

Breastfeeding in peripartum cardiomyopathy mothers: A systematic review

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Abstract

Introduction: Peripartum cardiomyopathy (PPCM) develops around the end of pregnancy or in the initial months after delivery. PPCM is induced by vasculotoxic chemicals secreted from the placenta and pituitary. Prolactin is one of these hormones that could be harmful. The maternal pituitary release prolactin in response to breastfeeding. The advantages of nursing for both mother and child must be taken seriously while deciding whether to breastfeed with PPCM. This systematic review aims to analyze the existing scientific evidence on breastfeeding in PPCM patients.

Method: To ensure comprehensive retrieval of relevant research we search the following key databases: PubMed and ScienceDirect through 1000 for peer reviewed articles (in all languages) evidence related to breastfeeding in peripartum cardiomyopathy.

Results: The studies suggest that PPCM influenced by the hormone prolactin which related to breastfeeding. Therapy of prolactin inhibitors is given to inhibit the worsening of PPCM patients, but with side effects patients cannot provide exclusive breastfeeding. From the study, breastfeeding has no significant effect on the LVEF of mothers with PPCM, but in PPCM conditions that are not well compensated, breastfeeding is not recommended and patients should undergo therapy with bromocriptine.

Conclusion: Breastfeeding and bromocriptine go opposite but both have benefits for PPCM patients, consideration for breastfeeding or bromocriptine administration must considering the patient's condition. Administration of bromocriptine for certain conditions such as severe PPCM can accelerate LV function recovery. There will be side effects for both children and mothers who are not breastfed.

Keywords: Peripartum Cardiomyopathy; Breastfeeding; Prolactin

1. Introduction

Peripartum cardiomyopathy is a condition of heart failure that occurs in women during pregnancy or within one year after delivery. A potentially fatal illness known as peripartum cardiomyopathy (PPCM) develops idiopathically around the end of pregnancy or in the initial months after delivery.¹ Depending on the locale, the reported incidence varies greatly. Nigeria had the greatest incidence (1 in 102) and Japan the lowest (1 in 15,533 births). It is important to highlight that the prevalence is higher in African nations, African Americans, and Haitians, indicating that the black race is extremely vulnerable to PPCM.²

The development of left ventricular systolic dysfunction and a corresponding decline in left ventricular ejection fraction (LVEF) to less than 45% are the conditions hallmarks.^{3,4,5} The reported mortality rates differ from nation to nation, and after five years of diagnosis, the reported maternal mortality in underdeveloped nations neared 25%.⁶ To address PPCM, a multidisciplinary strategy encompassing high-risk obstetrics, cardiology, neonatology, and intensive care is

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necessary. The following treatments have been suggested for patients with acute PPCM under the BROAD label, according to the European Society of Cardiology (ESC): bromocriptine, oral heart failure medicines, anticoagulants, vaso-relaxing medications like nitrate and hydralazine, and diuretics.⁷

It is a serious disease that can endanger the health of both the mother and the growing infant. Proper nutrition plays a crucial role in the management of peripartum cardiomyopathy, and the decision to breastfeed may present a complex choice for these patients. Breastfeeding is the preferred and recommended method of infant nutrition by national and international health organizations. However, for mothers with peripartum cardiomyopathy, the decision to breastfeed may involve more complex considerations. Several questions arise, including whether breastfeeding will impact the health of the mother and infant, whether breastfeeding can affect the progression of the heart disease, and whether the risks involved are outweighed by the benefits of breastfeeding.

The notion that PPCM is induced by vasculotoxic chemicals secreted from the placenta and pituitary during late gestation and the early postpartum periods has been promoted by multiple investigations in model species.⁸ These harmful hormones harm the heart microvasculature, which causes malfunction in the cardiomyocytes and contractile failure. Prolactin is one of these hormones that could be harmful. Late in the pregnancy, the maternal pituitary begins to release prolactin, and it does so even after delivery in response to breastfeeding. Prolactin stimulates milk production by directly affecting mammary glands. Prolactin, however, can occasionally be broken down by extracellular proteases into a 16 kD peptide that is severely vasculotoxic.

The advantages of nursing for both mother and child must be taken into account while deciding whether to breastfeed with PPCM. Breast milk is a vital conduit for the transmission of important nutrients and components to the infant from the mother. It can be disastrous for the baby to stop nursing in developing nations, where undernutrition and contaminated water sources cause the bulk of young deaths and when breast milk substitutes are expensive.⁹ Breastfeeding decreases the risk of abrupt infant death and fosters connection, immunity, metabolic protection, a healthy microbiome population, and substantial protection against diarrheal, respiratory, and otitis media conditions.

This systematic review aims to gather and analyze the existing scientific evidence on breastfeeding in patients with peripartum cardiomyopathy. By analyzing the available research, we hope to provide comprehensive information regarding the benefits, risks, and implications of breastfeeding in this specific patient population. The findings from this review will assist healthcare professionals and families in making informed decisions regarding breastfeeding in peripartum cardiomyopathy patients.

2. Methods

We searched PubMed, ScienceDirect, and Proquest databases from inception through 2000 for peer reviewed articles (in all languages) evidence related to breastfeeding in peripartum cardiomyopathy patients. We used the phrases “PubMed ((breastfeed OR breastfeeding OR lactation) AND (peripartum cardiomyopathy OR PPCM))”; ScienceDirect with the keyword (Breastfeeding AND peripartum cardiomyopathy); Proquest with the word (Breastfeeding) and (peripartum cardiomyopathy). Reference list from articles identified by the search, as well as key review articles conducted by author and we did not impose any language or other restrictions on the beginning of searches.

2.1. Study selection

Our search generated a list of abstracts. Any uncertainty on the eligibility of the studies that was based on title and abstract made the reviewers read full paper. The study flow diagram was shown in Flowchart 1.

To be considered for inclusion, studies must explicitly define and describe the study population, the interventions, and outcomes. For the proposed comparative effectiveness review, the population of interest includes women with symptomatic cyclic or irregular problem bleeding of three months or longer duration. The population of interest excludes individuals with abnormal uterine bleeding that is caused by systemic disease, structural abnormalities, cancer, or medication side effect. To be considered for inclusion, clinical research studies must evaluate a nonsurgical intervention. Study design and setting reported in table 1.

Table 1 Article Inclusion and Exclusion Criteria

| | Inclusion Criteria | Exclusion Criteria |
|-----------------------|---|---|
| Types of studies | Controlled clinical trials (randomized control trials), observational studies | Did not describe the effect of breastfeeding on PPCM or vice versa Did not describe LV function of PPCM patients with or without breastfeeding |
| | All evidence levels by clinical examination and was accepted for safety analysis inclusion | Non clinical studies Review High bias studies Expert opinions or commentary paper |
| Types of Participants | Female patients with heart failure in the late trimester pregnancy period up to 1 year postpartum and have not been detected to have heart disease before | |

2.2. Assessment of study quality

All authors participated in summarizing and systematically assessing the evidence through the use of standard abstraction forms. The team will test the screening and abstraction forms on multiple articles before beginning the abstraction and review process. Screening and data collection forms may undergo revisions by the team. The results are presented in the evidence tables (Table 1).

2.3. Data synthesis

We did not conduct quantitative syntheses because of four factors. They are wide differences in how the condition being treated is operationally define across studies, large variety of interventions with rare replication of trials using the similar interventions, and disparate primary and secondary outcomes measure.

2.4. Data Extraction

Data extracted from the identified publication included: study design, locations, methods, participants, results, discussion, conclusions and comments. We used a table where each piece of information was written descriptively (Table 1).

3. Results

Our search identified 943 studies and 4 paper were included in our study. Three of the twelve included studies were randomized control trials, and one was a pilot study describing abnormal uterine bleeding. The flowchart literature through the assessment process for the update of this review is shown in Figure 1.

Table 2 Characteristics and outcomes of the included studied

| No. | Author | Locations | Methods | Participants | Results | Conclusions |
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| 1. | Koczko et al, 2019 ¹⁰ | Multicenter IPAC (30 centers) | Prospective Cohort Study | In the first 13 weeks postpartum, 100 women with newly diagnosed PPCM were enrolled at 30 facilities between December 2009 and September 2012. At the time of enrollment, all of the women were at least 18 years old, had no prior history of cardiac disease, had estimated left ventricular ejection fractions (LVEF) of $\leq 45\%$, and had evaluations that were consistent with recent-onset nonischemic cardiomyopathy. | <p>CD3 and CD8 levels increase in PPCM patients, and as prolactin increases, CD3 and CD8 also increase.</p> <p>There was no improvement or increase in LVEF at months 6 and 12 of PPCM patients who breastfed and prolactin cannot be used to predict LVEF of PPCM patients at months 6 and 12</p> <p>Breastfeeding has a high EF at entry, at 6 months and 12 months and less ill than non-breastfeeding patients</p> <p>Increased prolactin regulates Th-1 types of cytokines thereby stimulating an increase in CD3 and CD8</p> <p>As a result of prolactin regulating Th-1 types, it interferes with the regulatory suppression of T cells</p> <p>Increased prolactin, CD3, and CD8 do not have a significant impact on EF and myocardial recovery</p> <p>Breastfeeding patients have better EF within 6 months than NBF patients</p> <p>Patients with well-compensated PPCM are not recommended to non-breastfeeding</p> | The lack of an apparent effect of BF on the results contradicts the inflammatory hypothesis. In fact, the lack of any risk for BF in IPAC provides evidence against the importance of prolactin as a mediator and bromocriptine as a treatment. This paper found no data that supports recommendations against BF for well compensated women who come with PPCM. Patients with PPCM who are more seriously unwell at the time of diagnosis may benefit from bromocriptine medication, which forbids BF. |
| 2. | Douglas et al, 2021 ¹¹ | Mayo Clinic and Olmsted Medical Center, Olmsted County, Minnesota | Observational Study | 1177 patients potentially diagnosed with PPCM from 3 regions using diagnostic criteria from the National Heart, Lung and Blood Institute of Health Workshop on Peripartum Cardiomyopathy. Of the 1177 patients with | <p>Women with PPCM are more likely to have a history of hypertension ($p=0,01$), anxiety ($p=0,03$) and migraines ($p<0,001$) than controls due to hormonal imbalances and angiogenic factors, one of which is prolactin.</p> <p>There is no significant difference between BF and NBF patients in the diagnosis of PPCM ($p=0,06$)</p> | Most women experienced LV function recovery from days to years after diagnosis. A small percentage of women with restored LV function afterwards reported LVEF decrease months or years following restoration. Low birth weight and preterm were elevated risks for children of |

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| | | | | <p>potential PPCM, only 48 confirmed cases of PPCM were obtained. And 96 women identified controls based on age, nationality (race) and number of babies born during pregnancy.</p> | <p>After being diagnosed with PPCM, BF decreases ($p=0,009$)</p> <p>Some of the reasons why mothers stop BF after being diagnosed with PPCM are because of their physical or mental health, mothers being treated in hospitals that do not allow BF, lack of education about patient's heart drugs that are safe to give to breastfeeding mothers</p> <p>WHO recommends BF (exclusive breastfeeding) for 6 months and continued BF for up to 1-2 years to reduce the risk of diabetes mellitus, ovarian and breast cancer and postpartum depression that increases maternal mortality.</p> | <p>women with PPCM. There is no significant difference between BF and NBF patients in the diagnosis of PPCM. Last but not least, women whose LVEF had recovered before a subsequent pregnancy did not experience a long-term reduction in LVEF after giving birth.</p> |
| 3. | McNamara et al, 2015 ¹² | Multicenter IPAC (30 centers) | Prospective Cohort Study | <p>100 women with newly diagnosed PPCM were enrolled within the first 13 weeks post-partum, minimum age 18 years, LVEF $\leq 45\%$, nonischemic idiopathic cardiomyopathy.</p> <p>Exclusion criteria: significant valvular disease, ongoing bacterial septicaemia, ongoing drug or alcohol abuse, history of chemotherapy or chest radiation in the last 5 years</p> | <p>80% of the subjects get HF therapy (beta blockers, ACE inhibitors or ARBs). Only 1 patient was given bromocriptine therapy and 15% of BF patients</p> <p>In univariate analysis for LVEF predictors at 12 months, there was no difference in LVEF at 12 months of observation in PPCM patients who were BF with non-BF ($p=0,10$)</p> <p>Although the use of bromocriptine as a prolactin inhibitor in 2013 in a German study giving a combination of HF therapy with bromocriptine showed good improvement. However, researchers did not find a significant difference in PPCM patients given HF + bromocriptine combination therapy with HF therapy alone.</p> <p>The limitation of this study is the variation in postpartum time to study entry</p> | <p>The majority of the women in a prospective cohort with PPCM recovered, although 13% experienced significant episodes or had permanent severe cardiomyopathy. Less recovery was linked to severe LV dysfunction and more remodelling at study entrance. At 12 months of monitoring, there was no difference in LVEF between PPCM patients who were BF and non-BF.</p> |

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| 4. | Haghikia et al, 2019 ¹³ | 12 participating centers in Germany | Randomized Control Trial | <p>68 people were included in the trial after 140 patients were screened at 12 centers for eligibility. There were 40 patients with PPCM included, and 24 of them had a low RV ejection percentage (RVEF \leq45%).</p> | <p>Bromocriptine administration for 8 weeks has a higher LV recovery during 6 months follow-up compared to bromocriptine administration for 1 week. But the results did not differ significantly ($p=0,211$)</p> <p>However, the administration of bromocriptine as an addition to HF therapy in PPCM with RV involvement showed a better increase in LV and RV function</p> <p>Administration of bromocriptine (prolactin antagonist) in addition to standard HF therapy plays a role in fully cardiac recovery of high risk PPCM patients regardless of duration of administration</p> <p>50% of the 1W group and 64% of the 8W group had complete LV recovery ($p = 0.678$). 40% of the 1W group and 79% of the 8W group had complete RV recovery ($p = 0.092$).</p> <p>Administration of bromocriptine as a prolactin inhibitor can be a fairly effective option for PPCM patients with RV dysfunction involvement. This study showed that administration of bromocriptine with a longer duration showed improved RV and LV function in population studies</p> | <p>Bromocriptine treatment in PPCM patients with RV involvement was associated with a high rate of complete RV and LV recovery, despite the fact that patients with baseline RV dysfunction had a generally worse outcome. No statistically significant differences were found between the short-term and long-term bromocriptine treatment regimes. These results imply that bromocriptine may be beneficial for PPCM patients with biventricular dysfunction in addition to normal heart failure treatment.</p> |
| 5. | Sieweke et al, 2020 ¹⁴ | Department of Cardiology and Angiology, Hannover Medical School, | Prospective Cohort Study | <p>All patients in Hannover Medical School's cardiology department are admitted to the ICU with Cardiogenic Shock</p> | <p>Patients are given bromocriptine at a dose adjusted to the measurement of prolactin levels, and guidelines for HF are also given, namely beta blockers, ACE inhibitor, MRA's and ivabradine.</p> <p>After bromocriptine administration, prolactin levels decreased significantly</p> | <p>In patients with rCS complicating PPCM, intensive care treatment involving MCS and bromocriptine medication is linked to a good survival rate. Bromocriptine is necessary in patients with cardiogenic shock, and significantly lowers prolactin levels so that mothers with PPCM</p> |

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| | | Germany | | | <p>after 72 hours and 7 days compared to baseline</p> <p>Prolong catecholamine administration in cardiogenic shock (PPCM) patients has the potential to cause damage that cannot be overcome by giving bromocriptine, so LVAD implantation is needed (in 3 patients)</p> <p>The limitations of this study are there's no control group is available but the results can help strengthen the hypothesis. In addition, because PPCM cases are rare, especially with cardiogenic shock, only a few cases are obtained</p> | cannot perform breastfeeding while in critical condition and require bromocriptine as adjuvant therapy |
| 6. | Tremblay-Gravel et al, 2019 ¹⁵ | 17 independent medical centres covered by Four Faculties of Medicine in the Province of Quebec, Canada | Retrospective Cohort Study | 76 women included and fulfilled the PPCM diagnostic criteria by the National Heart, Lung and Blood Institute and National Institutes of Health | <p>Patients were compared between patients taking bromocriptine during hospitalization at a dose of 2.5 mg given 2 times daily for 2 weeks followed by administration at a dose of 2.5 mg once a day for 6 weeks compared to PPCM patients who were not given adjunctive bromocriptine</p> <p>There were 76 female patients diagnosed with PPCM who were included in the inclusion criteria, of which 8 (11%) were given bromocriptine initiated since hospitalization</p> <p>Patients given bromocriptine therapy showed better recovery of LV function in 6 months and long-term follow-up compared to PPCM patients who were not given bromocriptine therapy. LVEF values were higher in PPCM patients who were given additional bromocriptine therapy compared to those who were not given bromocriptine.</p> | Administration of bromocriptine as adjuvant therapy in PPCM patients with critical conditions provided results that significantly improved her LVEF. It can be said that PPCM patients with critical conditions cannot breastfeed, so bromocriptine should be given to these patients in order to help improve the patient's condition |

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| | | | | | In this study the use of bromocriptine was more often used in patients with much lower LVEF, lower blood pressure, higher heart rate and much higher baseline lactate. From the low LVEF it shows a much more significant increase in LV function | |
| 7. | Ravi Kiran et al, 2021 ¹⁶ | Department of cardiology, Government general hospital, Kurnool, Andhra-pradesh, India, KIMS Hospital, Kurnool, India | Prospective Cohort Study | 43 patients with PPCM were monitored for 6 months. The primary objective (defined as left ventricular ejection fraction, LVEF: 45% at 6 months) was a composite incidence of decompensation-related rehospitalization, all-cause death, and poor recovery. | <p>Bromocriptine was given to 38 patients (88.3%), oral bromocriptine was given one to two times a day at a dose of 2.5 mg varying the duration of administration from 1 to 8 weeks</p> <p>26 patients (63.4%) full recovery and 11 patients (26.8%) poor LV recovery and the rest partial LV recovery</p> <p>The duration of bromocriptine administration in this study varied based on patient preference, low birth weight of new born child and availability of new clinical evidence</p> <p>This study reinforces that the administration of bromocriptine has no impact on the outcomes of PPCM patients</p> <p>In hospital mortality in this study was 4.7% which is higher than western studies. Where in this study has included Asian women. The difference in mortality in Asian women is due to delayed presentations, anaemia or infection in Asian women who are more prone to death from PPCM</p> | This investigation came to the conclusion that bromocriptine lactation suppression did not improve recovery. Approximately 61% of PPCM patients will have complete LV functional recovery six months after diagnosis with modern evidence-based therapy. Dobutamine and/or levosimendan inotropic treatment during the index hospitalization had no positive effects on patient outcomes. High left atrial volume index (LAVi >29.6 ml/m ² , with 72% accuracy) and low RV fractional area change (RVFAC 31.4%, with 86% accuracy) upon presentation are independent predictors of adverse outcomes. |

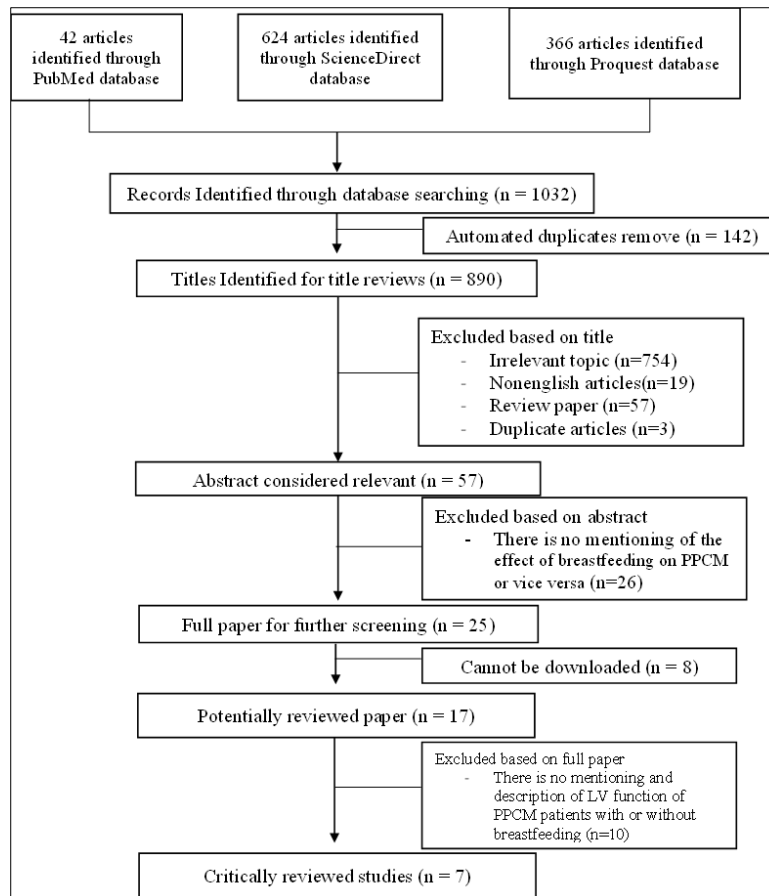


Figure 1 Study flow diagram in this review

4. Discussion

This study looked for the effect of breastfeeding on the condition of patients with peripartum cardiomyopathy by analyzing the available research, to provide comprehensive information regarding the benefits, risks, and implications of breastfeeding in this specific patient population. In a 2019 study by Koczo et al that examined 100 women diagnosed with PPCM, this study was examine how breastfeeding affected cellular immunity and cardiac healing in women with peripartum cardiomyopathy. Breastfeeding women exhibited higher levels of prolactin, and higher CD8+ T cell counts were also connected with prolactin levels. However, despite increased prolactin and cytotoxic T cell subsets, breastfeeding women's cardiac healing was unaffected. Patients with well-compensated PPCM are not recommended to non-breastfeeding. Despite the fact that BF and prolactin seem to modify CD3+ CD8+ levels, this study investigation found no proof that this had a clinical effect on LVEF at presentation or subsequent myocardial recovery. The observations do not suggest that cytotoxic T lymphocytes play a substantial part in the pathophysiology of PPCM or the subsequent recovery. Recently, Koczo et al showed that patients with PPCM had lower levels of natural killer cells than healthy postpartum control subjects, but that there was no significant difference between the two cohorts in terms of circulating cytotoxic T cell and T helper cell levels.¹⁰ In areas of Africa, Asia, and Haiti where PPCM is widespread, BF in postpartum mothers has significant maternal and neonatal advantages that may have an impact on health well beyond the months spent actually breastfeeding.¹⁷ BF is vitally important in underdeveloped nations, where PPCM is more prevalent than in the United States, not just as food and nutrition but also for newborn immunity.¹⁷ The risk of negative health effects on infants of PPCM woman who are prohibited from BF remains high.¹⁸ The Heart Failure Association of the European Society of Cardiology Study Group criticized the use of BF and suggested that patients with PPCM instead utilize bromocriptine to suppress prolactin.¹⁹ This advice is not supported by Koczo et al study, which found that women who breastfed had significantly higher LVEFs at 6 months and does not support a retrospective Internet-based study from the US that found better outcomes for women with PPCM who breastfed. Additionally, a recent single center investigation found that there was no statistically significant difference between the recovery status of NBF and breastfeeding patients for 27 of 63 patients with PPCM at 1 year.²⁰

Second study that we reviewed is an observational study with case control design conducted by Douglas et al on 1117 women who have the potential to experience PPCM and found that there is no significant difference between BF and NBF patients in the diagnosis of PPCM ($p = 0.06$) After being diagnosed with PPCM, BF decreases ($p = 0.009$).¹¹ Women stopped breastfeeding for a variety of reasons, such as feeling as though their physical or mental health was compromised, not being able to easily access their babies while in the hospital, treating physicians not being aware of the safety of cardiac medications during lactation, and/or a worry that breastfeeding might be harmful to the mother's recovery based on the proposed mechanistic link between PPCM and the nursing hormone prolactin.²¹ Increased mortality rates, infections, eczema, asthma, childhood obesity, diabetes, leukemia, and lower IQ in children, as well as an increased risk of diabetes, ovarian and breast malignancies, as well as postpartum depression in women.²² Increased information and understanding about which cardiac drugs are safe to take during nursing and that breastfeeding seems to have no negative effects on outcomes among women with PPCM would likely be beneficial to mothers with PPCM and their doctors.²³ In order to give moms and babies the right counseling and care, additional research into the short- and long-term outcomes of newborns delivered to mothers with PPCM is required.

Study conducted by McNamara et al in multicenter IPAC on 100 women with newly diagnosed PPCM found that there was no difference in LVEF at 12 months of observation in PPCM patients who were BF with non-BF.¹² A targeted treatment for PPCM that uses bromocriptine to prevent prolactin secretion has recently been recommended. According to a 2013 report of a significant series from Germany, patients with PPCM who received a combination of conventional medication (beta-blockers and angiotensin-converting enzyme inhibitors) and bromocriptine showed the most improvement.²⁴ However, these researchers found no difference between the groups of PPCM women who received bromocriptine and those who did not in terms of the proportion of these women who recovered fully. In fact, the recovery rate in this German study is on par with the most recent study that only looked at conventional therapy of beta blockers, ACE inhibitors or ARBs for HF_{rEF}. Based on the book therapy for peripartum cardiomyopathy, some HF drugs such as captopril and enalapril detected very low concentrations in human milk only about 1%, as well as beta blockers such as bisoprolol only detected <2%. Although data on the use of diuretics during lactation are limited, it was found that furosemide is not excreted in breast milk, but for side effects are not elucidated. From the study, human milk did not have an effect on babies.²⁷ From the case report that has been made shows that breastfeeding women given captopril (4.7 ng / ml) and enalapril (< 2 ng / ml) show no side effects in their babies. Breastfeeding prolongs the rise in prolactin during the postpartum period, hence some people advise against it for moms experiencing the PPCM. Given the significance of nursing for child survival in underdeveloped countries, this ban has a significant financial impact in regions of Africa, Asia, and the Caribbean where PPCM is more common.²⁵ Recommendations to curb this practice would also have unintended consequences in more developed nations because nursing has advantages over alternatives in terms of immunology, development, and nutrition. Breastfeeding was not linked to a reduced rate of recovery in the current investigation.

Haghikia et al in 2019 in their study conducted on 40 patients with PPCM using bromocriptine co therapy in 2 different groups for 1 week and 8 weeks, found that 50% of the 1W group and 64% of the 8W group had complete LV recovery ($p = 0.678$). 40% of the 1W group and 79% of the 8W group had complete RV recovery ($p = 0.092$). Administration of bromocriptine (prolactin antagonist) in addition to standard HF therapy plays a role in fully cardiac recovery of high risk PPCM patients regardless of duration of administration. Administration of bromocriptine as a prolactin inhibitor can be a fairly effective option for PPCM patients with RV dysfunction involvement. This study showed that administration of bromocriptine with a longer duration showed improved RV and LV function in population studies although not statistically significant.¹³ In PPCM patients with right ventricular involvement, bromocriptine treatment in addition to guideline-based heart failure therapy is associated with a high rate of RV and LV improvement, a high probability of full RV and LV recovery, and no significant differences were found between the short-term and long-term bromocriptine treatment regime with regard to RV and LV improvement or full recovery. The long-term bromocriptine treatment group, however, showed a propensity for higher levels of RV and LV improvement as well as a higher likelihood of cardiac recovery after 6 months.¹³ Bromocriptine works as a prolactin inhibitor. The pathogenesis of PPCM is thought to be primarily influenced by the nursing hormone prolactin and its cleaved 16 kDa form.²⁴ Nevertheless, despite improvements in our understanding of many PPCM features, there have only been a small number of clinical trials evaluating disease-specific treatments.²⁶ The limitation of Haghikia et al's study was that the placebo group did not get permission from the Ethics Committee and the risk of mastitis from stopping breastfeeding without medical support. Due to the limitations of the control group, which is still a question of the real effect of giving bromocriptine to PPCM patients.

The fifth paper that we reviewed is conducted by Sieweke et al in 2020 in Germany which discusses PPCM patients with complications in the form of cardiogenic shock. PPCM patients with this complication have a critical condition so breastfeeding their babies is impossible. Research subjects who received adjuvant therapy in the form of bromocriptine got better results on their LVEF.¹⁴ Some claim that bromocriptine administration is associated with increased

thromboembolic events during percutaneous mechanical circulatory support (MCS), therefore additional anticoagulant therapy such as unfractionated heparin is needed to reduce the risk of thromboembolism. In patients with rCS complicating PPCM, intensive care treatment involving MCS and bromocriptine medication is linked to a good survival rate. Bromocriptine is necessary in patients with cardiogenic shock, and significantly lowers prolactin levels so that mothers with PPCM cannot perform breastfeeding while in critical condition and require bromocriptine as adjuvant therapy.

Tremblay-Gravel et al in their research paper stated that when compared to PPCM patients who did not receive bromocriptine medication, patients who received it demonstrated a greater recovery of LV function in the 6-month and long-term follow-up periods. When compared to patients with PPCM who did not receive further bromocriptine medication, LVEF values were higher in the former group. In this study, patients with significantly poorer LVEF, lower blood pressure, greater heart rates, and significantly higher baseline lactate used bromocriptine more frequently. It is clear that LV function has increased significantly from the poor LVEF. Patient's LVEF was dramatically enhanced by the administration of bromocriptine as adjuvant therapy in PPCM patients with critical circumstances.¹⁵ It is important to evaluate the complex relationship between bromocriptine and the recovery of LV function in light of earlier studies that consistently showed lower recovery rates among women with severely depressed baseline LVEF.²⁸ A larger burden of myocardial fibrosis may be the cause of this obstruction to recovery, as shown by cardiac magnetic resonance studies that connected chronic LV dysfunction in PPCM women with myocardial late gadolinium enhancement.²⁹ Using bromocriptine early in the illness process could decrease the level of permanent damage rather than waiting until significant LV dysfunction has established. Although cleaved 16 kDa prolactin unifies all PPCM phenotypic subtypes, molecular investigations indicate that additional hits are required for the development of heart failure in the peripartum period.³⁰

Ravi Kiran et al in 2021 in their study of 43 PPCM patients, found that bromocriptine lactation suppression did not improve LVEF recovery. Bromocriptine as a new adjuvant therapy for PPCM patients has some limitations, from previous studies that most of these studies used observational studies. In a randomized trial study conducted in Germany showed that giving bromocriptine for 1 week with a control study or placebo for 8 weeks showed the same value in terms of LV recovery function.¹⁶ In addition, most studies only show clinical usefulness of bromocriptine in PPCM patients and do not show mortality and rehospitalization rates in PPCM patients given bromocriptine. The BRO-HF study showed that giving combination therapy of HF with bromocriptine did not decrease all cause death and HF events. The results of this study do not state anything similar to some of the studies above. This can be due to differences in the number of samples, and the race of the patient. In this study, the study subjects were Asian women, who came for treatment when the condition was critical, so that the administration of bromocriptine did not significantly help the patient's condition. This study's in-hospital death rate was 4.7%, which is higher than studies conducted in the west but on par with research involving Asian women.^{31,32} Since Asian females are more susceptible to dying from PPCM, this difference of greater mortality rates in Asians may be caused by a number of variables, including delayed presentation, related anemia, or infections.³³ In the majority of trials, mortality rates ranged from 0% to 16%, and recovery rates (defined as an LVEF 50-55% at 6-12 months follow up) ranged between 14% and 85%. Different selection criteria, sociodemographic and genetic variances, patient risk factors, and advancements in the management of heart failure may all contribute to differences in recovery and mortality rates.

5. Conclusion

- Administration of bromocriptine (prolactin inhibitor release) for certain conditions such as severe PPCM, namely Cardiogenic Shock as an adjuvant to other HF therapies can accelerate LV function recovery. In critically ill states it is also not possible to be given breastfeeding.
- However, in the condition of PPCM patients with stable conditions, bromocriptine administration did not show significant improvement in LV function and did not reduce all cause death and HF events
- HF drug administration can still be tolerated in mothers with breastfeeding and can be given safely with breastfeeding including: loop diuretics, beta blockers, nitrates, digoxin, ACE Inhibitor (enalapril and captopril), aldosterone receptor antagonist (spironolactone). Even anticoagulants such as Low Molecular Weight Heparin (LMWH) and warfarin given to critically ill PPCM patients associated with thrombotic complications can be tolerated in breastfeeding PPCM mothers.
- Data from IPAC also show that breastfeeding is not associated with adverse outcomes or persistent myocardial dysfunction in PPCM patients
- There will be side effects for both children and mothers who are not breastfed. In children there will be increased mortality rates, infections, eczema, asthma, childhood obesity, diabetes, leukemia, and lower IQ, as

well as an increased risk of diabetes, ovarian and breast malignancies, as well as postpartum depression in mother.

Compliance with ethical standards

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Disclosure of conflict of interest

Author declares there is no conflict of interest during this research.

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