

# Peripartum cardiomyopathy: inflammatory markers as predictors of outcome in 100 prospectively studied patients

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## KEYWORDS

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Inflammatory markers;  
Fas/Apo-1;  
C-reactive protein

**Aims** Peripartum cardiomyopathy (PPCM) is a disorder of unknown aetiology with a course and outcome that is largely unpredictable. We evaluated the prognostic role of multiple inflammatory markers in the plasma of a large cohort of African patients with PPCM.

**Methods and results** The study of 100 patients with newly diagnosed PPCM was single-centred, prospective, and longitudinal. Clinical assessment, echocardiography, and blood analysis were done at baseline and after 6 months of standard therapy. Inflammatory markers were measured at baseline only. Fifteen patients died. Left ventricular ejection fraction (LVEF) improved from  $26.2 \pm 8.2$  to  $42.9 \pm 13.6\%$  at 6 months ( $P < 0.0001$ ). However, normalization of LVEF ( $>50\%$ ) was only observed in 23%. Baseline levels of C-reactive protein correlated positively with baseline LV end-diastolic ( $r_s = 0.33$ ,  $P = 0.0026$ ) and end-systolic ( $r_s = 0.35$ ,  $P = 0.0012$ ) diameters and inversely with LVEF ( $r_s = -0.27$ ,  $P = 0.015$ ). Patients who died presented with significantly lower mean EF and higher Fas/Apo-1 plasma values ( $P < 0.05$ ). Fas/Apo-1 and New York Heart Association functional class (NYHA FC) predicted mortality at baseline.

**Conclusion** Plasma markers of inflammation were significantly elevated and correlated with increased LV dimensions and lower LVEF at presentation. Baseline Fas/Apo-1 and higher NYHA FC were the only predictors of mortality. Normalization of LVEF was only observed in 23% of this African cohort.

## Introduction

Peripartum cardiomyopathy (PPCM) is a disorder of unknown aetiology in which symptoms of heart failure occur between the last month of pregnancy and 5 months post-partum. Adherence to this time interval was emphasized to exclude pre-existing causes of heart failure that may be exacerbated by pregnancy rather than arising as a result of pregnancy.<sup>1,2</sup> The aetiology and pathogenic mechanisms have been difficult to study as its incidence and prevalence at any single institution or geographically circumscribed area are very low in western countries to allow meaningful evaluation. The incidence varies among geographic regions and has been estimated to be 1:15 000 in the USA,<sup>3</sup> 1:400 in Haiti,<sup>4</sup> and 1:1000 in South Africa.<sup>5</sup> Except for Haiti, published reports are based on data that were either derived from studies that included a small number of patients,<sup>6,7</sup> or collected from retrospective studies in which serial echocardiography was not performed in a systematic fashion.<sup>8</sup>

The high incidence of PPCM at a single centre in South Africa therefore provides a unique opportunity to initiate studies of the mechanism of pathogenesis, clinical features, and prognostic markers in this disease. Heart failure is characterized by activation of pro-inflammatory cytokines and elevation of C-reactive protein.<sup>9,10</sup> C-reactive protein is an acute-phase protein which, due to its binding specificity for phosphocholine present in a large variety of molecules, recognizes a range of pathogenic targets including membranes of apoptotic and reactive cells.<sup>11</sup> As this inflammatory marker is associated with adverse prognosis in patients with idiopathic dilated cardiomyopathy,<sup>9,10</sup> we investigated whether levels of plasma C-reactive protein at baseline could predict clinical outcome in patients with PPCM. In chronic heart failure, low levels of total cholesterol have been found to be a predictor of impaired survival.<sup>12</sup> The lipid profile in patients with PPCM has not been studied to date. In addition, cardiac myocytes have been noted to undergo apoptosis in animal models of PPCM,<sup>13,14</sup> as well in the failing human heart.<sup>15,16</sup> These findings prompted us to carry out a more detailed study aimed at correlating clinical evaluation with plasma levels of

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C-reactive protein and tumour necrosis factor (TNF)-alpha, as well as Fas/Apo-1, an apoptosis-signalling surface receptor known to trigger programmed cell death,<sup>15,16</sup> in a large cohort of African patients with PPCM.

## Methods

### Study design and patient enrolment

The protocol was approved by the Committee for Research on Human Subjects of the University of the Witwatersrand, Johannesburg, South Africa and complies with the Declaration of Helsinki. All patients and controls gave written informed consent before study entry. The objective of the study was to recruit a total of 100 consecutive patients (who happened to be black and who represent the population being seen at that clinic) with PPCM which required screening of a total of 144 patients, 44 of whom did not fit the inclusion criteria of the study. The study was conducted at the Chris Hani Baragwanath Hospital, a tertiary hospital linked to the University of the Witwatersrand, located in Soweto, South Africa, which is the sole tertiary medical facility for this community. Patients were referred from local clinics, secondary hospitals, and the Department of Obstetrics of the Chris Hani Baragwanath Hospital. History of pre-eclampsia and mode of delivery were obtained from the patient and confirmed by examining the obstetric card carried by each patient. The history of onset of symptoms and signs were recorded at the first presentation of the patients at the Chris Hani Baragwanath Hospital cardiac clinic (baseline) and after a follow-up period of 6 months (6 months visit). These were the two time points of the study.

Inclusion criteria: (i) age  $\geq 16$  and  $\leq 40$ , (ii) New York Heart Association functional classes (NYHA FCs) II–IV, (iii) symptoms of congestive heart failure that developed in the last month of pregnancy or during the first 5 months post-partum, (iv) no other identifiable cause for heart failure, (v) left ventricular ejection fraction (LVEF)  $\leq 40\%$  by transthoracic echocardiography, and (vi) sinus rhythm.

Exclusion criteria: (i) significant organic valvular heart disease, (ii) systolic blood pressure (SBP)  $>160$  mmHg and/or diastolic blood pressure  $>100$  mmHg, (iii) clinical conditions other than cardiomyopathy that could increase inflammatory markers by screening serum for rheumatoid arthritis and HIV and evidence of sepsis, (iv) treatment with anti-inflammatory drugs, (v) severe anaemia (haemoglobin concentration  $<9$  g/dL), and (vi) metabolic disorders affecting lipoprotein metabolism, i.e. thyroid disease.

Clinical assessment, echocardiography, and blood analysis were done at baseline and after 6 months of standard therapy. Inflammatory markers were measured at baseline only. All patients received treatment with diuretics and the angiotensin-converting enzyme inhibitor acupril. Patients with an EF  $\leq 25\%$  or LV thrombus received anti-coagulation therapy. Carvedilol was added after resolution of overt heart failure, and the dose was slowly titrated up to a target of 25 mg twice daily as long as SBP was  $>100$  mmHg or symptoms such as dizziness did not occur. Patients attended the cardiac clinic at least once a month for routine follow-up.

Plasma levels of C-reactive protein were measured as part of routine investigation by the hospital laboratory using a commercially available enzyme-linked immunosorbent assay (Roche Diagnostics GmbH, Mannheim, Germany). The assay used had a sensitivity of 0.1–10 mg/L and included standards that were run in parallel. Obtained values were used to calculate plasma levels in patient and control samples.

### TNF-alpha and Fas/Apo-1 levels

Fifteen millilitres of blood were drawn from each patient and controls during the day time (10.00 to 12.00 a.m.) from the antecubital vein and collected into pre-chilled vacutainer tubes containing ethylenediaminetetraacetic acid. Plasma was separated by centrifugation at

2500 r.p.m. for 12 min within 15 min of collection. Aliquots were stored at  $-80^{\circ}\text{C}$ . Plasma levels of TNF-alpha and Fas/Apo-1 were measured using commercially available enzyme-linked immunoassays (Amersham, Maidstone, USA and Calbiochem, San Diego, CA, USA, respectively) and performed according to manufacturers' instructions. The manufacturer supplied a reference range for normal values. However, as those values are obtained in samples from western population groups, we collected blood from 20 otherwise healthy, age, race, sex, body mass index, and parity comparable controls recruited from the local population.

### Functional class, echocardiography, and cardiac scintigraphy

A physician who was provided the clinical data, but was blinded to the protocol and unaware of the results of the laboratory tests, performed the assignments of each patient to the NYHA FC during baseline and follow-up visits. The same physician evaluated all patients.

A multiple-gated equilibrium cardiac blood pool scintigraphic technique (MUGA) was used to measure LVEF (Elscint Apex 409, Chicago, IL, USA), and calculations of LV performance were made as previously described.<sup>17</sup>

Two-dimensional targeted M-mode echocardiography with doppler colour flow mapping was performed using a Hewlett Packard Sonos 5500 (Philips, Bothell, WA, USA) echocardiograph attached to a 2.5 or 3.5 MHz transducer. All studies were performed and interpreted by the same operator who was unaware of the other parameters investigated. All studies were recorded on videotape. LV dimensions were measured according to the American Society of Echocardiography Guidelines.<sup>18</sup> Measurements of LV dimensions and function were determined on an average of  $\geq 3$  beats.

### Statistical analysis

Data were analysed using the SAS version 9.1 statistical programme (SAS, Cary, NC, USA). Results are expressed as mean  $\pm$  SD or median (range). The paired *t*-test was used for the comparison of baseline data with the 6 months data, whereas the Wilcoxon matched pair test was used for variables measured in a continuous scale and with a non-normal distribution. The McNemar test was used for calculating the differences on the basis of the NYHA FC by grouping the patients into two classes (I + II and III + IV). Comparison of numerical data between groups of patients was carried out using non-parametric Mann–Whitney–Wilcoxon test. Significance was assumed at a two-tailed value of  $P < 0.05$ . Spearman correlation coefficients were calculated for continuous data. Univariate logistic regression was used to select possible predictors of mortality. Continuous variables were tested for linearity generating partial residual plots. As non-linear effects were detected for all the variables, they were transformed into an ordinal scale by tertiles. The multiple logistic regression was performed including predictor variables [NYHA FC, end-diastolic diameter (EDD), end-systolic diameter (ESD), EF, Fas/Apo1, aspartate amino transferase (AST) and SBP] that had a *P*-value less than 0.15 from the univariate analysis. A good fitting model was indicated in stepwise, forward, and backward logistic regression. The resulting model for mortality selected Fas and NYHA FC as explanatory variables with a *P*-value less than 0.05 being considered significant.

## Results

### Study characteristics

The characteristics of the study population at first presentation to the cardiac clinic (baseline) are shown in *Table 1*. Although 91% of the study patients were diagnosed as PPCM patients for the first time, the remaining 9 (9%) PPCM patients had been diagnosed at a previous pregnancy. These nine patients had recovered their LV function and

**Table 1** Baseline characteristics of study population ( $n = 100$ )

Age (years)	31.6 ± 6.6
Gravidity (median)	3 (1–7)
Type of delivery (%)	89% vaginal 11% caesarean
Onset of clinical symptoms (months)	Pre-partum = 0 Within 1 month post-partum = 49% Within 2–3 months post-partum = 36% Within 4–5 months post-partum = 15%
Body mass index (kg/cm <sup>2</sup> )	25.6 ± 5.1
Blood pressure (mmHg) systolic	111.1 ± 17.4
Blood pressure (mmHg) diastolic	70.4 ± 13.5
Heart rate (b.p.m.)	93.5 ± 18.5
Left ventricular EDD (mm)	61.6 ± 7.1
Left ventricular ESD (mm)	53.1 ± 7
Ejection fraction	25.9 ± 8.2
echocardiography (%)	
Ejection fraction MUGA (%)	23.6 ± 7.8
C-reactive protein (mg/L), median (range)	10 (1–90)
Glucose (mmol/L)	4.8 ± 1.1
Total cholesterol (mmol/L)	4.2 ± 0.8
Haemoglobin (g/dL)	12.5 ± 1.7
Fas/Apo-1 (U/L), median (range)	5.5 (0.4–18.4)
TNF alpha (pg/mL), median (range)	3.6 (0.2–20.0)

experienced a subsequent episode of PPCM. None of the patients had identifiable causes for heart failure. There was no association between history of hypertension and eclampsia during pregnancy (2%) or use of tocolytic agents (9%). At the day of first presentation at the clinic (baseline), 26 patients were in NYHA FC II, 49 were in FC III, and 25 were in FC IV. LV thrombi were detected on echocardiography in 16% of the patients.

### Follow-up

Fifteen patients died within the follow-up period of 6 months, and eight patients moved to remote areas and were not available for full follow-up assessments. Patients lost to follow-up were observed for a median of 3 months (range 1–5 months). They were contactable through phone and were alive. Eleven patients died despite optimal medical therapy because of progression of heart failure in hospital and the other four patients experienced sudden death. All the patients died during the first 3 months after enrolment in the longitudinal study. Women who had a prior history of PPCM had no difference in mortality when compared with the women who had no previous history of PPCM. However, they had an intensive monitoring by the cardiologist and obstetrician throughout their pregnancy and post-partum. Baseline characteristics of patients that were not available for full follow-up assessment did not differ from the others. None of these patients died. Cardiac transplantation or LV assist device for the population studied was unavailable for the duration of the trial because of economic reasons. During the first months after enrolment, patients received standard therapy for heart failure, which included furosemide [ $n = 96$ , median daily dose 160 mg (80–250)], accupril [ $n = 96$ , median daily dose

**Table 2** Clinical variables and left ventricular function at baseline and after 6 months follow-up of survivors ( $n = 77$ )

	Baseline	6 months	P-value
Systolic BP (mmHg)	111.6 ± 16.8	116.1 ± 17.6	0.018
Diastolic BP (mmHg)	71.0 ± 12.6	72.6 ± 11.3	0.37
HR (b.p.m.)	92.8 ± 18.4	74.2 ± 12.9	0.001
NYHA FC ( $n$ )	FCs I + II = 23	FCs I + II = 72	<0.001
	FC III + IV = 54	FCs III + IV = 5	
EDD (mm)	61.2 ± 7.1	55.6 ± 8.9	<0.0001
ESD (mm)	53.4 ± 7.7	43.7 ± 10.3	<0.0001
Echo EF (%)	26.2 ± 8.2	42.9 ± 13.6	<0.0001
MUGA EF (%)	23.9 ± 8.1	43.1 ± 15.1	<0.0001

BP, blood pressure; HR, heart rate.

10 mg (10–20)], and carvedilol [ $n = 95$ , median daily dose 25 mg (6.25–50)]. Carvedilol was uptitrated as long as SBP was >100 mmHg or symptoms such as dizziness occurred. Clinical data and NYHA FC were compared at first presentation at the cardiac clinic at baseline ( $n = 100$ ) and after 6 months of standard care ( $n = 77$ ) as detailed in Table 2.

### LV function, dimension, and heart rate

Patients who completed 6 months of standard care showed a significant reduction of heart rate, LV dimensions, and significant improvement in scintigraphic and echocardiographic LVEF ( $P < 0.0001$ , Table 2) and NYHA FC ( $P < 0.001$ ). However, normalization of LVEF (>50%) was only observed in 18 (23%) patients.

### Levels of haemoglobin, glucose, and cholesterol

Mean plasma levels of haemoglobin and glucose of the PPCM patients were within the normal range (Table 1). The range of total cholesterol for the 100 PPCM patients was 2.2–6.6 mmol/L with a mean of 4.2 ± 0.9 mmol/L. There was an inverse correlation between baseline total cholesterol level and LV EDD ( $r_s = -0.35$ ,  $P = 0.0009$ ) and ESD ( $r_s = -0.38$ ,  $P = 0.0001$ ), and therefore, a positive correlation to EF ( $r_s = 0.36$ ,  $P = 0.0006$ ) was observed (Figure 1).

### Levels of C-reactive protein and pro-inflammatory cytokines

The median plasma level of C-reactive protein for the 100 PPCM patients was 10.0 mg/L (range 1–90) with 45% of patients having values of >10 mg/L (Table 2). Only 10 patients had a C-reactive protein level of <3 mg/L. Baseline plasma levels of C-reactive protein correlated positively with LV end-diastolic ( $r_s = 0.33$ ,  $P = 0.0026$ ) and end-systolic dimensions ( $r_s = 0.35$ ,  $P = 0.0012$ ), whereas the correlation with LVEF ( $r_s = -0.27$ ,  $P = 0.015$ ) was inverse (Figure 1). Plasma C-reactive protein levels also correlated inversely with levels of total cholesterol ( $r_s = -0.29$ ,  $P = 0.01$ ).

Baseline plasma levels of C-reactive protein, TNF-alpha, and Fas/Apo-1 were elevated in patients with PPCM when compared with 20 age, sex, body mass index, and parity comparable healthy volunteers (TNF-alpha 4.9 ± 4.2 vs. 1.4 ± 1.3 pg/mL, Fas/Apo-1 6.3 ± 4.1 vs. 0.84 ± 0.2 U/L, C-reactive protein 10.8 ± 13.2 vs. 3.1 ± 0.9 mg/L,  $P < 0.01$ ).

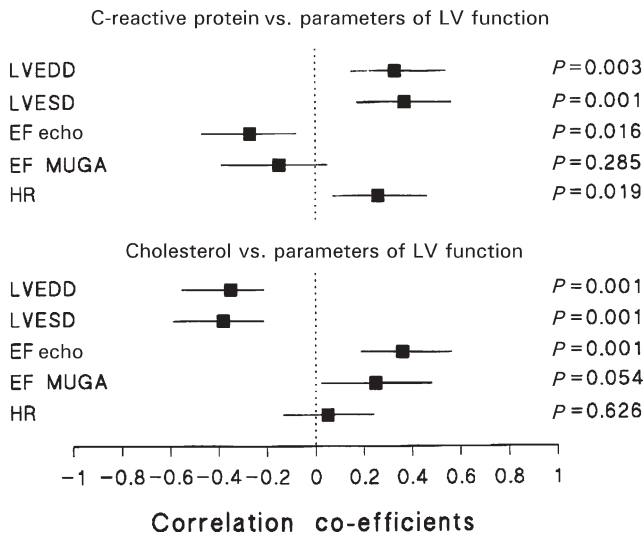


Figure 1 Correlation co-efficients of total cholesterol and C-reactive protein vs. parameters of LV dimensions and function.

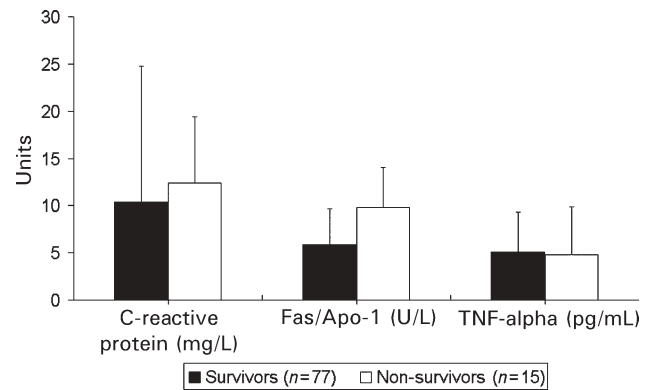


Figure 2 Baseline plasma inflammatory markers of deceased patients vs. survivors. Only differences in baseline plasma levels of Fas/Apo-1 were significant,  $P=0.002$ .

Table 3 Baseline characteristics of deceased vs. surviving patients

	Deceased (n = 15)	Survivors (n = 77)	P-value
Age (years)	28.9 ± 1.2	32 ± 6.4	0.30
No. of children (n), median (range)	2 (1-4)	3 (1-7)	0.14
Onset of symptoms after delivery (months), median (range)	1 (1-5)	2 (1-5)	0.68
HR (b.p.m.)	98.4 ± 21.0	92.2 ± 18.4	0.29
Systolic BP (mmHg)	102.1 ± 22.1	111.6 ± 16.8	0.03
NYHA FC	3.3 ± 0.7	2.0 ± 0.8	0.04
EDD (mm)	64.9 ± 5.8	61.2 ± 7.2	0.03
ESD (mm)	57.7 ± 7.3	53.4 ± 7.7	0.03
Echo EF (%)	22.2 ± 6.0	26.2 ± 8.2	0.04
AST (IU/L) median (range)	45 (12-151)	30 (1-154)	0.04
C-reactive protein (mg/L), median (range)	11.5 (2-27)	8 (1-90)	0.10
Total cholesterol (mmol/L)	4.3 ± 1.1	4.3 ± 0.9	0.87
Fas/Apo-1 (U/mL), median (range)	9.6 (2-18.4)	5.4 (0.4-14.9)	0.002
TNF (pg/mL)	3.2 (0.8-20.0)	3.6 (0.2-19.1)	0.30

BP, blood pressure; HR, heart rate.

There was no correlation between baseline plasma levels of C-reactive protein, TNF-alpha, and Fas/Apo-1 among the PPCM patients.

### Predictors of mortality

In the population studied, mortality remained high (15%). Significant differences in the baseline data between deceased patients and survivors were seen in NYHA FC, and values of SBP, end-diastolic and end-systolic dimensions, LVEF, plasma AST, a marker of hepatic congestion and liver cell death (Table 3), and plasma levels of Fas/Apo-1 (Table 3 and Figure 2). Logistic regression analysis of NYHA FC, SBP, EDD, ESD, EF, AST, and Fas/Apo-1 revealed that only the baseline plasma levels of Fas/Apo-1 (OR = 3.56, CI 95% = 1.35-9.42) and NYHA FC (OR = 2.67, CI 95% = 1.04-6.83) were independent predictors of death (Tables 4 and 5).

### Discussion

This study documented the clinical profile of 100 PPCM patients recruited prospectively at a single tertiary level hospital in South Africa and examined the role of inflammatory markers at time of diagnosis and clinical outcome after 6 months of standard clinical care. Of these, 15% of patients died and only 23% of the studied population normalized their LVEF after 6 months of therapy. Patients who died had lower NYHA FC, LVEF, and larger LV dimensions at diagnosis compared with those who survived, whereas age, parity, or onset of symptoms did not appear to play a role.

None of the patients with PPCM presented with symptoms during the pre-partum period. This is in contrast with studies performed by others,<sup>3,19</sup> and more in keeping with a study from Haiti<sup>4</sup> documenting that 96% of patients with PPCM developed heart failure in the post-partum period. Our failure to include PPCM patients during the pre-partum period in the present study was not due to lack of identifying

**Table 4** Univariate logistic regression analysis of survivors vs. deceased

	Odds ratio	95% Confidence interval	P-value
Age (years)	0.96	0.89–1.04	0.30
SBP (mmHg)	0.96	0.93–1.00	0.06
NYHA FC	2.35	1.03–5.34	0.04
EDD (mm)	1.07	0.99–1.16	0.07
ESD (mm)	1.07	0.99–1.15	0.06
Echo EF (%)	0.95	0.89–1.02	0.14
Fas/Apo-1(U/mL)	1.25	1.08–1.45	0.003
AST (U/L)	1.02	0.99–1.04	0.07
TNF-alpha (pg/mL)	0.99	0.86–1.14	0.83

**Table 5** Backward logistic regression analysis\*

	Odds ratio	95% Confidence interval	P-value
Fas/Apo-1(U/L) (tertiles)	3.56	1.35–9.42	0.01
NYHA FC	2.67	1.04–6.83	0.04

\*All variables from univariate analysis were included ( $P < 0.15$ ), but were not part of the final model, as they were not significant.

such patients as the cardiologists at the Chris Hani Baragwanath Hospital are routinely involved in the care of pregnant patients presenting with symptoms and signs of congestive cardiac failure. We could not confirm factors mentioned by others,<sup>3,19</sup> such as multi-parity, older age, or long-term use of tocolytic agents, to be associated with the development of PPCM. At presentation, this group of patients had acute-onset heart failure of short duration. There was no evidence of chronic disease or cardiac cachexia, which could account for a low lipid profile being a marker of severe chronic disease. Mean plasma levels of total cholesterol of the population studied was  $4.2 \pm 0.8$  mmol/L and low when compared with that reported in other studies.<sup>13,20,22</sup> In a study by Rauchhaus and colleagues with an established plasma cholesterol cut-off level of  $<5.2$  mmol/L, low total cholesterol level was found to be predictive for impaired 1-year survival.<sup>22</sup> In line with findings by others<sup>20,21</sup> demonstrating an increase in the rate of mortality with low serum total cholesterol levels, we found an association of low total cholesterol levels with larger LV dimensions and lower EF. There was a trend, but no significant association with the rate of mortality which could possibly be explained by the short duration of the trial, the limited number of patients studied, and the spontaneous recovery rate typical for patients with PPCM. Levels of low plasma cholesterol correlated positively with the levels of the inflammatory marker C-reactive protein. Plasma sampled from almost half of the population studied had raised levels of C-reactive protein reflecting possibly the presence of a low-grade chronic inflammatory process due to the release of endotoxin or endotoxin-like substances and subsequent release of pro-inflammatory cytokines.<sup>22</sup> As C-reactive protein measurements are relatively inexpensive, they could provide us with a readily

available tool to identify patients with an ongoing inflammatory process. A recent trial by Albert *et al.*<sup>23</sup> showed a significant variation in the distribution of plasma C-reactive protein levels among various ethnic groups living in the USA. Median plasma C-reactive protein levels were significantly higher among black women when compared with their white, Hispanic or Asian counterparts. As 40% of the variance of plasma C-reactive protein plasma levels is genetically determined and PPCM is much more frequent in black patients, one could hypothesize that an increase in the intensity of an inflammatory response could be one of many factors contributing towards the development of PPCM. This is supported by our previous research in PPCM patients presenting with subsequent pregnancy where we observed an exaggerated post-partum pro-inflammatory cytokine surge possibly playing a role in the development of PPCM.<sup>24</sup>

Plasma levels of Fas/Apo-1 as markers of potential cardiac myocyte loss were significantly higher in PPCM patients when compared with healthy controls and a predictor of mortality. A recent study by Podewski *et al.*<sup>14</sup> documented a high incidence of post-partum mortality in a cardiac tissue-specific signal transducer and activator of transcription 3 (STAT 3) knock out strain of mice. Prior to death, those female mutant mice presented with symptoms of heart failure, reduced cardiac function, and significant levels of cardiac myocyte apoptosis. Their data suggested that the cardiac myocyte-specific STAT3 pathway is necessary for the protection of the heart from post-partum stress. In addition, data from another mouse model of PPCM suggest that the apoptosis of cardiomyocytes is the basis for the development of PPCM and that pharmacological inhibition of apoptosis by a caspase inhibitor might offer novel therapeutic strategies.<sup>13</sup> These data and the finding of raised Fas/Apo-1 plasma levels in humans with PPCM indicate that cardiac myocyte apoptosis may contribute to the pathogenesis of PPCM.

This idea is further supported by a study in patients with PPCM where we have demonstrated improved clinical outcome in patients receiving pentoxifylline, an immunomodulating agent, added to conventional therapy.<sup>6</sup> Pentoxifylline has been shown to inhibit apoptosis in different human cell lines *in vitro*<sup>25</sup> and *in vivo*.<sup>26</sup> In addition, a study by Tsutamoto *et al.*<sup>27</sup> found plasma sFas as a useful prognostic marker, independent of neurohormonal factors.

### Study limitations

Our study was not designed to investigate the causes for raised plasma levels of TNF-alpha, C-reactive protein, and Fas/Apo-1. We therefore did not measure various other inflammatory markers such as plasma levels of soluble TNF-receptor plasma levels or endotoxin levels. Owing to limited funding available at the onset of this study, patients were only followed-up for 6 months.

### Conclusions

Plasma markers of inflammation were significantly elevated in PPCM patients and correlated with increased LV dimensions and lower EF at presentation. Baseline Fas/Apo-1 and higher NYHA FC were the only predictors of mortality. These results contribute to previous findings by our group

and others that apoptosis and inflammation may contribute to the pathogenesis of PPCM<sup>6,13,28</sup> and deserves further investigation. Despite standard medical therapy, normalization of LVEF was only observed in 23% of this African cohort.

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**Conflict of interest:** none declared.

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