

Research Article

Bromocriptine in Management of Peripartum Cardiomyopathy: A Randomized Study on 96 Women in Burkina Faso

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Abstract

In order to assess the role of bromocriptine in management of peripartum cardiomyopathy (PPCM), we conducted a randomized study from April 1, 2010 to June 30, 2012. Patients randomized for standard heart failure therapy (Br⁻) received heart failure conventional therapy and those randomized for bromocriptine (Br⁺) received standard heart failure therapy plus bromocriptine 2.5 mg twice daily for 4 weeks. Clinical assessment, electrocardiogram, and echocardiography were performed at baseline, 2 weeks, 1, 3, 6 and 12 months. Endpoints criteria were mortality, changes in dyspnea and evolution of echocardiographic parameters: End diastole Left Ventricular Diameter, End Systole Left Ventricular Diameter, Left Ventricular Ejection Fraction and Tricuspid Annular Plan Systolic Excursion (TAPSE).

Results: Ninety six (96) women were included for the study. There were no significant differences in baseline characteristics. The mean value of EDLVD was 58.7 mm in Br⁺ and 57.6 mm in Br⁻ ($p = 0.091$) while the ESLVD was 48.4 mm in Br⁺ and 48.8 mm in Br⁻ ($p = 0.074$). The mean LVEF was 37.2% in Br⁺ and 37.5% in Br⁻ ($p = 0.129$) and the mean TAPSE was 19.9 mm in Br⁺ and 18.9 mm in Br⁻ ($p = 0.718$). At Six months, cumulative death were stayed 8 (16.6%) in Br⁺ but 14 (29.1 %) in Br⁻ ($p = 0.0001$). Echocardiographic findings demonstrated better improvement in ventricles function in Br⁺. Mean EDLVD was 53.4 mm in Br⁺ and 55.1 mm in Br⁻ ($p = 0.002$). The mean LVEF was 49.9% in Br⁺ and 40.9% in Br⁻ ($p = 0.001$) and the mean TAPSE was 22.0 mm in Br⁺ and 20.7 mm in Br⁻ ($p = 0.001$). At 12 months, mean LVEF was 53.9 % in Br⁺ and 45.9 % in Br⁻ ($p = 0.001$) and mean TAPSE was 22.7 mm in Br⁺ and 20.9 mm in Br⁻ ($p = 0.001$). LVEF increased from 37.2% on admission to 49.9% at six months and to 53.9% at 12 months in Br⁺ while it increased from 37.5% on admission to 40.9% at six months and to 45.9% at 12 months in Br⁻.

INTRODUCTION

Peripartum cardiomyopathy (PPCM) is a life-threatening heart disease of unknown etiology characterized by a sudden onset of heart failure in the last month of pregnancy and/or in the first months postpartum [1]. PPCM is very rare in Europe [2], but common in West Africa [3].

In general, treatment of PPCM was considered to be similar

to other types of congestive heart failure [4,5]. But recently, the anti angiogenic 16-kDa N-terminal prolactin fragment (16K PRL), produced by the full-length nursing hormone prolactin (PRL) cleavage by cathepsin D, has been discovered with a potential factor initiating and driving PPCM [6]. Bromocriptine that reduces the prolactin production by its dopamine agonist actions may improve outcomes in patients with peripartum cardiomyopathy by eliminating the cleaved form of prolactin despite the activation of the cleaving enzyme.

The aim of this study was to assess the effectiveness of bromocriptine in the treatment of peripartum cardiomyopathy

METHODS

Study Design and Patient Recruitment

Our study was approved by the human research ethics committee of the Yalgado OUEDRAOGO Teaching Hospital, Ouagadougou, Burkina Faso, and complies with the declaration of Helsinki. All patients and control subjects were given a consent form duly signed before being recruited. Ninety six consenting consecutive patients diagnosed with PPCM and fulfilling the inclusion criteria were enrolled in the study. All patients were included and randomized; the decision for the first patient to receive bromocriptine depends on the outcome of a coin of 10 Francs CFA played "heads or tails". Once drawn "heads", the patient was put under bromocriptine (subgroup Br⁺) and the next patient did not received the bromocriptine but only standard therapy of heart failure (Subgroup Br⁻) and so on.

The study was conducted at the Yalgado OUEDRAOGO Teaching Hospital. Patients were referred from local clinics, secondary hospitals, emergencies unit, and the Obstetrics department of the Yalgado OUEDRAOGO Teaching Hospital. Past medical history of preexisting cardiac symptoms and signs, occurrence of preeclampsia, and mode of delivery were obtained from the patient and confirmed by examination of the obstetric file carried by each patient.

Symptoms and signs were recorded during the first consultation at the cardiology unit at the Yalgado Ouedraogo Teaching Hospital (baseline) and during a follow-up period of 12months. Clinical assessment, electrocardiogram, chest x-ray, echocardiography, and blood analysis were performed at baseline. Clinical assessment and echocardiography were then performed at 2 weeks, 1, 3, 6 and 12 months.

Inclusion criteria were symptoms of congestive heart failure developed in the last month of pregnancy or during the five months postpartum, with no other identifiable cause for heart failure, and left ventricle ejection fraction (LVEF) < 45% by transthoracic echocardiography. Exclusion criteria were composed by systolic blood pressure >150 or <95 mm Hg or diastolic >105 mm Hg, sepsis, autoimmune disease, HIV serology positivity, impaired renal function (defined as urea and/or creatinine >1.5 times the normal upper limit) and any clinical condition that precluded inclusion in the study such as ischemic heart disease, anemic heart or malignancy.

All patients received standard heart failure treatment with the diuretic furosemide and the angiotensin-converting enzyme (ACE) inhibitor captopril. Patients with an LVEF < 35% or ventricular thrombus received anticoagulation therapy with fluindione for 6 months. Captopril doses were titrated upward as tolerated during the first 4 weeks after diagnosis and then maintained throughout the 12-month study period remaining. Furosemide dose was decreased as indicated according to clinical assessment during the 12-month study period.

The 48 patients randomized to standard therapy (Br⁻) were treated as outlined above. The 48 patients randomized to standard therapy plus bromocriptine (Br⁺) received bromocriptine 2.5 mg

twice a day for 4 weeks. After the initial screening and baseline visits, monthly outpatient visits were scheduled for clinical assessment and evaluation of medication compliance. Clinical status of hospitalized patients was evaluated each day until its improvement before discharge. The study has been conducted from April 1, 2010 to June 30, 2012.

Endpoints criteria were mortality, changes in dyspnea (NYHA class) and evolution of echocardiographic parameters: End diastole Left Ventricular Diameter (EDLVD), End Systole Left Ventricular Diameter (ESLVD), Left Ventricular Ejection Fraction (LVEF) and Tricuspid Annular Plan Systolic Excursion (TAPSE).

All patients were informed from impossibility to breastfeed their babies and then all babies benefit from artificial lactation. Data analysis was realized from SAS V9.0 statistical software. Comparison of means and proportions between subgroups was performed by Chi-square statistics and independent t test. Significance was assumed at a value of $p < 0.05$.

RESULTS

We enrolled 99 black-african women but 3 were excluded because of their HIV serology positivity. Then, 96 women were included for the study. On admission, all of them had at least stage III NYHA dyspnea.

Sociodemographic characteristics

The mean age of the sample was 29.4 ± 3.4 years (16 and 36 years). The age group of 20-25 years was the most represented (29.16%). Patients' distribution by age group is summarized in Figure (1). The mean age was 29.1 ± 3.1 years in Br⁺ and 29.5 ± 3.8 years in Br⁻. The difference was not statistically significant ($p = 0.449$). More than two thirds of the patients had a low socioeconomic level (77.1% or 74 patients), while a high socioeconomic level was found in nine (09) patients (9.4%).

Patients' past medical history

No past medical history of hypertension or heart disease was found. There was no concept of smoking. The average of pregnancies per woman was 3.6 ± 1.5 pregnancies (1 and 9). More than the half had at least four pregnancies. The average gravidity was 3.6 ± 1.4 in Br⁺ and 3.2 ± 1.1 pregnancies in Br⁻. There was no significant difference between the two subgroups ($p = 0.615$). Twin pregnancies was noted in 10 cases, including

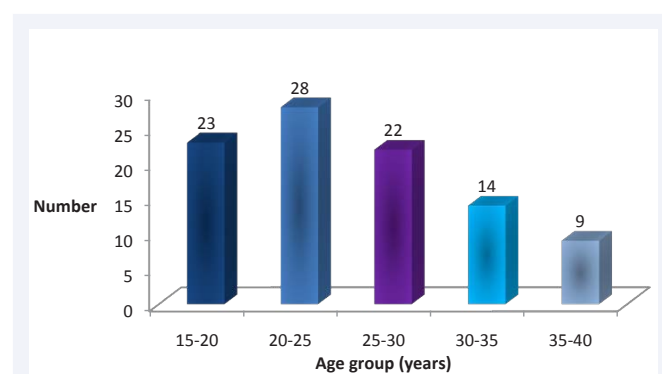


Figure 1 Patients' distribution by age range.

four (04) cases in the Br⁺ and six (06) in the Br⁻. The first heart failure symptoms on set after delivery were observed in 83.33% (80 women) and before delivery in 16 patients. Table (1) presents the period of symptoms onset by subgroup.

Follow up of Clinical signs and Para clinical findings at admission

Clinical signs: All women suffered from dyspnea. Thus, 69.7% presented a stage IV NYHA dyspnea and stage III was found in 30.3%. Women distribution by NYHA functional stage is presented on Table (2). Heart failure, cough and chest pain were present in 51 (53.12%) and 44 (45.84%) cases respectively. Table (3) summarizes physical examination results.

Paraclinical findings:

Biology: The hemoglobin was 11.9 ± 2.4 g/dl (9.1 and 13.6 g/dl) in Br⁺ and 11.7 ± 2.1 g/dl (9.3 and 14.4 g/dl) in Br⁻ without statistically significant difference between the two groups ($p = 0.899$). Creatinin value was normal in every subgroup.

Chest x-ray: The mean cardiothoracic rate was $57.4 \pm 2.2\%$ (49.7 and 61.1%) in Br⁺ and $57.2 \pm 1.8\%$ (49.5 and 62.1%) in Br⁻ ($p = 0.684$). Pleural effusion was present in 6 cases that is 4 in Br⁺ and 2 in Br⁻. Infectious lung was found in 8 cases in Br⁺ and 6 cases in Br⁻.

Electrocardiogram: The sinus rhythm was found in majority of women. A trial fibrillation and a trial tachysystoly was found in 1 case respectively. Electrocardiogram signs are summarized in Table (4).

Echocardiography data: Cardiac cavities were enlarged in all cases. The mean value of EDLVD was 58.7 ± 3.3 mm (55.2 and 63.2 mm) in Br⁺ and 57.6 ± 3.8 mm (52.3 and 63.0 mm) in Br⁻ ($p = 0.091$) while the ESLVD was 48.4 ± 4.1 mm (42.0 and 53.1 mm) in Br⁺ and 48.8 ± 3.9 mm (44.1 and 53 mm) in Br⁻ ($p = 0.074$). The mean LVEF was $37.2 \pm 6.6\%$ (22.3 and 44.4 %) in Br⁺ and $37.5 \pm 4.8\%$ (22.3 and 44.0%) in Br⁻ ($p = 0.129$) and the mean TAPSE was 19.9 ± 3.1 mm (10.3 and 28.6 mm) in Br⁺ and 18.9 ± 0.9 mm (10.1 and 26.2 mm) in Br⁻ ($p = 0.718$).

Thrombus and spontaneous contrast were present in 13 cases (13.5%). Left ventricle thrombus was present in 12 cases that 7 in Br⁺. Biven tricle thrombus were found in 2 cases (Figure 2,3) and right atrium thrombus in 1 case (Figures 4,5). Echocardiography data are summarized in Table (5).

There were no significant differences in baseline characteristics.

Table 1: Patients' distribution according to period of symptoms onset by subgroup.

Onseta	Br+	Br-	Total
Before delivery	11 (22.9 %)	5 (10.4 %)	16 (16.6 %)
With in 1 month after delivery	18 (37.5 %)	23 (47.9 %)	41 (42.7 %)
2 to 3 months after delivery	11(22.9 %)	12 (25 %)	23 (23.9 %)
4 to 5 months after delivery	8 (16.6 %)	8 (16.6 %)	16 (16.6 %)
Total	48 (100 %)	48 (100 %)	96 (100 %)

Table 2: Women distribution by NYHA functional stage on admission.

Functional stage	Br+	Br-	p
NYHA I	0	0	
NYHA II	0	0	
NYHA III	14 (29.16)	13 (27.08)	0.73
NYHA IV	34 (70.83)	35 (72.91)	0.66
Total	48 (100%)	48 (100%)	

Table 3: Distribution of physical examination findings by subgroup on admission.

Parametera	Br+	Br-	p
Systolic blood presure (mmHg)	109.9 ± 14.7	110.7 ± 15.3	0.846
Diastolic blood presure (mmHg)	62.2 ± 3.3	60.6 ± 3.5	0.819
Cardiacfrequency (bpm)	101.6 ± 12.4	97.7 ± 10.6	0.277
Height (cm)	162.4 ± 5.1	161.8 ± 6.4	0.951
Weight (kg)	65.7 ± 8.6	66.9 ± 6.8	0.696
Heart failure signs	100%	100%	

Table 4: Distribution of electrocardiogram abnormalities on admission.

Electrocardiograma	Br+ n (%)	Br- n (%)	p
Leftventricular hypertrophy	42 (87.5)	40 (83.3)	0.086
Left atrium hypertrophy	36 (75)	33 (68.7)	0.064
Right bundle branche block	10 (20.8)	13 (27.0)	0.071
Ventricular premature beat	5 (10.4)	3 (6.2)	0.053
Negative T waves	9 (18.7)	11 (22.9)	0.051
Atrial fibrillation	1 (2.0)	0	
Atrial tachysystoly	1 (2.0)	0	
Early repolarisation	1 (2.0)	3 (6.2)	0.055

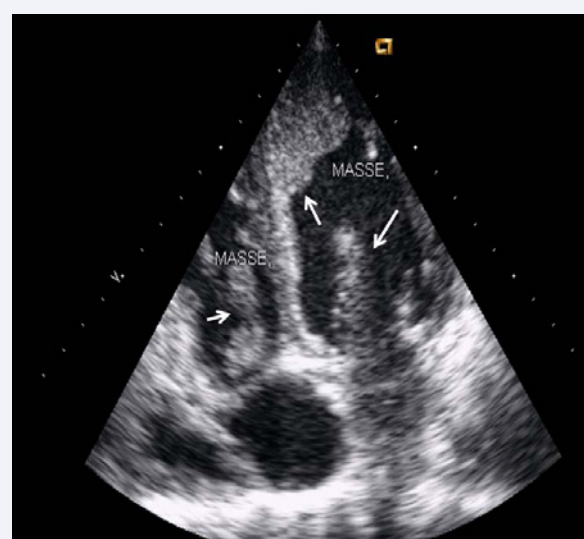


Figure 2 Biventricular and left atrium thrombi in a woman suffering from peripartum cardiomyopathy.

At two weeks: Functional stage: no patient had a stage IV NYHA dyspnea in both Br⁺ and Br⁻. Three patients in Br⁺ and 4 in Br⁻ group presented stage III NYHA. Table (6) shows functional stage at 2 weeks. v

Complications and death: Death was observed in 2 cases (4.1 %) in Br⁺ and in 4 cases (8.3 %) in Br⁻ (p = 0.001) during the 2 weeks follow up. Stroke was found in 7 cases that is 4 in Br⁺. Pulmonary embolism and lower limb ischemia occurred in the same Br⁺ woman who then undergoes thrombolysis.

Echocardiographic findings showed better improvement in Br⁺ compared to Br⁻. Mean EDLVD was 56.2 ± 1.9 mm (53.2 and 58.4 mm) in Br⁺ 57.2 ± 0.9 mm (53.2 and 59.0 mm) in Br⁻ (p = 0.001) while the ESLVD was 43.1 ± 2.6 mm (36.0 and 48.7 mm) in Br⁺ and 46.7 ± 3.5 mm (42.1 and 50.3 mm) in Br⁻ (p = 0.001). The

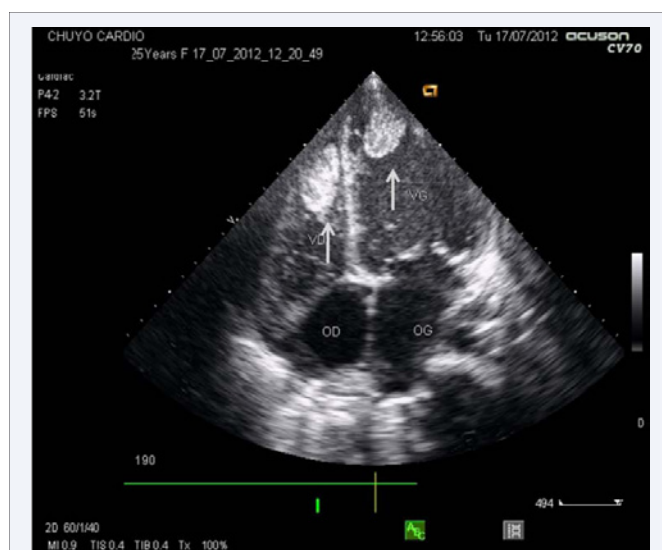


Figure 3 Biventricular apex thrombi in a woman suffering from peripartum cardiomyopathy (arrows).

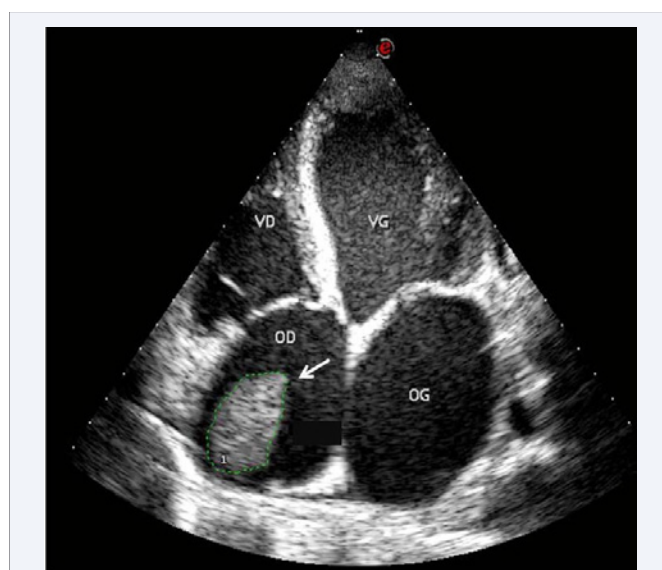


Figure 4 Right atrium thrombus (arrow) in a woman suffering from peripartum cardiomyopathy.

Table 5: Comparative echocardiographic data in global population and the two groups on admission.

Echocardiographic data	Total group	Br ⁺	Br ⁻	p
EDRVD (mm)	21.6 ± 4.8 (15.4 and 34)	23.4 ± 4.2 (15.4 and 31.8)	22.1 ± 7.1 (14.2 and 34.0)	0.623
EDLVD (mm)	58.7 ± 3.1 (55.2 and 63.2)	58.7 ± 3.3 (55.2 and 63.2)	57.6 ± 3.8 (52.3 and 63.0)	0.091
ESLVD (mm)	48.4 ± 4.5 (42.0 and 53.1)	48.4 ± 4.1 (42.0 and 53.1)	48.8 ± 3.9 (44.1 and 53)	0.074
ED IVS (mm)	7.2 ± 1.7 (5.1 and 9.2)	7.7 ± 0.9 (5.8 and 9.2)	7.3 ± 0.9 (5.1 and 8.6)	0.084
ED PW (mm)	7.5 ± 1.6 (5.4 and 9.9)	7.9 ± 1.8 (6.1 and 9.9)	7.5 ± 1.6 (5.4 and 9.7)	0.056
LVEF (%)	36.4 ± 5.5 (22.3 and 44.4)	37.2 ± 6.6 (22.3 and 44.4)	37.5 ± 4.8 (22.3 and 44.0)	0.129
LVSF (%)	18.2 ± 2.2 (14.5 and 22.8)	18.6 ± 2.8 (14.5 and 22.8)	17.9 ± 2.7 (14.5 and 21.6)	0.104
ESLAD (mm)	36.9 ± 5.8 (29.2 and 45.1)	36.6 ± 6.4 (29.2 and 44)	37.1 ± 4.9 (33.0 and 45.1)	0.031
ESLAS (cm ²)	16.7 ± 5.0 (11.0 and 26.4)	16.7 ± 3.0 (11.0 and 24.2)	17.2 ± 4.8 (12.2 and 26.4)	0.448
ESLAV (mL)	51.2 ± 13.6 (21.6 and 81.1)	50.06 ± 11.1 (21.6 and 77.9)	51.4 ± 8.8 (47.3 and 81.1)	0.114
IVCD (mm)	15.5 ± 3.2 (11.9 and 24.7)	16.7 ± 2.2 (11.9 and 24.0)	16.7 ± 4.2 (12.4 and 24.7)	0.517
SPAP (mmHg)	35.7 ± 10.2 (19.4 and 56.8)	35.7 ± 9.6 (20.1 and 56.8)	35.9 ± 11.1 (19.4 and 49.9)	0.613
TAPSE (mm)	19.5 ± 4.9 (10.1 and 28.6)	19.9 ± 3.1 (10.3 and 28.6)	18.9 ± 0.9 (10.1 and 26.2)	0.718

Abbreviations: EDRVD: End Diastolic Right Ventricular Diameter; EDLVD: End Diastolic Left Ventricular Diameter; ESLVD: End Systolic Left Ventricular Diameter; ED IVS: End Diastolic Interventricular Septum; ED PW: End Diastolic Posterior Wall; LVEF: Left Ventricular Ejection Fraction; LVSF: Left Ventricular Shortening Fraction; ESLAD: End Systolic Left Atrium Diameter; ESLAS: End Systolic Left Atrium Surface; ESLAV: End Systolic Left Atrium Volume; IVCD: Inferior Vena Cava Diameter; SPAP: Systolic Pulmonary Arterial Pressure; TAPSE: Tricuspid Annular Plane Systolic Excursion.

mean LVEF was 41.1 ± 2.1 % (37.2 and 48.9 %) in Br⁺ and 39.6 ± 5.9 % (30.2 and 48.2 %) in Br⁻ (p = 0.012) and the mean TAPSE was 21.9 ± 1.1 mm (15.7 and 28.6 mm) in Br⁺ and 19.3 ± 1.9 mm (12.3 and 24.4 mm) in Br⁻ (p = 0.001). Echocardiographic data at 2 weeks are summarized in Table (7).

At three months: Three Br⁻ women worsen in stage IV NYHA. Cumulative death was 8 in Br⁺ (16.6 %) and 12 in Br⁻ (25.0 %) p = 0.001. Comparative echocardiographic data showed more important improvement in Br⁺. Mean EDLVD was 56.0 ± 2.0 mm (53.1 and 58.0 mm) in Br⁺ and 57.2 ± 1.9 mm (53.2 and 59.0 mm) in Br⁻ (p = 0.001) while the ESLVD was 42.9 ± 2.3 mm (36.0

Table 6: Distribution of patients according to functional stage at 2 weeks.

NYHA	Br+	Br-	p
NYHA I	0	0	
NYHA II	13 (27.0)	21 (43.7)	0.0001
NYHA III	3 (6.2)	4 (8.3)	0.0872
NYHA IV	0	0	

Table 7: Comparative echocardiographic data in global population and the two groups on 2 weeks.

Echocardiographic data	Total group	Br+	Br-	P
EDRVD (mm)	20.7 ± 4.9 (14.5 and 29.0)	20.1 ± 4.2 (15.4 and 28.8)	21.9 ± 2.4 (14.5 and 29.0)	0.027
EDLVD (mm)	57.1 ± 1.1 (53.2 and 59.0)	56.2 ± 1.9 (53.2 and 58.4)	57.2 ± 0.9 (53.2 and 59.0)	0.001
ESLVD (mm)	48.1 ± 1.9 (36 and 50.3)	43.1 ± 2.6 (36.0 and 48.7)	46.7 ± 3.5 (42.1 and 50.3)	0.001
EDIVS (mm)	7.3 ± 1.7 (5.2 and 9.2)	7.7 ± 0.9 (5.8 and 9.2)	7.5 ± 0.9 (5.2 et 8.9)	0.061
EDPW (mm)	7.6 ± 1.2 (6.1 and 9.9)	7.9 ± 1.3 (6.4 and 9.9)	7.5 ± 1.0 (6.1 and 8.9)	0.055
LVEF (%)	39.2 ± 3.2 (30.2 and 48.9)	41.1 ± 2.1 (37.2 and 48.9)	39.6 ± 5.9 (30.2 and 48.2)	0.012
LVSF (%)	23.0 ± 2.3 (19.0 and 28.0)	24.7 ± 2.4 (19.9 and 28.0)	20.1 ± 1.0 (19.0 and 28.0)	0.021
ESLAD (mm)	36.9 ± 5.8 (29.2 and 43.1)	36.6 ± 2.4 (29.2 and 42.4)	37.1 ± 2.9 (33.0 and 43.1)	0.031
ESLAS (cm ²)	16.6 ± 5.0 (11.0 and 24.4)	15.7 ± 3.0 (11.0 and 22.2)	17.0 ± 4.1 (12.2 and 24.4)	0.001
ESLAV (mL)	50.2 ± 7.6 (21.6 and 60.3)	45.6 ± 4.9 (21.6 and 50.9)	47.6 ± 2.8 (21.6 and 60.3)	0.001
IVCD (mm)	15.1 ± 3.2 (10.9 and 20.7)	12.9 ± 1.2 (10.9 and 20.1)	15.9 ± 3.0 (11.4 and 20.7)	0.001
SPAP (mmHg)	26.4 ± 6.2 (18.4 and 36.9)	26.4 ± 6.6 (18.4 and 36.9)	27.9 ± 9.1 (18.4 and 36.9)	0.003
TAPSE (mmHg)	20.2 ± 5.1 (12.3 and 28.6)	21.9 ± 1.1 (15.7 and 28.6)	19.3 ± 1.9 (12.3 and 24.4)	0.001

and 48.2 mm) in Br⁺ and 46.3 ± 2.0 mm (36.0 and 49.7 mm) in Br⁻ (p = 0.001). The mean LVEF was 47.1 ± 4.0 % (39.1 and 52.0 %) in Br⁺ and 39.9 ± 5.9 % (30.2 and 48.9 %) in Br⁻ (p = 0.001) and the mean TAPSE was 21.9 ± 1.1 mm (15.9 and 28.6 mm) in Br⁺ and 20.3 ± 1.9 mm (14.8 and 24.4 mm) in Br⁻ (p = 0.001). Echocardiographic data at 3 months are presented on Table (8).

At Six months: Two women in Br⁺ (4.1%) and 6 in Br⁻ (12.5%) were re-hospitalized (p = 0.0001). Cumulative death were stayed 8 (16.6%) in Br⁺ but 14 (29.1 %) in Br⁻ (p = 0.0001). Echocardiographic findings demonstrated better improvement in ventricles function in Br⁺. Mean EDLVD was 53.4 ± 2.0 mm (50.2 and 58.0 mm) in Br⁺ and 55.1 ± 2.0 mm (51.2 and 58.2 mm) in Br⁻ (p = 0.002) while the ESLVD was 40.0 ± 2.4 mm (36.0 and 48.3 mm) in Br⁺ and 43.3 ± 2.0 mm (44.1 and 49.7 mm) in Br⁻ (p = 0.001). The mean LVEF was 49.9 ± 2.1 % (43.1 and 52.7 %) in Br⁺ and 40.9 ± 5.9 % (32.2 and 48.9 %) in Br⁻ (p = 0.001) and the mean TAPSE was 22.0 ± 1.2 mm (16.9 and 28.6 mm) in Br⁺ and 20.7 ± 2.0 mm (14.9 and 24.4 mm) in Br⁻ (p = 0.001). Table (9) shows comparative echocardiographic data at 6 months. Given symptoms onset, ventricles systolic function improvement was better when onset occurred before delivery and more preferably within 1 month after delivery although there was difference between subgroups (Table 10).

At 12 months: Neither other death nor re-hospitalization was noted. Mean LVEF was 53.9 ± 4.1 % (39.1 and 64.6 %) in Br⁺ and 45.9 ± 5.9 % (32.6 and 55.4 %) in Br⁻ (p = 0.001) and mean TAPSE was 22.7 ± 1.1 mm (15.7 and 28.9 mm) in Br⁺ and 20.9 ± 1.7 mm (15.7 and 24.7 mm) in Br⁻ (p = 0.001). Echocardiographic data at 12 months are summarized in Table (11) and Figure (5) shows LVEF evolution during follow up. LVEF increased from 37.2% on admission to 49.9% at six months and to 53.9% at 12 months in Br⁺ while it increased from 37.5% on admission to 40.9% at six months and to 45.9% at 12 months in Br⁻.

DISCUSSION

Peripartum cardiomyopathy (PPCM) remains a disease with misunderstood etiopathogenesis. It is the major cause of pregnancy-induced heart failure and is associated with high morbidity and mortality [8-11]. The true incidence of PPCM is unknown, as clinical presentation varies. Current estimates ranging from 1:299 (Haiti), 1:1000 (South Africa) to 1:3186 in the USA are primarily based on case series from single center or retrospective questionnaires [12, 13]. No data exists on the frequency of the disease in West Africa but primary studies shown that the disease seemed to be frequent. The extensive research undertaken since these last year's helped in identifying etiologic

Table 8: Comparative echocardiographic data in global population and the two groups on 3 months.

Echocardiographic data	Total group	Br+	Br-	P
EDRVD (mm)	20.6 ± 4.7 (14.5 and 29.0)	20.1 ± 3.2 (15.4 and 28.8)	21.2 ± 2.4 (14.5 and 29.0)	0.021
EDLVD (mm)	56.6 ± 2.3 (53.2 and 59.0)	56.0 ± 2.0 (53.1 and 58.0)	57.2 ± 1.9 (53.2 and 59.0)	0.001
ESLVD (mm)	48.1 ± 1.3 (36.0 and 49.7)	42.9 ± 2.3 (36.0 and 48.2)	46.3 ± 2.0 (36.0 and 49.7)	0.001
EDIVS (mm)	7.3 ± 1.7 (5.2 and 9.2)	7.7 ± 0.9 (5.8 and 9.2)	7.5 ± 0.9 (5.2 and 8.9)	0.061
EDPW (mm)	7.6 ± 1.0 (6.4 and 9.9)	7.9 ± 1.2 (6.4 and 9.9)	7.5 ± 1.0 (6.4 and 8.9)	0.055
LVEF (%)	44.2 ± 3.2 (30.2 and 52.0)	47.1 ± 4.0 (39.1 and 52.0)	39.9 ± 5.9 (30.2 and 48.9)	0.001
LVSF (%)	23.0 ± 2.3 (20.1 and 31.3)	26.4 ± 3.4 (20.1 and 31.3)	23.1 ± 2.0 (20.3 and 28.0)	0.001
ESLAD (mm)	36.9 ± 5.8 (29.2 and 43.0)	36.6 ± 4.2 (29.2 and 42.0)	37.1 ± 4.9 (31.0 and 43.0)	0.021
ESLAS (cm ²)	16.6 ± 5.0 (11.0 and 24.1)	15.7 ± 2.1 (11.0 and 22.1)	17.0 ± 4.1 (12.2 and 24.1)	0.001
ESLAV (mL)	49.2 ± 1.6 (20.6 and 50.9)	45.3 ± 4.2 (20.6 and 50.3)	48.2 ± 2.4 (21.1 and 50.9)	0.001
IVCD (mm)	15.1 ± 3.2 (10.9 and 19.0)	12.7 ± 1.3 (10.9 and 17.0)	13.9 ± 3.0 (10.4 and 19.0)	0.051
SPAP (mmHg)	26.4 ± 6.2 (18.4 and 36.9)	26.4 ± 6.6 (18.4 and 36.9)	27.9 ± 7.1 (18.4 and 36.9)	0.003
TAPSE (mm)	21.2 ± 5.0 (14.8 and 28.6)	21.9 ± 1.1 (15.9 and 28.6)	20.3 ± 1.9 (14.8 and 24.4)	0.001

Table 9: Echocardiographic data on six months.

Echocardiographic data	Total group	Br+	Br-	P
EDRVD (mm)	20.1 ± 4.7 (14.5 and 28.4)	20.0 ± 3.0 (14.5 and 28.1)	21.0 ± 1.0 (16.5 and 28.4)	0.027
EDLVD (mm)	56.1 ± 1.9 (50.2 and 58.2)	53.4 ± 2.0 (50.2 and 58.0)	55.1 ± 2.0 (51.2 and 58.2)	0.002
ESLVD (mm)	44.2 ± 2.8 (36.0 and 49.7)	40.0 ± 2.4 (36.0 and 48.3)	43.3 ± 2.0 (44.1 and 49.7)	0.001
ETD IVS (mm)	7.3 ± 1.7 (5.2 and 9.2)	7.7 ± 0.9 (5.8 and 9.2)	7.5 ± 0.9 (5.2 and 8.9)	0.069
ETD PW (mm)	7.6 ± 1.0 (6.4 and 9.9)	7.9 ± 1.1 (6.4 and 9.9)	7.5 ± 0.9 (6.4 and 8.6)	0.054
LVEF (%)	45.7 ± 3.2 (32.2 and 52.7)	49.9 ± 2.1 (43.1 and 52.7)	40.9 ± 5.9 (32.2 and 48.9)	0.001
LVSF (%)	24.0 ± 2.3 (20.1 and 35.1)	28.9 ± 3.4 (23.1 and 35.1)	24.1 ± 2.0 (20.3 and 28.0)	0.001
ESLAD (mm)	36.9 ± 5.8 (29.2 and 43.0)	36.2 ± 6.2 (29.2 and 43.0)	36.9 ± 4.0 (32.0 and 43.0)	0.021
ESLAS (cm ²)	16.6 ± 5.0 (11.0 and 24.1)	15.7 ± 2.1 (11.0 and 22.1)	17.0 ± 4.1 (12.2 and 24.1)	0.001
ESLAV (mL)	49.2 ± 1.6 (21.1 and 51.9)	45.3 ± 3.2 (20.6 and 50.3)	48.2 ± 2.4 (21.1 and 51.9)	0.001
IVCD (mm)	14.1 ± 3.2 (10.4 and 19.0)	12.7 ± 1.3 (10.4 and 17.0)	13.9 ± 3.0 (10.4 and 19.0)	0.051
SPAP (mmHg)	26.4 ± 6.0 (17.0 and 36.9)	21.4 ± 3.1 (17.4 and 29.9)	26.9 ± 9.1 (17.0 and 36.9)	0.003
TAPSE (mm)	21.2 ± 5.0 (14.9 and 28.6)	22.0 ± 1.2 (16.9 and 28.6)	20.7 ± 2.0 (14.9 and 24.4)	0.001

factors. Enhanced oxidative stress and the subsequent cleavage of the nursing hormone prolactin into an anti-angiogenic 16 kDa sub fragment emerged as a potential causal factor of the disease [7]. Therefore, Bromocriptine that block Prolactin production has been identified as a therapy way. From there, a small pilot study suggested that prolactin blockade by Bromocriptine in addition to standard therapy prevents repeated episodes of peripartum cardiomyopathy in patients presenting with a subsequent pregnancy [15]. A survey of more than 1400 pregnant women

who took Bromocriptine primarily during the first few weeks of pregnancy found no evidence of increased rates of spontaneous abortion or congenital malformations [16]. However, safety issues were raised for patients taking Bromocriptine in the early postpartum phase: a few case reports describe an increased risk of thrombotic events, such as myocardial infarction and retinal vein occlusion, in these patients [17- 19]. But in fact, never thrombotic events in peripartum cardiomyopathy patients treated with Bromocriptine and heparin have been observed [20]. In a proof of

Table 10: Improvement of LVEF at 6 months in the two groups according to dyspnea onset period.

Dyspnea on set period	LVEF (%)		p
	Br+	Br-	
Before delivery	55.5 ± 5.7	51.8 ± 5.7	0.004
With in 1 month after delivery	62.3 ± 3.9	55.5 ± 5.8	0.0001
2 to 3 months after delivery	54.8 ± 3.4	48.1 ± 4.9	0.002
4 to 5 months after delivery	51.3 ± 2.9	48.0 ± 3.3	0.003

Table 11: Comparative echocardiographic data at 12 months.

Echocardiographic data	Total group	Br+	Br-	P
EDRVD (mm)	20.0 ± 4.2 (14.0 and 28.0)	19.3 ± 3.0 (14.0 and 23.1)	19.8 ± 2.6 (14.5 and 28.0)	0.028
EDLVD (mm)	54.0 ± 2.1 (49.7 and 57.2)	52.0 ± 2.0 (49.7 and 55.3)	54.3 ± 2.7 (50.2 and 57.2)	0.001
ESLVD (mm)	44.1 ± 2.3 (36.0 and 49.4)	39.6 ± 2.1 (36.0 and 46.0)	43.0 ± 1.7 (40.1 and 49.4)	0.001
EDIVS (mm)	7.3 ± 1.7 (5.2 and 9.2)	7.7 ± 0.9 (5.8 and 9.2)	7.5 ± 0.9 (5.2 and 7.9)	0.067
EDPW (mm)	7.6 ± 1.0 (6.5 and 9.9)	8.2 ± 0.8 (6.5 and 9.9)	7.5 ± 0.8 (6.5 and 8.9)	0.053
LVEF (%)	49.4 ± 3.2 (32.6 and 64.6)	53.9 ± 4.1 (39.1 and 64.6)	45.9 ± 5.9 (32.6 and 55.4)	0.001
LVSF (%)	26.0 ± 2.3 (21.4 and 36.4)	29.7 ± 3.4 (21.4 and 36.4)	25.4 ± 2.0 (21.4 and 29.7)	0.001
ESLAD (mm)	36.9 ± 5.2 (29.2 and 43.0)	35.3 ± 4.8 (29.2 and 42.0)	36.2 ± 4.0 (30.0 and 43.0)	0.021
ESLAS (cm ²)	16.1 ± 2.3 (11.0 and 20.1)	15.1 ± 2.0 (11.0 and 20.1)	16.9 ± 2.9 (12.2 and 20.1)	0.051
ESLAV (mL)	44.2 ± 2.6 (20.6 and 50.4)	42.3 ± 3.4 (20.6 and 49.6)	45.2 ± 4.4 (21.1 and 50.4)	0.001
IVCD (mm)	14.0 ± 2.9 (10.9 and 18.3)	12.7 ± 1.3 (10.9 and 17.0)	13.9 ± 3.0 (10.9 and 18.3)	0.051
SPAP (mmHg)	26.1 ± 6.0 (15.4 and 36.0)	20.2 ± 3.7 (15.4 and 29.9)	26.3 ± 4.1 (17.0 and 36.0)	0.003
TAPSE (mm)	21.3 ± 4.0 (15.7 and 28.9)	22.7 ± 1.1 (15.7 and 28.9)	20.9 ± 1.7 (15.7 and 24.7)	0.001

concept study, Sliwa (South Africa) included 20 patients suffering from PPCM. The 10 patients randomized to standard therapy (PPCM-Std group) were treated by conventional heart failure therapy. The 10 patients randomized to standard therapy plus Bromocriptine (PPCM-Br) received Bromocriptine 2.5 mg twice a day for 2 weeks followed by 2.5 mg daily for 6 weeks in addition to standard heart failure therapy. After the initial screening and baseline visits, monthly outpatient visits were scheduled for clinical assessment and evaluation of medication compliance. Treatment with Bromocriptine resulted in a significantly larger

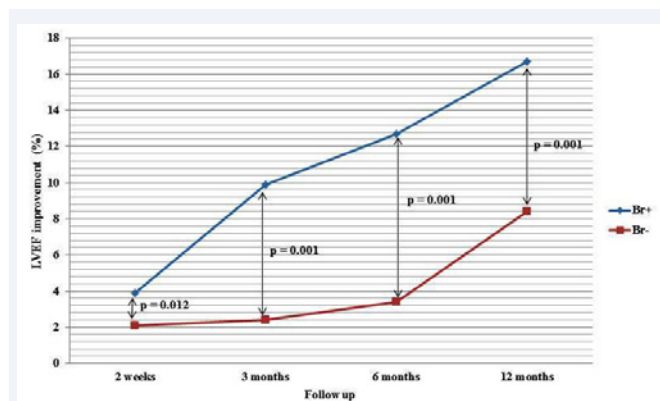


Figure 5 Evolution of left ventricular ejection fraction during follow up.

rate of LV recovery at 6 months compared with a comparable group of 10 women with PPCM treated with standard heart failure therapy alone. PPCM-Br patients displayed greater recovery of left ventricular ejection fraction (27% to 58%) compared with PPCM-Std patients (27% to 36%) ($P = 0.012$) at 6 months. In addition, there was a lower rate of mortality in PPCM-Br (1 versus 4 patients) [14]. German registry analysis demonstrated that pregnancy-associated hypertension was associated with a better outcome while a baseline LVEF < 25 % was associated with a worse outcome [20]. In our study, clinical and echocardiographic improvement was already marked the second week follow up. Clinical and echocardiographic parameters improvement was constant throughout the follow up. But echocardiographic parameters, including left ventricular systolic function were significantly improved at 6 months in the subgroup Br⁺ with a statistically significant difference. At 6 months indeed, cumulative death were 8 (16.6%) in Br⁺ and 14 (29.1 %) in Br⁻ ($p = 0.0001$). Echocardiographic findings demonstrated better improvement in ventricles function in Br⁺. Mean EDLVD was 53.4 mm in Br⁺ and 55.1 mm in Br⁻ ($p = 0.002$) while the ESLVD was 40.0 mm in Br⁺ and 43.3 mm in Br⁻ ($p = 0.001$). The mean LVEF was 49.9 % in Br⁺ and 40.9 % in Br⁻ ($p = 0.001$) and the mean TAPSE was 22.0 mm in Br⁺ and 20.7 mm in Br⁻ ($p = 0.001$). Recovering LVEF was greater in patients whose symptoms appeared before the birth or within one month after delivery. Right ventricle function assessed by TAPSE was also more improved in subgroup Br⁺. No thromboembolic phenomenon due to Bromocriptine was observed. Mortality was significantly higher in the subgroup Br⁻. These results corroborate those of Sliwa. At 12 months, the recovery of ventricular systolic function was almost complete in subgroup Br⁺. Deaths were recorded up to 6th month. After this date, there has been no death up to 12 months. Deaths were most important in Br⁻ ($p = 0.0001$) as shown Sliwa [14]. This suggests that the critical phase of disease surveillance is in the range of diagnosis to 6th month.

CONCLUSION

This study shows that peripartum cardiomyopathy is common in cardiology practice in our context. It affects middle-aged women of 29.4 years, with low socioeconomic level and multi graveide. Bromocriptine associated with standard treatment of

heart failure leads to a rapid and almost complete recovery of left and right ventricular function and reduces mortality associated with this disease. The effectiveness of this drug is greater in patients whose symptoms on set occurred before delivery or in the first month following this event. No major adverse events associated with its use have been highlighted. In view of these results, bromocriptine should be the central molecule in the treatment of peripartum cardiomyopathy, in addition of course to conventional treatment of heart failure.

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