Iron balance in pregnancy in relation to anemia

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Summary: Blood levels of iron, transferrin and ferritin varied in the course of pregnancy (6th to 42nd week) in 136 women. Analysis of variance showed that the factor "weeks of pregnancy" ($\leq$ 27 or > 27 weeks) was correlated differently with the variables "ferritin" and "iron" according to the presence or absence of anemia (Hb $\leq$ or $\geq$ 11 g/dl). In anemic women the correlation was significant (F-ratio=5.90; P=0.018) for iron (which decreased from initial low level until term) but not ferritin, whereas in non-anemic women the correlation was significant (F-ratio=13.306; P=0.0006) for ferritin (which decreased to less than 20 μg/ml around the 34th week) but not iron. In both anemic and non anemic subjects, transferrin levels increased with weeks of pregnancy. It is concluded that towards the end of pregnancy, some decrease in ferritin ($\geq$ 15 μg/ml) is physiological, and in the absence of anemia (Hb > 11 g/dl) iron supplements are not necessary.

Key words: Pregnancy; Anemia; Iron balance.

INTRODUCTION

During pregnancy, there is a progressive increase in the volume of blood and metabolic demand, increase due to placental and fetal requirements ([1, 2, 3]). Iron, an essential component of hemoglobin (Hb), cytochrome and catalase and peroxidas enzymes, is almost completely bound to proteins in its transport and storage forms ([4, 5]).

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Cardiovascular modifications occurring in pregnancy are considered to compensate the reduction in Hb ([6]). In some circles, iron supplements are regarded as unnecessary ([7]) whereas in others it is thought that iron reserves may become depleted if supplements are not given ([8, 9]).

We therefore investigated the dynamics of the iron balance in pregnancy and the relationship of its characterising parameters (iron, ferritin and transferrin) to anemia and gestational age.

MATERIALS AND METHODS

Blood samples were taken in 136 pregnant women admitted to the Clinic in the 6th-42nd week of pregnancy, for the determination of red cell count, Hb, hematocrit, mean corpuscle volume etc. Only Hb values were used for our study. Hb was determined both by colorimetry and optical bench (Technicon H2 System).

At the same time a blood was taken to determine the serum iron balance: iron (129 cases),

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transferrin (118 cases) and ferritin (117 cases). All determinations were performed by the following methods in the central laboratory of the University: "ferrizzina" method for iron, nephelometry for transferrin and immunometry with chemical luminescence for ferritin.

All patients admitted to the Obstetric Pathology Ward, whether for anemia or otherwise, were included in the study. Women with twin pregnancies, preeclampsia, gestational hypertension, retarded fetal growth, gestational diabetes and all cases of severe organ miopragia and other initially severe conditions (sepsis, acute infection, hepatitis) were excluded.

STATISTICAL ANALYSIS

Iron, transferrin and ferritin values were divided into two groups according to initial Hb levels ($\leq$ or $>$ 11 g/dl: a) anemic; b) non anemic) and analysis of variance performed. A second analysis of variance was performed with the same dependent variables in anemic (62 cases) and non anemic (67 cases) subjects against two categories of gestational age: I: $\leq$ 27 weeks; II: $>$ 27 weeks. The statistical calculations were performed with software for PC [10].

The tests used were: calculation of the median and maximum and minimum values, calculation of the regression coefficient (multiple R^2) and the respective level of significance (F-ratio and P) and one-way analysis of variance with R and P. A graphics system Lowess was used to construct linear regression lines and curves [11].

RESULTS

The statistical division of anemic and non anemic patients is reported in Table 1. The number of cases in each of the groups was nearly the same. Minimum levels of Hb were never less than 8 g/dl and the difference between the median of the two groups was less than 2 g/dl.

The patterns of iron and ferritin showed a roughly parallel, decreasing trend as pregnancy progressed; the decrease was sudden after the 33rd week. Transferrin, on the other hand, increased as pregnancy progressed with a steeper slope after the 23rd week (Fig. 1).

Table 1. — *Medians, hinges, minima and maxima of haemoglobin in two groups of pregnant women: a) $\leq$ 11 g/dl and b) $>$ 11 g/dl.*

No. cases	Mini-	Lower hinge	Median	Upper hinge	Maxi-mum
a) 62	8.200	9.900	10.300	10.700	11.000
b) 74	11.070	11.600	12.150	12.600	15.500

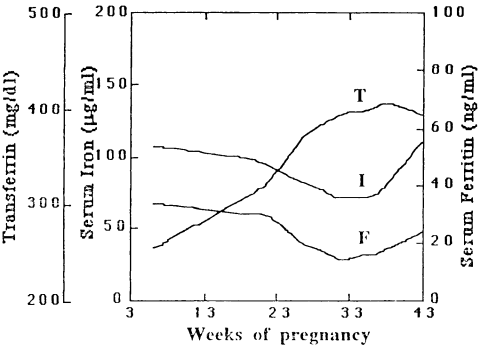

Fig. 1. — Variations in levels of ferritin (F), iron (I) and transferrin (T) throughout pregnancy in 136 patients, according to LOWESS regression curve.

One-way analysis of variance of the three parameters as dependent variables in relation to the factor Hb ($\leq$ or $>$ 11 g/dl) is shown in Table 2. The presence of anemia was influenced in a highly significant way by iron (F-ratio = 23.397; $P < 0.0001$), transferrin and ferritin being uninfluential. However transferrin was close to reaching minimum levels of statistical significance (F-ratio = 3.38; P = 0.069).

Table 2. — *One way analysis of variance of iron, transferrin and ferritin in two groups of pregnant women divided according to Hb values ($\leq$ or $>$ 11 g/dl).*

	No. cases	R 2	F-Radio	P
Iron	129	.156	23.397	.000 ***
Transferrin	118	.168	3.380	.069 N.S.
Ferritin	117	.007	.850	.359 N.S.

Dividing the patients on the basis of the factor "weeks of pregnancy", it emerged that the three variables had different pat-

terns in anemic and non anemic patients. In the former, weeks of pregnancy ($\leq$ or $>$ 27) affected iron (F-ratio=5.90; P=0.018), unlike the non anemic subjects. Ferritin, which was highly influenced by weeks of pregnancy in non anemic patients (F-ratio=13.306; P<0.001), ceased to be correlated with this parameter when Hb fell below 11 g/dl.

Transferrin varied with weeks of pregnancy, independent of Hb levels. The greatest variation was observed in non anemic subjects (Table 3).

Table 3. — *One way analysis of variance of iron, transferrin and ferritin in pregnant women in relation to the weeks of pregnancy ($\leq$ or $>$ 27th week): a) patients with Hb $\leq$ 11 g/dl; b) patients with Hb $>$ 11 g/dl.*

a)	No. cases	R 2	F-Ratio	P
Iron	62	.090	5.908	.018 *
Transferrin	57	.194	13.266	.0006 ***
Ferritin	56	.037	2.078	.155 N.S.
b)	**No. cases**	**R 2**	**F-Ratio**	**P**
Iron	67	.008	.554	.459 N.S.
Transferrin	61	.265	21.261	.00002***
Ferritin	61	.194	13.306	.0006 ***

Figure 2 shows the time course of iron and ferritin which, according to analysis of variance, had different patterns in anemic and non anemic subjects. Apart from the height of the iron curve which was about 20% lower in anemic subjects up to the 34th week (37 non anemic vs 36 anemic subjects: means 100.85±38.87 SD vs 78.70±34.74 SD, P=0.001), values rase rapidly and significantly after the 34th week (28 cases, P=0.007) whereas in anemic subjects they continued to fall.

The decrease in ferritin in non anemic women was very regular until 32 weeks when it recovered slightly. These differences explain the results obtained with analysis of variance for iron and ferritin.

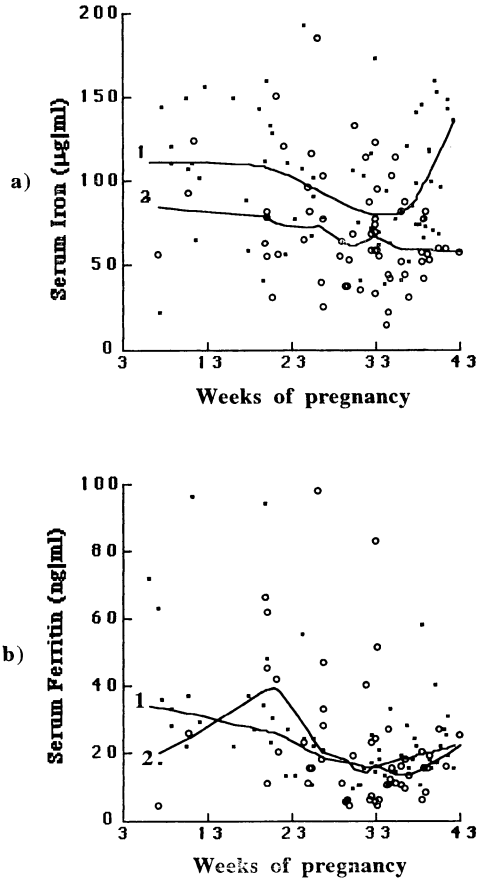

Fig. 2. — LOWESS regression curve of iron (a) and ferritin (b) in non anemic (1: Hb > 11 g/dl) and anemic (2: Hb $\leq$ 11 g/dl) subjects in relation to weeks of pregnancy.

DISCUSSION

The patterns of iron, transferrin and ferritin during pregnancy were not the same when the subjects were divided on the basis of initial Hb values. Although our population of women did not receive iron supplements in the Clinic, some of them may have taken iron independently. We did not consider this element because it was difficult to quantify and also because we were interested in the pattern of the iron balance starting from initial

values in a heterogeneous population of patients, taking a level of 11 g/dl of Hb as discriminant. The results should be unaffected by such iron supplements which would be randomly distributed in the 136 subjects. The same applies to diet.

Variations in iron (in anemic subjects) and transferrin (in anemic and non anemic subjects) were expected, but the lack of variation in ferritin in anemic subjects in relation to weeks of gestation was interesting. Figure 2b shows that this cannot be explained, as one would expect, by the fact that before the 27th week, ferritin levels were lower in anemic subjects and remained low. The pattern of the LOWESS curve was much more irregular and the variations probably annulled the differences related to gestational age. Transferrin levels always increased with gestational age, independent of anemia.

On the question of the use of iron supplements in pregnancy, our results introduce several new points. First of all, in women with Hb levels above 11 g/dl, not clinically anemic, the decrease in iron and ferritin during pregnancy is physiological, i.e. it occurs in the absence of iron supplements, in the vast majority of women.

In a recent article, Thompson [9] diagnosed iron depletion on the basis of ferritin levels below 20 μ/ml. With this criterion, as in the present study, he naturally saw an increase in the percentage of women with iron depletion in the second and third trimesters. He concluded that all pregnant women with ferritin levels below 20 μ/ml should be given iron supplements.

Our results lead us to disagree with this conclusion. Iron supplements seem to be useful in at least two types of patient with Hb below 11 g/dl: those with initially low levels of ferritin (20 μg/ml) and those showing a drop in serum iron after the 34th week. Ferritin levels of 20 μg/ml (±3.98) between the 34th and 40th weeks are physiological if Hb and iron are high, and do not seem to call for correction with supplements. There is no experimental evidence to suggest that when ferritin levels are not always above 20 μg/ml, clinical effects result in the mother and baby.

The present results suggest that it is opportune to follow the iron balance from the beginning of pregnancy so as to be able to evaluate any pathological changes and provide iron supplements if required.

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