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Maternal serum ferritin and hemoglobin values in patients with gestational diabetes mellitus

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A number of studies have linked increased maternal iron store and high serum hemoglobin (Hb) levels in pregnancy with increased incidence of adverse pregnancy outcomes, such as low birth weight and small-for-gestational age newborns, pre-term births, increased perinatal mortality, and preeclampsia.[1] In normal pregnancy, maternal serum ferritin level decreases with advancing gestation, even when iron supplementation has been given antenatally. Lao et al[2] identified high maternal hemoglobin and ferritin concentrations as a risk factor for gestational diabetes mellitus (GDM), however, there is no universal criterion of what constitutes a high hemoglobin concentration.

A case control study in Chinese women with a body mass index (BMI) of more than 26 kg/m^2, has shown that those who developed impaired glucose tolerance during pregnancy, had significantly increased Hb concentrations compared with BMI-matched groups.[3] In the non-pregnant population, an association between Hb values and red cell count with diabetes mellitus (DM) has been reported earlier. Diabetic subjects were found to have increased total red cell count compared with age and gender matched controls. Furthermore, it has been suggested recently that an elevated ferritin concentration is a part of the picture of insulin resistance. Since iron supplementation is often recommended to pregnant women, it is possible that iatrogenic iron excess can be induced in the non-anemic women. Therefore, the aim of this study is to clarify if there is a relationship between maternal iron status and Hb values and GDM in the third trimester, so that a rational approach can be formulated. The study group comprised 56 gestational diabetic patients and 56 patients for control group. The study protocol was approved by the hospital Ethical Committee, and all participants signed informed consents prior to sample collection. In our hospital, a multivitamin preparation containing 29 mg of elemental iron is offered to all patients after the initial visit. Since all patients were treated with multivitamin, there is no difference between the groups. Patients having hemoglobin level less than 10 g/dL at any time during pregnancy are diagnosed to have anemia, and these patients were not included to the study or the control group. All subjects were screened for GDM using a 50 g, 1-h glucose load administered 24-28 weeks' gestation. A positive screening test (plasma glucose ≥140 mg/dL) was followed by a 3-h oral glucose tolerance test (OGTT). Gestational diabetes mellitus was diagnosed according to the OGTT criteria of Carpenter and Coustan,[4] by which after a 100 g oral glucose load, 2 or more of the following plasma values was met or exceeded: fasting 95 mg/dL, 1 hour 180 mg/dL, 2 hours 155 mg/dL, and 3 hours 140 mg/dL. Diabetic patients were managed with a diet restriction first, and after this treatment all patients were followed up for their preprandial and postprandial second-hour plasma glucose levels weekly. If their preprandial glucose level was over 105 mg/dL or postprandial second-hour glucose level was over 120 mg/dL, insulin treatment was given. Anamnestic, clinical, and anthropometric parameters were recorded. The gestational age was estimated by last menstrual period, confirmed by ultrasonography. All subjects were followed until delivery, labor was not induced, and so, this will not have an impact on the gestational age of the offspring, birth weight, and Appearance, Pulse, Grimace, Activity, and Respiration (Apgar) scores were obtained. Maternal weight gain during pregnancy was defined as an increase in weight from pre-pregnant weight to weight at the last visit. Prepregnancy body mass index (p BMI) (weight [kg]/height [m]^2) was based on measured height and maternal self-report of prepregnancy weight at the initial visit. The women in both groups had the same socio-economic status and were non-smokers. Women with hypertensive disorders, blood disorders, multiple gestations, and renal or liver disease was excluded. At 28-30 weeks, after informed consent obtained, blood was taken for the study of maternal hemoglobin concentration, mean corpuscular volume, serum transferrin and ferritin concentration (Microparticle Enzyme Immunoassay, IMx System of Abbott Laboratories, Abbott Park, IL), and insulin levels. The patients subsequently diagnosed to have glucose intolerance were compared with control group. Statistical analysis was performed using the Mann-Whitney *U* test and Student's *t*-test using a commercial computer package (Statistical Package for the Social Sciences [SPSS] for Windows, SPSS Inc., Chicago, IL).

The maternal characteristics of the 2 groups are shown in **Table 1**. Significant difference was found among the 2 groups in the maternal age, gravida, and

Table 1 - Maternal characteristics, comparison of pregnancy and infant characteristics and laboratory values in 2 groups.

Characteristics	GDM (n=56)	Controls (n=56)	*p*-value
Gravida	2.45±1.45	1.93±1.16	<0.05
Age (years)	29.96±3.9	26.63±5.51	<0.001
Weight gain in pregnancy (kg)	13.75±3.2	12.54±2.46	<0.05
Gestational age (week)	38.13±1.65	39.04±1.43	<0.05
APGAR 5-minute	8.77±0.46	8.95±0.22	<0.05
Serum ferritin (ng/mL)	17.17±13.55	16.23±15.28	NS
Mean cell volume (fl)	90.2±5.0	89.3±4.7	NS
Hematocrit (%)	34.6±3.2	34.1±2.9	NS
Transferrin (µmol/L)	63,5±18,8	61,4±16,6	NS
Insulin (µIU/mL)	10.92±4.48	9.13±3,75	NS

NS - not significant, GDM - gestational diabetes mellitus, APGAR - Appearance, Pulse, Grimace, Activity, and Respiration, Results expressed in mean ±SD

maternal weight gain during pregnancy. The p BMI was 23.1±3.5 kg/m^2 for diabetic group and 22.8±3.1 kg/m^2 for control group (p>0.05). For the infants; there was a significant difference in the mean gestation and 5-minute APGAR scores between the 2 groups **(Table 1).** Birth weight was 3386±461 g for diabetic patients and 3256±329 g for control group (p>0.05). The Apgar scores and gestational age was significantly lower in diabetic group, although, labor was not induced for non of the diabetic woman. The incidence of male infants was higher in the GDM group. Approximately 28/56 of babies were male in the control group (50%) and 37/56 of babies were male in the diabetic group (66.1%) (p=0.085). Moreover, the incidence of male infants was significantly higher in the insulin treated group compared with diet treatment in the GDM group. The numbers of male infants were 19/34 (55.9%) in the diet treated group, and this number was 18/22 (81.8%) in the insulin treatment group (p=0.036). The comparisons of gestational mean maternal laboratory values for GDM and control groups are shown in **Table 1.** The mean cell volume and hematocrit values were higher in the GDM group, but these did not reach statistical significance. Hemoglobin values at the beginning of the study were 12.05±1,71 g/dL for diabetic patients and 11.89±1,57 g/dL for control group (p>0.05). These values were 11.83±1.65 g/dL and 11.77±1.38 g/dL (p>0.05). Transferrin and ferritin values were also higher in GDM group, and these differences were not statistically significant. When we compare the insulin values for both groups, it was 10.92±4.48 for diabetic patients and 9.13±3,75 for control group (p>0.05). For the entire group of GDM and controls, correlation analysis indicated that the

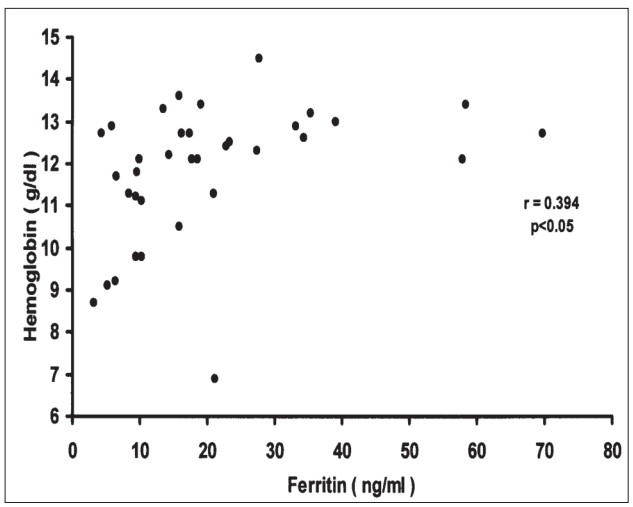

Figure 1 - Correlation between ferritin and hemoglobin values for control group.

serum ferritin concentration was positively correlated with hemoglobin values **(Figure 1).** The measurement of hemoglobin at the first antenatal visit has become a standard investigation in the pregnant woman. This result could be useful for the identification of women who are at risk not only for complications, such as fetal growth restriction and pre-term birth, but also for GDM if there is really an association between high hemoglobin concentration and DM. In non-pregnant subjects, the association between high hemoglobin concentration and red cell count with DM is attributed to the increased proportion of glycosylated hemoglobin in diabetic subjects.[3] Lower

Apgar scores may be the result of lower gestational age or due to the general problems of diabetic mother baby, such as hypoglycemia, electrolyte imbalance, intrauterine growth retardation. Rjasanowski et al[5] has been reported that insulin requirement was increased in pregestational diabetic pregnancies carrying a female fetus, and that diabetic women had increased numbers of female offspring. Different from these results, we found increased incidence of male infants in the GDM group, furthermore, in diabetic group, women carrying male fetus were more prone for insulin treatment. Lao et al[2] has found that even with mild GDM diagnosed in the third trimester, maternal serum ferritin concentrations were significantly higher than in controls. In this study, we could not find an association between high hemoglobin and ferritin concentration and development of GDM. Moreover, similar to the study of Lao et al,[2] there was no difference in the serum transferrin saturation according to results of this study. Our results indicate that in Turkish women, there is no association between high hemoglobin or ferritin concentrations and development of GDM.

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