Interrelationship Between Serum Iron Concentration and Pregnancy-induced Hypertension and Chronic Hypertension in Pregnancy

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Abstract : *It is important to distinguish pregnancy-induced hypertension(PIH) from pregnancy complicated by chronic hypertension(CHT). Retrospective case-control studies demonstrated a correlation between serum iron concentration and PIH. This study is a cross-sectional study to compare the serum iron concentration among three groups of pregnant women i.e. normotensive (control), CHT and PIH. Of 180 pregnant women recruited, there were 45 CHT and 45 PIH. 90 controls were selected by matching to CHT and PIH for age group, gestational age, hemoglobin and history of iron supplementation. The serum iron was determined in three phases i.e. antepartum, intrapartum and postpartum. It was shown that serum iron was significantly higher in delivery phase of PIH group both comparing to its own control or in pooled data and PIH group itself also demonstrated a peak of mean serum iron concentration during intrapartum when comparing to antepartum and postpartum phases. (Thai J Obstet Gynaecol 1991;2: 59-65.)*

Key words : serum iron concentration, pregnancy-induced hypertension, chronic hypertension

It is practically important to make an early diagnosis of pregnancy-induced hypertension (PIH) and to distinguish it from underlying chronic hypertension (CHT) due to their different management. In severe PIH, pregnancy must be rapidly terminated, while those of CHT could usually safely go on to term. This is of special importance since some patients attend the antenatal clinic very late in their pregnancy. It may be very difficult to differentiate between CHT and PIH, especially those first seen in late

pregnancy presenting with hypertension without any previous information on early pregnancy blood pressure and no definite sign of PIH. Many laboratory measurements, therefore, have been developed to differentiate these two diseases, i.e. determining the level of uric acid, antithrombin III, platelets, or liver enzymes[1]. There is, however, no laboratory technique able to effectively differentiate the two entities.

In 1981, Entman and associates[2] reported a retrospective case-control study to evaluate the clinical course and mean serum iron concentrations among the patient groups of PIH, CHT and normotensive pregnant women. The study demonstrated that mean serum iron concentrations in the antepartum and intrapartum phases of PIH group were significantly higher than in CHT and normotensive controls and the concentrations in the PIH group were highest at the intrapartum phase. For postpartum phase, there was no significant difference among the three groups. In addition, it was demonstrated that the peak of serum iron concentration at intrapartum phase was well-related to the severity of the disease. In 1982, Entman and associates[3] reported another study whose results confirmed the previous findings. They, furthermore, found that serum iron was sensitive and specific parameter for PIH, and the predictive value was high exceeding any other test so far employed for this disease. They, therefore, concluded that the serum iron has transient but striking changes during the course of PIH, and that in their opinion this test was the most sensitive and specific for diagnosis and predicting the severity of the disease. So far, this finding has not been substantiated by any other group of investigators, especially in subjects who have different racial and nutritional characteristics from those of the American counterpart. It is highly desirable, therefore, to conduct a similar study to document whether or not the above observation could be reproduced in a pregnant PIH population of northern Thailand.

Materials and Methods

A cross sectional case-control study was conducted at Maharaj Nakorn Chiang Mai Hospital, Department of Obstetrics and Gynaecology, Faculty of Medicine, Chiang Mai University, from September 1, 1985 to August 31, 1990. The study population i.e. PIH, CHT and normotensive pregnant controls were recruited from the antenatal clinic and obstetrical wards. Of the 180 singleton and nonanemic pregnant women recruited, there were 45 CHT, 45 PIH and 90 controls. PIH group consisted of pregnant women who met the criteria of PIH[1]. Again,CHT patients were those diagnosed before pregnancy, and who met the criteria of CHT[1]. Controls were healthy, normotensive pregnant women having no other signs and symptoms of PIH. 90 controls were selected, case by case, by matching CHT or PIH for age group, trimester

of gestational age at delivery and first antenatal clinic visit, hemoglobin concentrations (10-12, 12-14 gm %), and history of iron supplementation.

For PIH and CHT patients, blood samplings were taken the first time that PIH or CHT was diagnosed, which might be during the antepartum, intrapartum or postpartum periods. If the antepartum specimen had been obtained, the next specimen would be taken serially at the following conditions:1) the time that PIH was considered to become worse i.e. from mild to severe and/or, 2) immediatedly before induction of labor and/or, 3) during the active phase of intrapartum and/or, 4) 72 hours postpartum. If the first specimen obtained was the intrapartum one, the next specimen would be taken during 72 hours postpartum.

In controls, antepartum specimens were obtained during trimester of gestation matching to the cases. Intrapartum and postpartum specimens were obtained as they were in the cases.

Total serum iron determination was based on the extraction of iron by using precipitating agent and then treated with chormogenic reagent bathophenanthroline sulfonate gives pink color solution which could be absorbed at 535 mm[4].

Calculation of the mean value and standard deviation of serum iron concentration of each study group was done. The statistical significance for mean difference was tested by analysis of variance. If there was statistically significant difference in the mean values among the three groups. The fluctuation of serum iron concentrations was compared between cases and controls.

Results

The important characteristics of each pair of control and study group are described in Table 1. In comparision, the PIH group was not significantly different from its control in mean age, parity, gestational age at first antenatal visit, number of visits, percentage of iron supplemetation, gestational age at delivery, mode of delivery, except for fetal birthweight which was significantly lower in the PIH group. For the pair CHT group and its control, there was no difference in many characteristics except that the CHT group had a significantly higher parity.

When comparing the mean serum iron concentration for each pair of control and study group it was found that there was statistical difference ($p<0.05$) only between PIH and its control during the delivery phase. The mean($\pm$1 SD) serum iron concentration of PIH and controls during intrapartum phase were 115.98$\pm$78.08 and 77.11$\pm$35.20 μg% respectively.

When pooling the data of controls for either CHT or PIH groups into one control group and comparing the mean serum iron by analysis of variance, the statistically significant difference was only for the intrapartum phase. The mean serum concentration of controls, CHT and PIH dur-

ing intrapartum phase was 77.89± μg% respectively.
38.17, 83.49±38.17 and 115.98±78

Table 1 Characteristics of study population

Study groups	n	Mean age (years)	Parity O (%)	Parity 1 (%)	Parity>1 (%)	GA at 1st ANC	No.of ANC
CHT	45	28.2±5.2	46.7	31.1	22.2	20.8±8.8	7.2±3.4
Control	45	27.3±4.7	60.0	37.8	2.2	20.6±8.5	7.3±3.1
p value	-	0.365	<----------0.015---------->			0.894	0.974
PIH	45	26.5±5.6	62.2	26.7	11.1	21.9±7.8	6.2±3.2
Control	45	25.2±5.6	75.	22.2	2.2	21.1±7.5	6.9±3.4
p value	-	0.231	<----------0.18---------->			0.621	0.267

Table 1 Characteristics of study population (continued)

Study groups	Hb (g %)	% Iron supplement	GA(wks) at delivery	Vaginal delivery	Cesarean delivery	Birth weight (g)
CHT	12.14±1.15	97.4	37.47±3.96	38(84.4%)	7(15.6%)	2778.00±521.68
Control	11.73±0.96	84.4	37.60±3.22	41(91.1%)	4(8.90%)	2917.33±22.17
p value	0.069	0.064	0.140	<--------0.218------->		0.209
PIH	11.82±1.13	95.6	36.24±3.56	35(77.8%)	10(22.2%)	2525.78±656.72
Control	12.14±1.15	100.0	37.47±3.96	41(91.1%)	4(8.90%)	2778.00±521.68
p value	0.199	0.475	0.127	<--------0.146------->		0.047

Table 2 Mean serum iron of CHT and controls

Phase of iron taken	CHT	Control	p value
Antepartum	73.39±30.49(n=18)	86.85±35.41(n=13)	0.266
Intrapartum	83.49±38.17(n=45)	78.67±41.72(n=45)	0.569
Postpartum	75.32±36.27(n=44)	65.89±35.89(n=44)	0.223

Table 3 Mean serum iron of PIH group and controls

Phase of iron taken	PIH	Control	p value
Antepartum	88.00±34.41(n=26)	78.92±34.70(n=26)	0.078
Intrapartum	115.98±78.08(n=43)	77.11±35.20(n=45)	0.004*
Postpartum	69.10±42.33(n=42)	63.60±25.10(n=45)	0.468

*Statistically significant

Table 4 Mean serum iron by study groups and pooled controls

Phase	Control	CHT	Control	p value
Antepartum	84.42±34.30(n=26)	73.39±30.49(n=18)	88.00±34.41(n=26)	0.076
Intrapartum	77.89±38.38*(n=90)	83.49±38.17*(n=45)	115.98±78.08*(n=43)	0.003**
Postpartum	64.73±30.74(n=89)	75.32±36.27(n=44)	69.10±42.33(n=42)	0.264

* Statistically significant for Scheffe's test
**Statistically significant for analysis of variance

Table 5 Mean serum iron by phase of blood samplings

	Antepartum	Intrapartum	Postpartum	p value
Control	84.42±34.30*(n=26)	77.89±38.38*(n=90)	64.73±30.74*(n=89)	0.009**
CHT	73.39±30.49(n=18)	83.49±38.17(n=45)	75.32±36.27(n=44)	0.463
PIH	88.00±34.41*(n=26)	115.98±78.08*(n=43)	69.10±42.33*(n=42)	0.008**

* Statistically significant by Scheeffe's test
**Statistically significant by analysis of variance

The PIH group also demonstrated a peak of the mean serum iron con centration during the intrapartum phase. The mean serum iron in the PIH group during ante-, intra-and postpartum phases were 88.00±34.41, 115.92 ±78.08 and 69.42 ± 42.33 μg% respectively.

Discussion

The results of this case-control study indicate that there is a transient but significant increase in the level of serum iron concentrations during intrapartum period of pregnancy-induced hypertensive patients, as documented by Entman et al[1]. The mean serum iron concentrations for the control and chronic hypertension groups, however, do not significantly change at the time of delivery. This finding is consistent with the value documented by Kaneshige[5], who also showed that mean serum iron concentrations in late pregnancy, intrapartum and

postpartum were not significantly different.

Iron metabolism of pregnancy has been studied extensively, it has been generally related only to anemia[6-9]. There have only been reports demonstrating the relationship between ferrokinetic changes and PIH[1,2].

In order to control the variables, 90 controls of this study were selected by matching to CHT or PIH patients for hemoglobin concentrations, history of iron supplementation, age group, and trimester of gestational age. It is well documented that hemoconcentration occurs commonly in PIH patients, especially in severe cases, and concern could be raised that the iron concentration changes are a reflection of the hemoconcentration. Among the patients in this study, hemoconcentration was, however, corrected by adequate hydration during the delivery phase, and clinical parameters of hemoconcentration, i.e. hemoglobin and hematocrit during labour did not show marked hemoconcentration. The hemoglobin, of course, was influenced by both hemoconcentration and blood loss.

Ferrokinetic changes in PIH group may be explained by the possible mechanism of increasing red cell destruction associated with either intravascular or extravascular hemolysis. There was evidence of erythrocyte destruction characterized by hemolysis, schizocytosis, spherocytosis, reticulocytosis, hemoglobinuria and occasionally hemoglobinemia[10,11]. These dearrangements result in part from microangiopathic hemolysis, which is the characteristic of PIH. It is likely that plasma erythrocyte membrane lipid changes that accompany pre-eclampsia are magnified by decreased serum albumin concentration and these serve to intensify fragmentation hemolysis. Hemolysis may be the explanation of ferrokinetic changes in PIH but the definite mechanism requires further ivestigation.

Serum iron concentration is influenced by biologic and laboratory variation on serial samplings. Although samples were drawn at various times, effectively randomizing the data, the degree to which diurnal variation might have an impact on the data should be considered. Winkel and associates[12] reported a 12.9% variation with higher levels in the afternoon, and they also noted an average 29% day-to-day variation for individuals[13]. Long and coworkers[14] reported that 18 of 25 subjects showed an average 21% decrease in iron levels in the afternoon, and 7 of 25 individuals showed an average of 20% higher levels in the afternoon, and of 25 individuals showed an average of 20% higher levels in the afternoon. These reports suggest that the impact of biological variation should be of minimal magnitude on the data presented.

These data suggest an acute and significant increase in serum iron concentrations associated with PIH, but not in CHT and normotensive pregnant women. The findings confirm those of Entman's studies[2,3]. The mean serum iron concentration in the antepartum phase was, however, not significantly different among the three groups, this result did not support the findings in

another Entman's report[3]. It may be possible that the population for the antepartum phase was too small to show the difference. The increase in serum iron concentration during delivery may not only serve as an adjunct to distinguish PIH from underlying CHT but might also be one of the parameters to reflect the severity of the disease.

The investigators concluded that the serum iron concentration increased during the delivery phase of pregnant women complicated with PIH compared with CHT and normotensive pregnant women and it might serve as adjunct to differentiate between PIH and CHT.

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