

Prospective study on changes in blood variables in pregnant women at higher risk of peripartum cardiomyopathy

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Abstract

Aims Echocardiography is necessary for the diagnosis of peripartum cardiomyopathy (PPCM). Multifetal pregnancies (MFP) and hypertensive disorders (HD) are prominent risk factors for PPCM. To determine which blood variables exhibit greater change in a late stage of pregnancy in women with MFP and/or HD compared with women with normotensive singleton pregnancies.

Methods and results Serum levels of six variables—high-sensitive troponin I (hs-TnI), N-terminal fragment of precursor protein brain-type natriuretic peptide (NT-proBNP), myoglobin, creatine kinase-myocardial band, ferritin, and prolactin—were compared between 29 women with MFP ($n = 13$) and/or HD ($n = 18$) and 100 women with normotensive singleton pregnancies (control group). None of 129 women developed PPCM. All variables increased significantly peripartum in both groups. In 29 women with MFP and/or HD, the elevated hs-TnI and NT-proBNP levels (median) were significantly higher compared with the control group (5.4 vs. 3.7 pg/mL for hs-TnI with $P = 0.002$, 185 vs. 68 pg/mL for NT-proBNP with $P = 0.007$), and the prevalence rate of more than 90th percentile value specific for the 129 women was significantly more frequent for hs-TnI (>12.2 pg/mL; 31% [9/29] vs. 4.0% [4/100], $P < 0.001$) and tended to be more frequent for NT-proBNP (>342 pg/mL; 21% [6/29] vs. 7.0%, $P = 0.072$).

Conclusions Both hs-TnI and NT-proBNP were likely to increase markedly in women with MFP and/or HD. The combination of hs-TnI and NT-proBNP may contribute to better selection of candidates for echocardiography.

Keywords Cardiac biomarkers; Maternal mortality; Peripartum cardiomyopathy; Pre-eclampsia; Twin pregnancy

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Introduction

Peripartum cardiomyopathy (PPCM) is a cause of pregnancy-associated heart failure and occurs typically peripartum (during the last month and up to 6 months after pregnancy) in women without known cardiovascular disease.¹ The estimated incidence of PPCM varies markedly 0.03% in the USA,² 0.1% in South Africa,³ and 0.3% in Haiti.⁴ As baseline cardiac function at the time of PPCM diagnosis can predict outcome,^{5–8} increased awareness of PPCM is required for early diagnosis and aggressive therapy to prevent

complications.⁷ However, diagnosis of PPCM is often delayed resulting in major adverse events, such as death or the necessity for heart transplantation,^{6,7} and the maternal mortality rate ranges from 4 to 15%.^{6,8–10}

It may be important to screen for women at higher risk of PPCM before a definite diagnosis of PPCM with echocardiography. Clinical symptoms associated with PPCM include dyspnoea, oedema, and large weight gain.⁹ However, oedema is common even in healthy pregnant women¹¹ and dyspnoea may be a late sign of PPCM. In epidemiological studies, multifetal pregnancy (MFP) and hypertensive disorder (HD)

in pregnancy, including gestational hypertension, pre-eclampsia, and chronic hypertension, are consistent and prominent risk factors for PPCM, accounting for 7–15% and 15–68% of all PPCM cases, respectively.¹² For example, in a study of 102 Japanese women with PPCM,⁸ 15 and 42 were complicated with MFP and HD, accounting for 15 and 41% of all PPCM cases, respectively. As MFP accounts for approximately 1.0% of all pregnancies in Japan¹³ and HD occurs in approximately 5% of all general pregnant Japanese women,¹⁴ these results indicated that women with MFP and HD were at approximately 15-fold and 8-fold higher risk of developing PPCM, respectively, compared with the general population.

As a result of elevated left ventricular filling pressure because of systolic dysfunction, women with PPCM commonly have an increased blood level of BNP or N-terminal fragment of precursor protein brain-type natriuretic peptide (NT-proBNP),¹ and a gradual increase in BNP before the development of PPCM is reported.¹⁵ Under such conditions of heart failure, other blood parameters can change. The serum levels of troponin I (TnI), myoglobin, and creatine kinase myocardial band (CK-MB) are elevated in patients with cardiac myocyte damage. Iron deficiency is common in patients with heart failure.¹⁶ The serum ferritin concentration is correlated with total body iron stores and is therefore a convenient laboratory test to assess iron stores. In the 2012 European Society of Cardiology guidelines for the diagnosis and treatment of heart failure, determination of serum ferritin level is recommended in all patients with suspected heart failure.¹⁷ Increased serum level of prolactin (PRL) was suggested to be involved in the pathogenesis of PPCM.¹⁸ If we assumed that these variables changed significantly before the clinical manifestation of PPCM, the degrees of change in these parameters would be greater for women with MFP and/or HD than for those with normotensive singleton pregnancies. Blood parameters that exhibit greater changes peripartum in women with MFP and/or HD than in women with normotensive singleton pregnancies may be candidates for blood variables to predict the risk of PPCM. However, to our knowledge, no systematic studies from the prospective viewpoint have been reported to date.

This partly longitudinal study was conducted to examine our hypothesis that some of the six blood variables, i.e. high-sensitive troponin I (hs-TnI), NT-proBNP, myoglobin, CK-MB, ferritin, and PRL, exhibit greater changes in perinatal women with risk factors of PPCM including MFP and HD than those with normotensive singleton pregnancies.

Methods

This partly longitudinal and prospective study was conducted after being approved by the Institutional Review Board of Hokkaido University Hospital, and written informed consent was obtained from all pregnant participants. This study was undertaken following the provisions of the Declaration of

Helsinki (Br Med J 1964;ii: 177). A total of 129 pregnant women participated in this study and provided a total of 332 blood specimens at various stages of pregnancy. All gave birth between October 2009 and August 2011 at our institution, and none developed cardiac dysfunction that was clinically detectable and left hospital without complications. HD was diagnosed in women who exhibited hypertension (systolic ≥ 140 mmHg or diastolic ≥ 90 mmHg) on at least two occasions, recorded 6 h apart during pregnancy.

Of the 129 women, 116, 12, and 1 had singleton, twin, and triplet pregnancies, respectively. Sixteen of the 116 women with singleton pregnancies developed HD, and the remaining 100 remained normotensive during pregnancy. These 100 women with normotensive singleton pregnancies served as a control group, and the remaining 29 women with MFP and/or HD were treated as the study group (*Table 1*). As two of 13 women with MFP developed HD, the study group included 18 women with HD. Demographic characteristics of the 129 women were obtained from medical charts. Blood sampling was performed at five different pregnancy stages, i.e. gestational week (GW) 23–28 (termed P1) and 31–38 (termed P2), and on postpartum days 2–3 (termed PPD1), 6–7 (termed PPD2), and 25–35 (termed PPD3) (*Table 1*). At any stage of pregnancy, more than 30% of participants provided blood specimens in both the control and study groups. The numbers of blood specimens (median and range) provided per woman were 3 (1–5) and 3 (1–5), respectively, and the numbers of specimens totalled 256 and 76 in the control and study groups, respectively (*Table 1*).

Serum were separated and stored at -40°C until assays of six blood variables, i.e. hs-TnI, NT-proBNP, myoglobin, CK-MB, ferritin, and PRL. Serum NT-proBNP levels were measured using a chemiluminescence immunoassay kit for NT-proBNP at Special Reference Laboratory Co., Tokyo, Japan. Serum levels of hs-TnI, myoglobin, CK-MB, ferritin, and PRL were measured using corresponding chemiluminescence immunoassay kits (ARCHITECT High Sensitive Troponin-I^{TR}, ARCHITECT Myoglobin^{TR}, ARCHITECT CK-MB^{TR}, ARCHITECT Ferritin^{TR}, and ARCHITECT Prolactin^{TR}, respectively; Abbott Japan Co., Ltd. Chiba, Japan). The intraassay coefficients of variation were less than 5.0% for all six variables. The interassay coefficients of variation were less than 5.0% for hs-TnI, NT-proBNP, CK-MB, and PRL, and less than 10% for myoglobin and ferritin. According to the manufacturer's data, the 99th percentile value is 15.6 pg/mL for hs-TnI among 764 healthy women aged 21–75 years old. Therefore, a laboratory threshold of 15.6 pg/mL hs-TnI was used in this study to rule out cardiac damage. A laboratory threshold of 125 pg/mL NT-proBNP was used to rule out cardiac dysfunction. However, as all of the above assays were performed after all participants gave birth and left hospital, medical interventions were not altered according to the data for these six variables.

Data are presented as the median (range) or median (25th–75th percentiles). Statistical analyses were performed

Table 1 Demographic characteristic of study subjects

	Control group	Study group	<i>P</i> value
Number of women	100	29	
Singleton pregnancy	100	16	
Twin pregnancy	0	12	
Triplet pregnancy	0	1	
Hypertensive disorder	0	18	
Age (years)	34 (20–42)	34 (22–43)	0.856
Primiparity (%)	62 (62%)	15 (52%)	0.067
Pre-pregnancy weight (kg)	52 (39–95)	53 (40–120)	0.209
Pre-pregnancy BMI (kg/m ²)	20.3 (16.6–44.6)	21.4 (16.7–44.6)	0.095
Weight gain in pregnancy (kg)	8.9 (–1.3–20.6)	10.8 (–8.1–16.7)	0.140
GW at delivery	38 (28–41)	36 (24–40)	< 0.001
<37	7 (7%)	16 (55%)	< 0.001
Caesarean section	49 (51%)	25 (86%)	< 0.001
No. of women who provided blood specimens at various pregnancy stages			
P1 (GW 23–28)	50 (50%)	16 (55%)	
P2 (GW 31–38)	71 (71%)	16 (55%)	
PPD1 (PPD 2–3)	46 (46%)	14 (48%)	
PPD2 (PPD 6–7)	31 (31%)	12 (41%)	
PPD3 (PPD 25–35)	58 (58%)	18 (62%)	
Total no. of specimens	256	76	
No. of specimens/woman	3 (1–5)	3 (1–5)	0.889

Data are presented as the median (range).

BMI, body mass index; GW, gestational week; P1 and P2, pregnancy stage 1 and 2, respectively; PPD, postpartum day; PPD1–3, postpartum day stages 1–3, respectively.

using JMP® Pro 11 statistical software package (SAS, Cary, NC). Differences in the means were tested using the Wilcoxon rank sum test between each group, and categorical variables were compared using Fisher's exact test. In all analyses, $P < 0.05$ was taken to indicate statistical significance.

Results

As the study group included 13 and 18 women with MFP and HD, respectively, delivery occurred significantly earlier and caesarean section rate was significantly higher for the study group than for the control group (*Table 1*).

Changes in serum levels of hs-TnI, NT-proBNP, myoglobin, CK-MB, ferritin, and PRL during pregnancy and postpartum

In comparison with baseline values determined at GW 23–28, all variables increased significantly peripartum irrespective of the presence or absence of MFP/HD except for PRL in the study group (*Figure 1*). The hs-TnI level that was already significantly higher during the third trimester in the study group than in the control group, peaked at PPD2 (in the study group) or PPD1 (in the control group), and then decreased at PPD3 to the level seen during the second trimester in both control and study groups. NT-proBNP exhibited a similar pattern of changes to hs-TnI. However, hs-TnI rather than NT-proBNP appeared to differentiate well between women with MFP/HD and controls. The antepartum ferritin level was

significantly higher in the study group than the control group, but this difference disappeared postpartum (*Figure 1*).

Variables prone to a greater change in women with MFP and/or HD

Maximum values of six variables for each woman were compared between two groups. The median values of hs-TnI, NT-proBNP, myoglobin, and ferritin were significantly higher in the study group than the control group (*Table 2*). In sub-analyses of the 29 women in the study group, the median hs-TnI (4.5 pg/mL), NT-proBNP (185 pg/mL), myoglobin (35.1 ng/mL), CK-MB (1.3 ng/mL), and PRL (305 ng/mL) values for 13 women with MFP were significantly higher than those for the 100 control women (*Table 2*). The median hs-TnI (5.8 pg/mL) value for 16 women with HD with singleton pregnancies was significantly higher than that for the 100 control women. The median NT-proBNP (184 pg/mL) value tended to be higher ($P = 0.052$), and the prevalence of NT-proBNP > 342 pg/mL was significantly higher for 16 women with HD with singleton pregnancies than those for the 100 control women.

For the 129 women in both control and study groups, the 90th percentile value for hs-TnI was 12.2 pg/mL, that for NT-proBNP was 342 pg/mL, that for myoglobin was 57.8 ng/mL, that for CK-MB was 1.6 ng/mL, that for ferritin was 91.2 ng/mL, and that for PRL was 434 ng/mL (*Table 2*). Nine (31%) of 29 women with MFP and/or HD showed hs-TnI values of > 12.2 pg/mL, while 4 (4.0%) of 100 women with normotensive singleton pregnancies showed this level of hs-TnI ($P < 0.001$). Thus, women with MFP and/or HD

Figure 1 Changes in serum levels of various biomarkers during pregnancy and postpartum. The dotted and solid lines indicate median values of control ($n = 100$) and the study ($n = 29$) groups, respectively. Numbers of data available for each stage of pregnancy in the control vs. study groups are shown in Table 1. *, $P < 0.05$ vs. baseline value determined at pregnancy stage P1; †, $P < 0.05$ between two groups; P1, pregnancy stage of gestational week 23–28; P2, pregnancy stage of gestational weeks 31–38; PPD1, postpartum days 2–3; PPD2, postpartum days 6–7; PPD3, postpartum days 25–35.

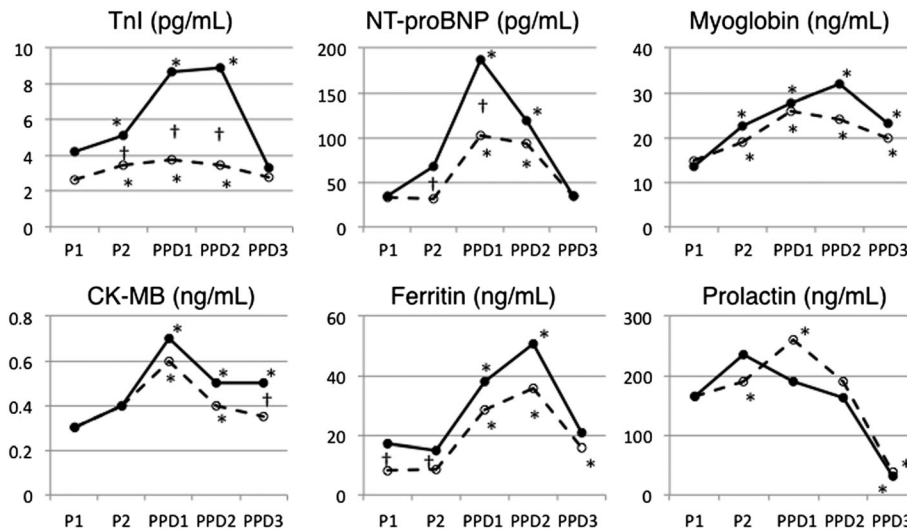


Table 2 Comparison of maximum values of six variables between two groups

	Control group ($n = 100$)	Overall ($n = 29$)	Study group MFP ($n = 13$)	HD ($n = 16$)
Number of women	100	29	13	16
TnI	3.7 (1.8–54.7)	5.4 (1.9–76.7)*	4.5 (2.3–32.7)*	5.8 (1.9–76.7)*
>12.2 pg/mL ^a	4 (4.0%)	9 (31%)*	3 (23%)*	6 (38%)*
NT-proBNP	68 (5–729)	185 (14–1086)*	185 (24–499)*	184 (14–1086)
>342 pg/mL ^a	7 (7.0%)	6 (21%)*	2 (15%)*	4 (25%)*
Myoglobin	26.6 (11.7–133)	32.5 (12.7–99.2)*	35.1 (12.7–67.0)*	27.0 (13.0–99.2)
>57.8 ng/mL ^a	9 (9.0%)	5 (17%)*	3 (23%)*	2 (13%)*
CK-MB	0.7 (0.1–2.7)	0.9 (0.2–9.3)	1.3 (0.2–3.9)*	0.6 (0.2–9.3)
>1.6 ng/mL ^a	9 (9.0%)	4 (14%)*	2 (15%)*	2 (13%)*
Ferritin	24.6 (3.51–688)	38.2 (4.27–259)*	38.2 (4.27–259)	37.8 (7.3–110)
>91.2 ng/mL ^a	9 (9.0%)	4 (14%)*	2 (15%)*	2 (13%)*
PRL	230 (27.2–680)	269 (130–607)	305 (157–607) *	239 (130–453)
>434 ng/mL	10 (10%)	2 (7%)*	1 (9%)*	1 (8%)*

The median (range) or number of women (percentage) is indicated. Two of 13 women with MFP were complicated with HD, and all 16 women with HD were singleton pregnancies.

^a90th percentile value for 129 women.

* $P < 0.05$ vs. control group.

were likely to exhibit >90th percentile hs-TnI value compared with controls. Although women with MFP and/or HD tended to exhibit NT-proBNP value of >342 pg/mL, neither the fraction size of women with >90th percentile value of NT-proBNP, myoglobin, CK-MB, ferritin, nor PRL differed significantly between the study and control groups (Table 2), suggesting that among the six variables, hs-TnI was the best biomarker for differentiation of women with MFP and/or HD from those with normotensive singleton pregnancies.

Chronological relationship between appearances of hs-TnI and NT-proBNP values above threshold

Six women exhibited both hs-TnI and NT-proBNP values above the respective thresholds (>15.6 pg/mL for hs-TnI and >125 pg/mL for NT-proBNP). Chronological changes in both values of these six women are shown in Figure 2. Five cases (Cases 1–5) were from the study group, and the remaining one (Case 6) was from the control group. The

appearance of NT-proBNP >125 pg/mL preceded that of hs-TnI >15.6 pg/mL in three cases (Cases 1–3) and occurred simultaneously in the remaining three (Cases 4–6) (Figure 2). Thus, the rise to a value above threshold was likely to occur earlier for NT-proBNP than for hs-TnI in pregnant women. The prevalence rate of women with both values above threshold was significantly greater in the study group than in the control group [17% (5/29) vs. 1.0% (1/100), $P=0.002$]. In the remaining 123 women, four (3 from the study group) and 40 (12 from the study group) exhibited hs-TnI >15.6 pg/mL alone and NT-proBNP >125 pg/mL alone, respectively. Thus, the number of women with either hs-TnI value >15.6 pg/mL [28% (8/29) vs. 2.0% (2/100), $P<0.001$] or NT-proBNP >125 pg/mL [59% (17/29) vs. 29% (29/100), $P=0.004$] was significantly greater in the study group than the control group, suggesting that women with MFP and/or HD were likely to exhibit the TnI level above threshold as well as the NT-proBNP level above threshold compared with women with normotensive singleton pregnancies.

Correlations between the six variables

There were six statistically significant correlations between log-transformed serum levels of the six variables examined in this study: between hs-TnI and three other variables (NT-ProBNP, myoglobin, and ferritin), between NT-proBNP and ferritin, between myoglobin and ferritin, and between CK-MB and myoglobin (Figure 3). Pearson correlation coefficients ranged from 0.189 (for hs-TnI and ferritin) to 0.561 (for NT-proBNP and ferritin) indicating that these correlations were not strong.

Discussion

The present study demonstrated that peripartum hs-TnI and NT-proBNP levels were significantly higher in women with than without MFP/HD. As both MFP and HD are prominent risk factors for PPCM^{8,12} and both hs-TnI and NT-proBNP levels are markedly elevated in women diagnosed with PPCM,^{19,20} our results suggest that these two variables may be useful to predict women at higher risk of PPCM. In addition, the results of this study may be helpful for clinicians in appropriate interpretation of data on six blood variables in pregnant women in various clinical settings.

PPCM is a distinct form of cardiomyopathy, associated with a high morbidity and mortality, but also with the possibility of full recovery.¹ As baseline cardiac function at the time of PPCM diagnosis can predict outcome^{5–8} and the final diagnosis of PPCM is made based on echocardiographic findings,¹ a high index of suspicion is required among obstetricians for early referral to cardiologists before profound cardiac dysfunction occurs. Therefore, a screening blood test for detection of candidates for echocardiography would be convenient for both pregnant women and physicians. In our previous experience in a patient with impending PPCM,¹⁵ gradual worsening of cardiac function and concomitant and gradual rise in plasma BNP occurred before fulfilling the criteria for diagnosis of PPCM with echocardiography, and an early termination of pregnancy after the diagnosis may have facilitated improvement of cardiac function.¹⁵

The serum NT-proBNP level is elevated in PPCM women^{19,20}: 940 ± 208 pg/mL for 52 PPCM women vs. 210 ± 68 pg/mL for 52 healthy pregnant women.²⁰ It also reflects the severity of PPCM: in PPCM patients with persisting cardiac dysfunction, NT-proBNP remains high, while it decreases

Figure 2 Chronological relationship between appearances of hs-TnI and NT-proBNP values above threshold in 6 women. The red and blue horizontal lines indicate hs-TnI (15.6 pg/mL) and NT-proBNP (125 pg/mL) threshold values, respectively. Six women exhibited both hs-TnI and NT-proBNP values above the threshold (5 and 1 from the study and control groups, respectively). NT-proBNP exceeded the threshold level earlier than hs-TnI in three cases (Cases 1–3).

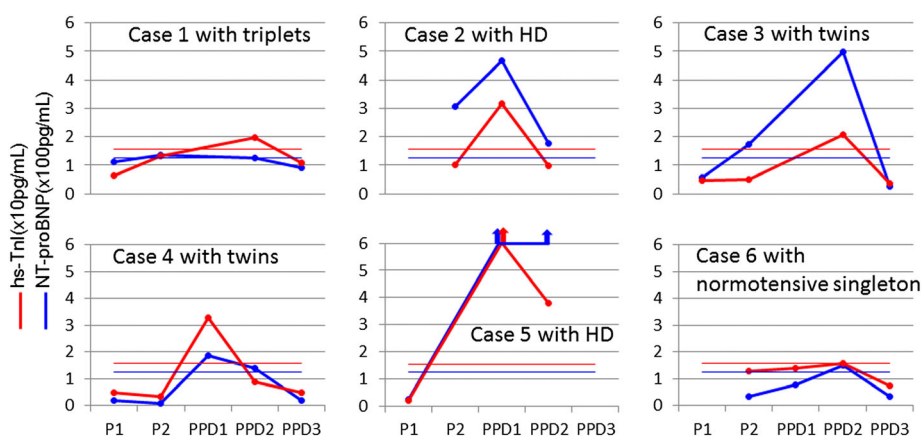
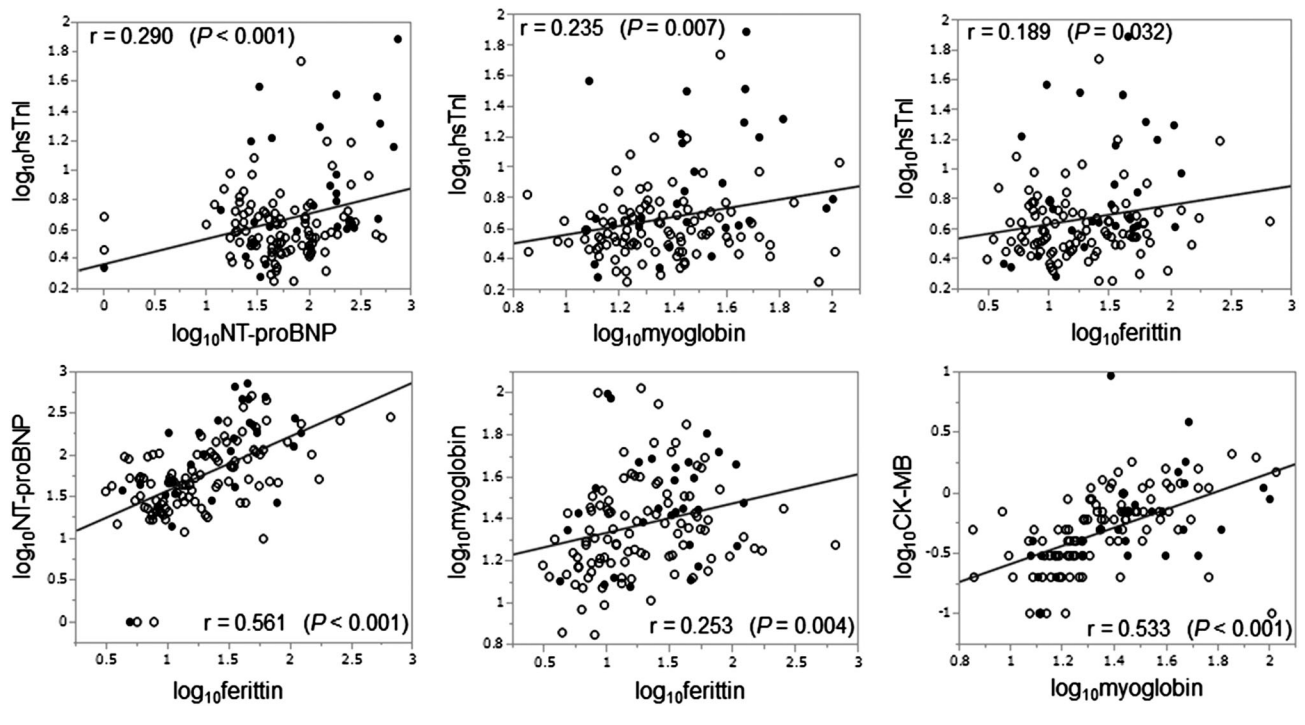


Figure 3 Correlations between six variables. The closed and open circles indicate women belonging to the study group ($n = 29$) and control group ($n = 100$), respectively. Analysed data on hs-TnI, NT-proBNP, myoglobin, CK-MB, and ferritin were those in the blood exhibiting the maximum hs-TnI value for each woman.



with improving cardiac dysfunction.¹⁹ In addition, as the serum NT-proBNP level was reported to increase in women at higher risk of PPCM, i.e. women with MFP²¹ and women with HD,^{22,23} the results of the present study regarding NT-proBNP were expected, and this variable may be a good choice for blood tests to detect women at higher risk of PPCM. However, the NT-proBNP level was much lower in women with MFP/HD compared with that reported in patients with PPCM.²⁰ As shown in this study, a considerable number of healthy pregnant women (29 of 100 normotensive singleton pregnancies in this study) exhibited NT-proBNP levels above the threshold, and an appropriate NT-proBNP cutoff level has not been determined. Some additional blood parameters may help to identify women with impending PPCM. Candidates for other possible blood parameters to predict the risk of PPCM included hs-TnI, a marker of cardiac myocyte damage that also increases in patients with heart failure,²⁴ myoglobin, CK-MB, ferritin, and PRL examined in this study. However, elevated levels of the latter four parameters did not differ between women at higher and lower risk of developing PPCM. Some of the four parameters may change greatly only around or after the development of PPCM.

To our knowledge, there have been only a few reports regarding TnI levels in pregnancy.^{20,25,26} In an earlier study in 1999,²⁶ examining 51 healthy women during parturition, demonstrated that none exceeded a TnI threshold of 150 pg/mL to rule out acute coronary syndrome. Another

study in 2000,²⁵ examining 43 healthy and 26 women with HD with singleton pregnancies around GW 35 demonstrated a significantly higher median TnI value in women with HD than in normotensive women (118 pg/mL vs. 30 pg/mL, $P < 0.0001$), consistent with the results of the present study, although absolute TnI values differed markedly from those in the present study, perhaps because of differences in assay methods used. In addition, a significantly higher TnI level was reported in PPCM women (170 ± 180 pg/mL for 52 PPCM women vs. 60 ± 50 pg/mL for 52 healthy pregnant women, $P < 0.01$).²⁰ It was speculated that the high level of TnI seen in PPCM patients may not have occurred abruptly based on our findings. The hs-TnI level began to increase during pregnancy, peaked within 7 days after delivery, and then decreased to the baseline level at approximately one-month postpartum, suggesting that termination of pregnancy decreased the hs-TnI level. If delivery did not occur in a timely manner, hs-TnI may have continued to rise until delivery. The present study also demonstrated that not only women with HD but also women with MFP were likely to exhibit raised hs-TnI levels, confirming our expectations. Taken together, these results indicate that hs-TnI may be a blood parameter that can predict the risk of PPCM.

Our study suggested that the combined use of hs-TnI and NT-proBNP would efficiently reduce the number of pregnant women who are recommended to undergo echocardiography for investigation of cardiac function. Cutoff values of 15.6 pg/mL

for hs-TnI and of 125 pg/mL for NT-proBNP yielded positivity rates of 7.8% (10/129) for hs-TnI test vs. 36% (46/129) for NT-proBNP test, and the prevalence rate of women with double positive test results was 4.7% (6/129) in this study population. However, PPCM is uncommon, occurring in 0.03–0.3% of women.^{2–4} It was speculated that PPCM is more likely to occur among women with double positive test results than those with other test results based on previous reports that women with PPCM exhibit higher levels of both NT-proBNP and TnI^{19,20} and the present findings that five of six women with double positive test results had demographic risk factors for PPCM, i.e. MFP and/or HD. The following screening and diagnostic procedures are suggested as a strategy for the early detection of reversible PPCM: first, screening for NT-proBNP targeting women with MFP, HD, dyspnoea, and/or oedema with marked weight gain; second, hs-TnI test in women with a positive NT-proBNP test result at a certain interval; and third, diagnostic echocardiography in women with double positive test results. As the present study included much higher percentages of women with MFP [10% (13/129) in this study vs. approximately 1% in the general population¹³] and HD [14% (18/129) in this study vs. approximately 5.0% in the general population¹⁴], accounting for 22% (29/129) of the study population, double positive test results occurred in 4.7% of women. However, in the general population, the number of candidates for echocardiography after obtaining double positive test results would be 1–3 per 100 women.

The serum levels of myoglobin and CK-MB rise during parturition,^{26,27} as confirmed in this study. This may be partly explained by the release of these molecules from the uterine muscle during labour. A weak but significant correlation between the serum levels of hs-TnI specific for cardiac myocyte damage and myoglobin (*Figure 3*) supported the suggestion that myoglobin derived from the cardiac muscle partially contributed to the rise in myoglobin level.

As PPCM occurs peripartum and iron deficiency occurs frequently in patients with heart failure,¹⁶ it was expected that the ferritin level would decrease peripartum. The implications of the unexpected rise in the serum ferritin level

observed in this study remain unclear. Although there have been few reports on changes in ferritin level in pregnancy, pregnant women with polycystic ovarian syndrome were shown in a previous prospective study to exhibit higher ferritin levels compared with normal pregnant women and a gradual increase in ferritin level during pregnancy.²⁸ As the serum ferritin can increase in inflammatory conditions, the authors suggested that there may be a low-grade chronic inflammation in pregnant women with polycystic ovarian syndrome.²⁸

The major limitation of this study was that no women with PPCM were included. However, it was considered that PPCM would occur in women with higher levels of NT-proBNP and hs-TnI. Therefore, it was important clinically to determine which women are likely to exhibit higher levels of NT-proBNP and hs-TnI.

In conclusion, this partly longitudinal study of 129 pregnant women indicated that women with MFP and/or HD were likely to exhibit higher levels of both NT-proBNP and hs-TnI than those with normotensive singleton pregnancies. Both MFP and/or HD are prominent risk factors for PPCM.^{8,12}

As median NT-proBNP and hs-TnI levels seen in women with MFP and/or HD, but not with PPCM were much lower than those²⁰ reported in PPCM patients, it was speculated that women with developing PPCM would exhibit a further increase in these parameters. The combined use of hs-TnI and NT-proBNP may contribute to better selection of candidates for echocardiography.

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Conflict of interest

None declared.

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