criteria was strictly followed to control bias in study results.

Data analysis

All the data was analysis in SPSS 22. Mean and standard deviations was computed for quantitative variables like age, gestation periods. Frequency and percentage were computed for qualitative variables like parity, obesity, Past history of PPCM and responsible factors (Pregnancy induced hypertension, Preeclampsia, Type 2 diabetes). Responsible factors were stratification with age, gestational age, parity, obesity, past history of PPCM to see effect modifiers. Post stratification chi square test was applied in which P value ≤ 0.05 was considered as significant value.

RESULTS

A total of 247 patients were included in this study. The baseline characteristics of the study population reveal that the majority of participants are in the age group of 31-40 years (170, 69%), with a smaller proportion aged 18-30 years (77, 31%), and the mean age is 33 ± 12.84 years. Regarding gestational age, most participants were between 37-38 weeks (163, 66%), while 84 (34%) were between 39-40 weeks, with an average gestational age of 38 ± 2.77 weeks. The majority of the participants were multiparous (203, 82%) compared to primiparous (44, 18%). In terms of obesity, 161 (65%) were classified as obese, while 86 (35%) were non-obese. Additionally, a small percentage (22, 9%) had a past history of peripartum cardiomyopathy (PPCM). **Table 1**

In this study out of 247 cases, the most frequent responsible factor was preeclampsia, which accounts for 109 cases (44%). This was followed by pregnancy-induced hypertension, responsible for 67 cases (27%). Lastly, type 2 diabetes is the least common factor, with 30 cases (12%). **Table 2 & Graph 1**

In this study of 247 patients, the frequency of pregnancy-related conditions was assessed by age, gestational age, parity, obesity, and past history of peripartum cardiomyopathy (PPCM). Pregnancy-induced hypertension was observed in 67 patients (27.1%), with 21 (31.3%) in the 18-30 years group and 46 (26.3%) in the 31-40 years group (p=0.9720). Preeclampsia occurred in 109 patients (44.1%), with 34 (50.7%) in the 18-30 years group and 75 (42.1%) in the 31-40 years group (p=0.9955). Type 2 diabetes was present in 30 patients (12.1%), with 9(13.8%) in the 18-30 years group and 21 (11.8%) in the 31-40 years group (p=0.8822). By gestational age, pregnancy-induced hypertension occurred in 67 patients (27.1%) with 44 (27.0%) in the 37-38 weeks group and 23 (27.4%) in the 39-40 weeks group (p=0.9483).

Preeclampsia was seen in 109 patients (44.1%), with 72 (44.1%) in the 37-38 weeks group and 37 (44.0%) in the 39-40 weeks group (p=0.9851). Type 2 diabetes was noted in 30 patients (12.1%), with 20 (12.3%) in the 37-38 weeks group and 10 (11.9%) in the 39-40 weeks group (p=0.9336). Regarding parity, pregnancy-induced hypertension was present in 67 patients (27.1%), with 12 (27.3%) in the Primi Para group and 55 (27.1%) in the Multi Para group (p=0.9806). Preeclampsia was found in 109 patients (44.1%), with 20 (45.5%) in the Primi Para group and 89 (43.8%) in the Multi Para group (p=0.8451). Type 2 diabetes was observed in 30 patients (12.1%), with 5 (11.4%) in the Primi Para group and 25 (12.3%) in the Multi Para group (p=0.8609). In terms of obesity, pregnancy-induced hypertension was seen in 67 patients (27.1%), with 44 (27.3%) in the obese group and 23 (26.7%) in the non-obese group (p=0.9215). Preeclampsia occurred in 109 patients (44.1%), with 71 (44.1%) in the obese group and 38 (44.2%) in the non-obese group (p=0.9895). Type 2 diabetes was noted in 30 patients (12.1%), with 20 (12.4%) in the obese group and 10 (11.6%) in the non- obese group (p=0.8555). For patients with a past history of PPCM, pregnancy-induced hypertension was found in 67 patients (27.1%), with 6 (27.3%) in the PPCM group and 61 (27.1%) in the non-PPCM group (p=0.9870). Preeclampsia occurred in 109 patients (44.1%), with 10 (45.5%) in the PPCM group and 99 (44.0%) in the non-PPCM group (p=0.8956). Type 2 diabetes was observed in 30 patients (12.1%), with 3 (13.6%) in the PPCM group and 27 (12.0%) in the non-PPCM group (p=0.8225). All p-values indicated that the differences between groups were statistically insignificant (p>0.05). **Table 3**

Table 1. Frequency of bassline and clinical characteristics (n = 247)

Baseline characteristics	Frequency	Percentage	Mean ± Standard Deviation
Age in groups 18-30 years 31-40 years	77 170	31% 69%	33 ± 12.84
Gestational age 37 - 38 weeks 39 - 40 weeks	163 84	66% 34%	38 ± 2.77
Parity Primi Para Multi Para	44 203	18% 82%	-
Obesity: Obese Non obese	161 86	65% 35%	-
Past History of PPCM	22	9%	-

Graph 1: Frequency of responsible factors (n = 247)
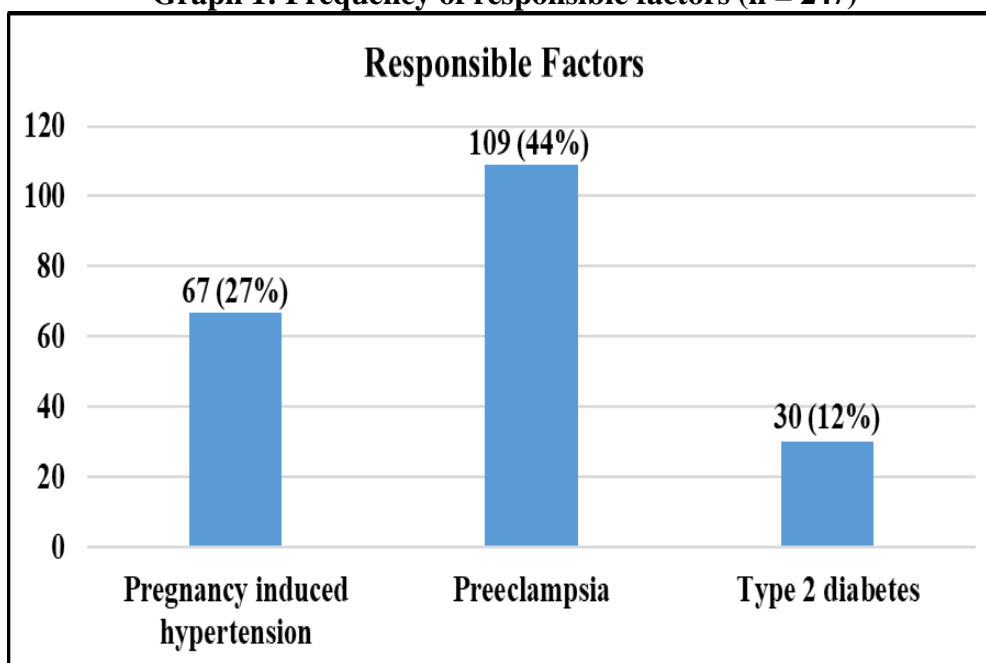
Table 2: Frequency of responsible factors (n = 247)

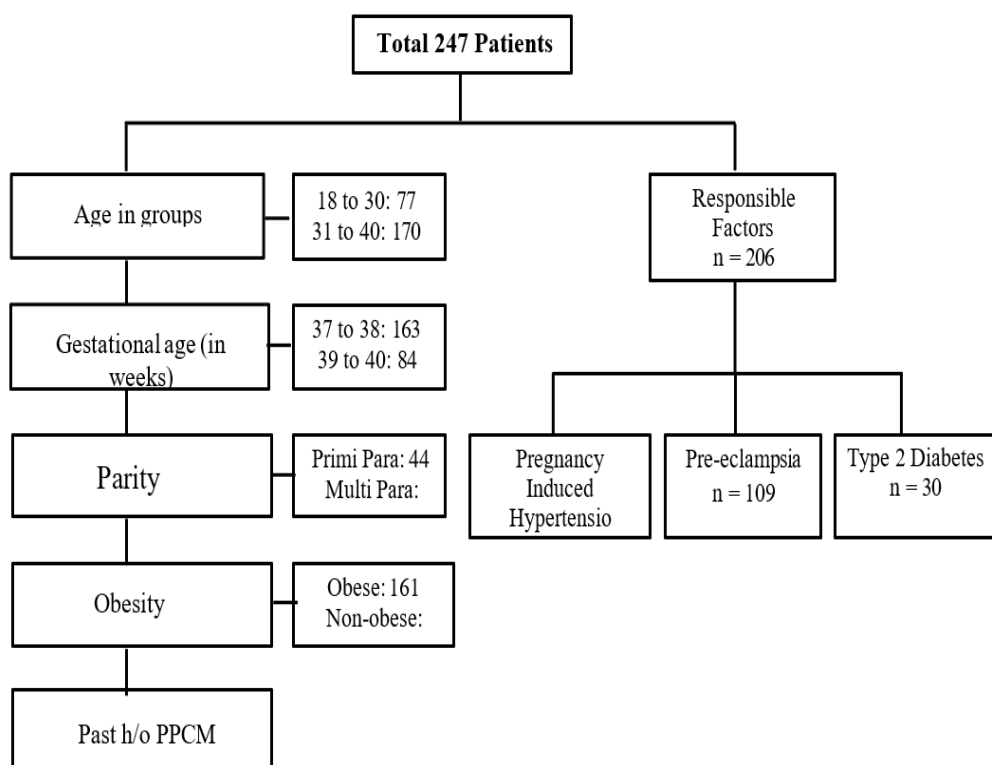| Responsible factor	Frequency	Percentage
Pregnancy induced hypertension	67	27%
Preeclampsia	109	44%
Type 2 diabetes	30	12%

Table 3. Frequency of Pregnancy-Related Conditions by Age, Gestational Age, Parity,Obesity, and Past History of Peripartum Cardiomyopathy (PPCM) (n = 247)

Age (in groups)		18-30 years	31-40 years	Total	P value
Pregnancy induced hypertension	Yes	21	46	67	0.9720
	No	56	124	180	
Preeclampsia	Yes	34	75	109	0.9955
	No	43	95	138	
Type 2 diabetes	Yes	9	21	30	0.8822
	No	68	149	217	
Gestational age (in weeks)		**37 - 38 weeks**	**39 - 40 weeks**	**Total**	**P value**
Pregnancy induced hypertension	Yes	44	23	67	0.9483
	No	119	61	180	
Preeclampsia	Yes	72	37	109	0.9851
	No	91	47	138	
Type 2 diabetes	Yes	20	10	30	0.9336
	No	143	74	217	
Parity		**Primi Para**	**Multi Para**	**Total**	**P value**
Pregnancy induced hypertension	Yes	12	55	67	0.9806
	No	32	148	180	
Preeclampsia	Yes	20	89	109	0.8451
	No	24	114	138	
Type 2 diabetes	Yes	5	25	30	0.8609
	No	39	178	217	
Obesity		**Obese**	**Non obese**	**Total**	**P value**

Pregnancy induced hypertension	Yes	44	23	67	0.9215
	No	117	63	180	
Preeclampsia	Yes	71	38	109	0.9895
	No	90	48	138	
Type 2 diabetes	Yes	20	10	30	0.8555
	No	141	76	217	
Past History Of PPCM		**Yes**	**No**	**Total**	**P value**
Pregnancy induced hypertension	Yes	6	61	67	0.9870
	No	16	164	180	
Preeclampsia	Yes	10	99	109	0.8956
	No	12	126	138	
Type 2 diabetes	Yes	3	27	30	0.8225
	No	19	198	217	

DISCUSSION

Peripartum cardiomyopathy (PPCM) is a kind of heart muscle disease that develops in the months after childbirth or close to the end of pregnancy and is characterized by heart failure brought on by impaired left ventricular (LV) pumping function [10]. Heart failure is the only cause of this condition. According to Rantner et al. (2015), there is nearly always a drop in ejection fraction (EF) below 45% in individuals with PAD even though there may not be an enlargement of the ventricle. [11]. The research suggests that the causes of PPCM include viral myocarditis, autoimmune reactions, aberrant reactivity to hemodynamic stress, hormonal imbalances, starvation, and genetic abnormalities of the heart muscle.[10]

In the present study mean age was 33 years with SD± 12.84. 66% patients had gestational age 37-38 weeks and 34% patients had gestational age 39-40 weeks. 18% patients were primi para and 82% patients were multi para. More over responsible factors for peripartum cardiomyopathy were pregnancy induced hypertension 67(27%), Preeclampsia 109(44%) and Type 2 diabetes mellitus was 30(12%).

In Pakistan, a study has been showed the higher incidence of PPCM in patients with type 2 diabetes (8.6%) and with pregnancy induced hypertension (22.9%)[7]. Some studies do not agree with the all risks factors stated above. For example, in contrast to higher incidence of PPCM in multigestation, PIH and Eclampsia (as above)[7], another study in the US concluded that the incidence of PPCM is higher in single gestation pregnancy (6.2% in multiple gestation and 10.5% in singleton pregnancy) with no effect of pregnancy induced hypertension (10.1 [95% CI 9.5 to 10.6] in PIH and 10.4 [95% CI 10.3 to 10.5] per 10 000 live births in without PIH)[3]. However complete data regarding this in other part of the world (including Pakistan) is scanty and should need to be confirm and well evaluated in further studies as different study show difference in risk factors[3,4,9].

Peripartum cardiomyopathy (PPCM) is a distinctive form of cardiomyopathy that develops in pregnant women either shortly before or after childbirth, resembling dilated cardiomyopathy. This condition exhibits a notable geographical distribution, with lower occurrence in European nations but higher prevalence in West Africa [1,12]. The reported incidence of PPCM varies from 1 in 350 to 1 in 15,000 pregnancies, with Haiti having particularly high rates where approximately one in every 350 to 400 women develops PPCM [12]. The prevalence of PPCM in China remains uncertain, although screening of 18,000 women at Liaocheng Hospital from 2007 to 2009 indicated that approximately 0.29% of hospitalized women for delivery were affected by PPCM.

Though its etiology is uncertain, PPCM most likely has a multifactorial etiology. Previous research revealed that multiparity, African ancestry, twin pregnancies, advanced maternal age, gestational hypertension, and long-term miscarriage prevention were risk factors of postpartum depression (PPCM) [12]. The observation of familial occurrences and clustering in PPCM suggests a potential role for genetic variables in the pathophysiology of PPCM [13].

Prolactin's proteolytic cleavage into a strong antiangiogenic, proapoptotic, and pro- inflammatory factor is connected to imbalanced peri/postpartum oxidative stress, according to experimental data. This might have a role in the pathophysiology of PPCM [14].

Patients with acute onset PPCM had better outcomes when bromocriptine was used in a pharmacological inhibition of prolactin, according to a recent proof-of-concept clinical trial (Sliwa, Blauwet, et al. 2010) Seventy Further evidence that aberrant immune activity and inflammatory mediators may contribute to the pathophysiology of PPCM comes from increased plasma concentrations of FAS/Apo-1, C-reactive protein, interleukin-6, and tumor necrosis factor-á in PPCM patients [15,16].

Multivariate logistic analysis showed that hs-CRP was an independent predictor of PCCM, and that the PPCM group in this study had significantly higher levels of this biomarker of chronic inflammation. These results suggest that PPCM may be related to chronic inflammation or pro-inflammatory cytokines.

Elkayam et al. (2005) and Gentry et al. (2010) have identified chronic and gestational hypertension as a risk factor for postpartum hemorrhage (PPCM) [17,18]. The correlation between race and hypertension may be shown in the increased prevalence of PPCM observed in some ethnic groups. The current investigation found that 11.5% of patients with PPCM had gestational hypertension, which was equivalent to the rate of 8% to 10% reported in the general pregnant population (Khan et al., PPCM.2022) but less than the 43% described by Elkayam et al. 2010 [17,18]. The results of our multivariate logistic analysis revealed that hypertension was a separate predictor of According to the current study, 25% of the PPCM patients also had laboratory evidence of a previous viral infection, and 36.5% of the patients had clinical signs of a respiratory illness. According to the analysis conducted today, PPCM and respiratory illness seem to be related. The significance of infection in the pathophysiology of PPCM in our patients is yet unknown because it was challenging to diagnose respiratory infections in patients with congestive heart failure.

Huang Qi, also known as radix astragali, is an antiviral medication that was used to treat twelve of the thirteen patients who had previously contracted a virus. Given that the primary chemical constituents of this medication are flavonoids and saponins [19]. This medicine doesn't seem to be related to PPCM, as none of them have been reported to cause cardiomyopathy or heart failure. Further, the group treated with Huang Qi had a mean left ventricular ejection fraction.
at the conclusion of the follow-up was comparable to that of the group that had not received Huang Qi treatment throughout their hospital stay.

One of the study's limitations is that the patient outcomes were only examined when they were hospitalized and right after they were discharged (mean follow-up period of 21.6 days). While the majority of patients healed, only one patient (1.9%) died, most likely from heart failure, raising questions about the long-term survival of PPCM in this demographic. All of our patients had postpartum PPCM, therefore ACE inhibitors and ARBs were often prescribed; nevertheless, it is important to keep in mind that these drugs should not be taken during pregnancy.

CONCLUSION

Our study concludes that responsible factors for peripartum cardiomyopathy were pregnancy induced

hypertension 27%, Preeclampsia 44%, and Type 2 diabetes mellitus was 12% in patient presenting to Gynea department Lady Reading Hospital Peshawar.

Conflict of interest
There was no any conflict of interest in this study

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