Brief Communication

Relationship of early hypertensive retinopathy to inflammation markers and microalbuminuria in hypertensive patients with regulated blood pressure

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Hypertensive retinopathy is the term used to describe the changes to the retinal vascular system that happen due to high blood pressure.1 It is believed that retinal assessment may be a valuable tool in gathering information regarding systemic micro vascular injury.2 Today, many guidelines define hypertensive retinopathy as target organ injury. Although the Joint National Committee (JNC) 7 report published in 2003 defines all retinopathy stages as target organ injury, World Health Organization (WHO) / International Society of Hypertension (ISH) 2003, British Hypertension Society (BHS) IV 2004, European Society of Hypertension (ESH)-European Society of Cardiology (ESC) 2003 guidelines suggest that only grades 3 and 4 should be accepted as target organ injury.2 However, the most common grades of retinopathy are 1 and 2.3 Therefore, it is important to understand the clinical significance of the retinal changes in these grades. Although certain large-scale studies conducted to understand the clinical significance of grade 1-2 retinopathy have yielded conflicting results. The aim of the present study is to investigate whether the routine inflammation markers and urinary albumin excretion are different in hypertensive patients with and without retinopathy, and also to assess whether these parameters are related to early retinopathy.

We carried out this study in Kirikkale University Medical School, between December 2004 and March 2005. A total of 118 hypertensive patients, comprising of 46 men and 72 female with ages ranging from 30-74 years were included in the study. None of them had any disease except regulated essential hypertension. All subjects were informed prior to the study and their written consent was obtained. Weight, height and waist circumference were measured and body mass index (BMI) was calculated. Blood pressure was measured 3 times following 15-minute rests and the average of these 3 measurements was taken. A blood sample was drawn in the fasting state: plasma fibrinogen C-reactive protein (CRP), hemoglobin, white blood cell, platelet, serum glucose, urea, creatinine, albumin and 24-hour urinary protein, albumin and creatin excretion were measured. Microalbuminuria was defined as urinary albumin excretion ≥30 mg/24h and <300 mg/24h. Oral glucose tolerance test was performed on subjects whose fasting blood sugar level was above 5.5 mmol/L. The funduscopic examination of all subjects was carried out using the ophthalmoscope. The Keith-Wagner-Baker classification was used to determine retinopathy level.1 Accordingly, only those patients with retinopathy grade 1-2 were included in the study. The subjects were then divided into 2 groups based on their funduscopic examination: subjects with retinopathy (grade 1-2 retinopathy, n=65) and subjects without retinopathy (no pathological findings in funduscopic examination, n=53). Retinopathy was analyzed as a dichotomous variable (such as retinopathy yes or no). Means were compared by Student's t test. Analysis of categorical data was carried out with the chi-square test. Multiple logistic regression analysis was also used to assess the independent relationship between retinopathy and study variables.

There were no significant differences in age, gender, smoking, BMI, waist circumferences, systolic and diastolic blood pressure between retinopathy and non-retinopathy groups (p>0.05). However, white blood cell, CRP, platelet, fibrinogen and 24-hour urinary albumin excretion showed significant differences with higher values for people with retinopathy (p<0.05). Multivariate analysis was performed using the logistic regression with retinopathy (yes/no) as the dependent variable and with white blood cell, platelet and CRP as independent variables. Retinopathy was positively and significantly associated with white blood cell (β=0.001, p=0.01) and CRP (β=0.289, p=0.03), whereas no significant association was found with platelet. Very similar results were obtained with the use of fibrinogen instead of CRP in the model (β=0.006, p=0.03). Chi-square analysis showed that microalbuminuria and retinopathy were statistically significantly related (p<0.01). Target organ injuries, which happen during the acute or chronic stages due to high blood pressure, indicate both a failure in controlling blood pressure and increased cardiovascular risk independent of the blood pressure.3 Today grades 1-2 retinopathies are the most common types whereas grades 3-4 are rare.3 That is why the clinical significance of grades 1-2 is crucial to understand. Our study focuses on hypertensive patients with regulated blood pressure and no additional diseases such as diabetes mellitus. However, other studies concerning this issue generally consist of patients with no prior treatment, blood pressure regulation or careful diabetes mellitus scans, therefore, results of the present study may be more significant.3 The present study also shows that grade 1-2 hypertensive retinopathy (55.1%) is more common than microalbuminuria (39%), another target organ.
injury. In the literature as well, grade 1-2 hypertensive retinopathy is generally found to be more common than other target organ injuries such as microalbuminuria or left ventricular hypertrophy. For this reason, recognition of the clinical value of grade 1-2 retinopathy may be more influential than other target organ injuries in the assessment of hypertensive patients. The present study has found a statistically significant relationship between microalbuminuria and retinopathy. As a result, it may be thought that togetherness of microalbuminuria and retinopathy develops due to systemic microvascular injury and, in relation to this; grade 1-2 retinopathy also indicates systemic microvascular injury. Another result of the present study is the relationship between grade 1-2 retinopathy findings and inflammation markers that are used frequently in clinical practice. A possible relationship between inflammation markers and retinopathy was suggested for the first time in the Atherosclerosis Risk in Communities Study study. Additionally, in the multivariate analysis that was conducted, grade 1-2 retinopathy development was seen to be influenced by white blood cell, CRP and fibrinogen, which are important parameters of inflammation. Inflammation is one of the triggering mechanisms in various cardiovascular and cerebrovascular events. Inflammation markers such as white blood cell, fibrinogen, CRP may be useful in identifying cardiovascular risk. Inflammation, which has a role in the development of retinopathy in hypertensive patients, may at the same time cause destruction in coronary, cerebral, renal and other similar microvascular structures and, as a result of this, grade 1-2 hypertensive retinopathy may also be exacerbating due to inflammation increase in these systems. Therefore, grade 1-2 retinopathy may be closely related to cardiovascular risk increase. Additionally, the significant togetherness of microalbuminuria, and retinopathy also supports this view. Hypertension generally brings with itself increased cardiovascular mortality and morbidity. However, this increase is not typical in all hypertensive patients. Therefore, identifying high-risk patient groups may help decrease cardiovascular morbidity and mortality. Displaying target organ injuries does not decrease the risk today. This makes it important to understand the clinical significance of grade 1-2 hypertensive retinopathy, which is easily and frequently identified in clinical practice.

The conclusions of the present study support the clinical significance of hypertensive grade 1-2 retinopathy. However, the limited number of subjects and the use of ophthalmoscope for retinal assessment somewhat reduces the significance of the findings. Nevertheless, they are similar to those obtained in other studies that used the fundus photography method to make a more detailed retinal assessment.

In conclusion, retinal examination may show the existence of systemic microvascular injury. Grade 1-2 hypertensive retinopathy is frequently seen in hypertensive subject groups with regulated blood pressure. Microalbuminuria, a serious target organ injury, is related to grade 1-2 retinopathy, whose development is induced by increased inflammation. Therefore, grade 1-2 retinopathy may be important in both assessing the effectiveness of treatment and identifying cardiovascular risk increase in hypertensive patients with regulated blood pressure.

References


Diabetic scenario in Arabs

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Diabetes is a metabolic disorder characterized by resistance to the action of insulin, insufficient insulin secretion, or both. It is estimated that diabetes affects approximately 5% of the population in the industrialized nations, majority (~90%) constitute type-2 diabetes. It is expected that diabetes will be one of the most challenging public health problems of the 21st century. It is now affecting more than 150 million...
people worldwide and is predicted to rise to 300 million by 2025. Overall prevalence of type-1 diabetes in Saudi Arabia was found to be 0.3%, type-2 was 4.53% and impaired glucose tolerance (IGT) 0.72% and for over the age of 60 years type-2 was increased to 26.87%. Recently in a seminar in the kingdom on “Diabetic Patient Empowerment” it was revealed that 25 to 30% of Saudi population is suffering from diabetes, and 52% of the population is obese. Interestingly, 34% army soldiers were also found to be obese. The prevalence of diabetes in Arab countries varies from 3% in Sudan to 35% in Bahrain. In Oman it is 21%, in Kuwait 17.78%, Lebanon 13.1%, Egypt 9.3%, Tunisia 4.05% and Libya 0.19%. Over 10 years of age, it was found to be 4.3% in urban and 5.7% in rural areas. In Arab Americans of 20-70 years of age, abnormal IGT increased by 41% and diabetes by 18% after 60 years to become 70% and 40% respectively, which was consistent with the rates reported for urban Arab populations. Obesity is defined as body mass index (BMI) >30 kg/m². Diabetes mellitus, hypertension and obesity are among the multifactorial disorders that occur at a higher prevalence in older age group. In Saudi population, obesity is 13.05% in adult male and 20.26% in adult females. In Kuwait 63% of diabetics reported a positive family history. The crude central obesity (abnormal weight hips ratio) in Oman was found to be 49.3% (31.5% males; 64.6% females). In Egypt, obesity was 27%, while in Kuwait obesity was found to be a significant risk factor. In Lebanon, the main risk factor for type-2 diabetes was obesity (55% in males, 67% in females). It was seen in 34% of the Arab Americans as compared to 26% reported for general US population. Hypertension and positive family history of diabetes in Saudi diabetic subjects were 27.6% and 41.7%. Maternal history was positive in 32% while paternal history in only 13% of men with diabetes. Transition to urban environments and greater economic affluence has been associated with changes in physical activity and dietary patterns that have promoted the development of non-communicable diseases. Population that formerly lived in harsh environmental conditions in the Middle East, had developed an efficient metabolism for better survival. This former metabolic advantage was lost once a modern life style, characterized by inactivity and high-energy diet, was adapted. Profound changes in the lifestyle of the people in the Arabian Peninsula during the last 30 years have been associated with the emergence of diabetes. Diagnostic criteria for diabetes mellitus is based on fasting plasma glucose above 108-116 mg/dl and 2 h postprandial above 185 mg/dl and a hemoglobin A1c greater than 5.9-6%. To minimize the discrepancy between fasting plasma glucose Oral Glucose Tolerance Test (OGTT), cut-off values of 126 mg/dl and 200 mg/dl respectively have been adopted by the World Health Organization in 1998. In addition, impaired fasting glucose is defined by plasma glucose ≥110 mg/dl but less than 126 mg/dl. This corresponds to the category of IGT, which is defined as a 2 h glucose value 140 mg/dl but less than 200 mg/dl during OGTT. Poor compliance (54.4%) and infection (28%) were the most common precipitating factors for type-1 diabetes among Saudi children. A low mortality rate of 2.9% suggested better medical care. Prevalence of diabetic retinopathy in Saudi population was 11.3%. The Saudi type 2 diabetics with nephropathy were presented nephrotic range of proteinuria in 5.6%, clinical proteinuria in 30.4% and microalbuminuria in 16.8% of cases. Hypertension and retinopathy were present in 36.8% and 37% of patients respectively. In Egypt, retinopathy was 42%; albuminuria 21%, neuropathy 22%; nephropathy 7%, and foot ulcers 1%. The most common complications of diabetes in Libya were neuropathy (45.7%). For an insulin-resistant population, however, cardiovascular mortality is higher in the Bahraini population. Diabetes is a complex disorder associated with several potentially preventable disabilities, such as blindness, amputation, neuropathy, nephropathy, and cardiovascular disease. Overweight and obesity are coexisting risk factors amongst hypertensive and diabetic adult patients. Most individuals with type 2 diabetes exhibit intra-abdominal or visceral obesity and surprisingly modest weight reduction markedly reduces the development of type 2 diabetes. Childhood obesity is a relatively recent phenomenon, and the emergence of type-2 diabetes in childhood is a serious development. Not all obese people eat more than the average person, but all obviously eat more than they need. In addition, the following steps may help ameliorate the current alarming condition of diabetes in Arabs in general and Saudis in particular: 1) Promote and improve the public education and awareness regarding diabetes mellitus in Saudi Arabia. The venue, date and time of such programs must be widely publicized before their commencement so that all those genuinely interested may reap its benefits. Publication of small booklets in Arabic, in lay man’s terms. 2) Discussion and lectures on television and public lectures. 3) Informative articles in news papers. 4) Inclusion of information in school curricula. 5) Education of patients: dietary measures to maintain glycemic control, foot care and importance of prompt contact with health care providers with special attention to villages, rural areas and older people in terms of method of approach. 6) Health care workers’ role in educating the family of the patient regarding: role of diet, exercise, weight control and compliance with the drug therapy. 7) Treatment of hypertension in those with signs of early nephropathy, even those with
mid hypertension. 8) Early detection and treatment of proliferative retinopathy.

These aforementioned approaches will also help reduce the cost of treatment, which is currently Saudi Riyals 3 billion per month in the Kingdom of Saudi Arabia. Eastern Mediterranean and Middle East in the outpatient care for people with diabetes is 2.6 times that for the people without diabetes. In Europe it is 28% extra cost of diabetes. In America, it has increased many folds. In South-East Asia it may be 25% of the average family income. In Western Pacific it is 4.3 times more in non diabetics.

References


Effect of Helicobacter pylori eradication on short-term control of glycemia in patients with type 2 diabetes mellitus

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Diabetes mellitus (DM) is one of the most prevalent endocrine diseases, and its precise control is important for prevention of serious vascular complications. The importance of glycemia control has been emphasized by studies, showing that diabetic patients with higher levels of glycosylated hemoglobin (HbA1c) have significantly more long-term complications of the disease, such as retinopathy, nephropathy, and neuropathy. Infections can lead to hyperglycemia in patients with DM and increase their drug requirement; the mechanisms are unknown, but are thought to include the secretion of counter-regulatory hormones due to stress, as well as the production of cytokines. Cytokines by themselves can stimulate the secretion of insulin counter-regulatory hormones, and they can directly affect carbohydrate metabolism. Infection with Helicobacter pylori (H. pylori) induces gastric inflammation in most subjects and has been associated with an increased production of cytokines such as tumor necrosis factor, interferon-γ, and interleukins. In some studies, patients with concomitant H. pylori infection requires higher doses of insulin and yet had higher levels of HbA1c than their uninfected counterparts. Our study designed to assess effect of H. pylori treatment on HbA1c level (Glycemic Control Index) in diabetic patients. Patients from January to June 2005 with type 2 DM in diabetes clinic of Fatemeh Hospital, had positive urea breath test (UBT), allocated randomly into 2 equal groups. The first group treated for H. pylori infection and UBT test repeated in them after 6 weeks of cessation of therapy. If the result were negative, the patient enrolled into study as case. The second group patients enrolled into study as control. HbA1c and fasting blood sugar (FBS) measured in all patients at the beginning of study and 3-month later. For each patient, the differences of HbA1c and FBS at the beginning and at the end of study calculated and the mean of these variables compared in 2 groups. The UBT did with Model 2000, Fluorescence Inc, Ontario, Canada instrument. HbA1c measured with Enzyme-linked immunosorbent assay (ELISA) method (Diaplus Company) and FBS with Glucose oxide method (Man Company). For treatment of H. pylori infection, Omeprazole 20 mg (by mouth [po], twice a day [bid]), Azithromycin 250 mg (po, bid), Bismuth subcitrate 240 mg (po, bid), and Metronidazole 500 mg (bid) for 10 days was used. For randomization (allocation) of data, we used Epi Info program (Version 6.04d - January 2000, CDC U.S.A, WHO Switzerland). Before allocation, patients that need to change their diet or drug regimens and had certain sport recommendations excluded from study. For comparing demographic and clinical data in the 2 groups, we used independent T-test for quantitative and Chi-square test for qualitative data. A
Effect of H. pylori eradication in DM2

Table 1 - Effect of Helicobacter pylori eradication on short-term control of glycemia in patients with type 2 diabetes mellitus.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group</th>
<th>Number</th>
<th>Mean</th>
<th>SD</th>
<th>t*</th>
<th>df</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1c decrease (%)</td>
<td>Control</td>
<td>22</td>
<td>0.019</td>
<td>0.22</td>
<td>0.612</td>
<td>39</td>
<td>0.54</td>
</tr>
<tr>
<td></td>
<td>Case</td>
<td>19</td>
<td>0.057</td>
<td>0.16</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FBS decrease (mg/dl)</td>
<td>Control</td>
<td>22</td>
<td>11.95</td>
<td>60.82</td>
<td>0.54</td>
<td>39</td>
<td>0.58</td>
</tr>
<tr>
<td></td>
<td>Case</td>
<td>19</td>
<td>3</td>
<td>39.51</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

HbA1c - Glycosylated hemoglobin, FBS - Fasting blood sugar, SD - Standard deviation, df - degrees of freedom, *Independent T-test

received statistical test was carried out with Statistical Package for the Social Sciences (SPSS) program (Version 11.5, 2002, SPSS Inc.) and two-sided p values lower than 0.05 were considered to be statistically significant. Nineteen cases and 22 controls enrolled in study. H. pylori eradication rate in patients in first group was 76% (19 from 25 patients, 95% confidence intervals: 54.4-89.8%). No significant difference observed in demographic and clinical aspects between the 2 groups (Age, Gender, Duration of DM, Oral or Insulin therapy). As shown in Table 1, the mean decrease of HbA1c level in case (treatment) is more than control (without treatment) group, however, this difference is not statistically significant and very small. Mean decrease of FBS shows no statistically significant difference between 2 groups as well. So, this study suggests that H. pylori treatment in patients with type 2 DM has no roles in short-term control of the disease.

The studies have been performed up to now, have differences in following point: different populations (adult/pediatric), different groups (type 1/type 2 diabetes) and different duration of follow-up (short-term/long-term). Thus, in most studies, number and type of evaluated cases has limitations and the results are different. In future, it is required to perform more extensive studies, using randomized clinical trials with long-term follow-up, and avoidance of all confounding variables, which can affect on glycemia control.

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References


Arabian incense exposure among Qatari asthmatic children. A possible risk factor

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Asthma is a multifactorial disease that is likely to be the result of interactions between a genetically determined predisposition to allergic diseases and environmental factors that serve to enhance allergic inflammation and target inflammation to the lower airway. The Expert Panel of the National Asthma Education and Prevention defined asthma as a chronic inflammatory disorder of the airways, in which many cells and cellular elements play a role, in particular mast cells, eosinophils, T-lymphocytes, neutrophils, and epithelial cells.1 People spend approximately 90% of their time indoors, where the levels of some pollutants often are higher than they are outdoors. Indoor pollutants that can trigger asthma include house dust, environmental tobacco smoke, pet dander, incense, and molds.2 Incense is a traditional perfume, which is commonly used in the Arabian Gulf area. It consists of charcoal, starch, karaya gum, aromatic chemicals, plant wood, perfume, and essential oils. Incense has appeared in many forms: raw woods, wood chips, resins, powders, and even liquids or oils. The Arabian Gulf people prefer to have fragrance of incense around, and they use various
Arabian incense exposure among Qatari asthmatic children

Perfumes on their body and clothes. A common ancient tradition to keep their houses and offices filled with fragrance by burning incense on hot coals in a special type of incense burner or Mabkhara. The most commonly used incense for burning is oud. The tree referred to as “oud” is Aquilaria agallocha, and is also known as lignum aloes, aloes wood, agarwood, and eaglewood. The unique aroma is due to a fungal infection of the heartwood, which causes the tree to secrete aromatic protective resin that has long been used in the Middle East as a source of incense and perfume. Other types of incense (such as bakhour) are derived from sandalwood and are usually mixed with other ingredients such as agarwood, natural oils, and other natural ingredients. Frankincens is a resin produced by small pine like trees of the genus Boswellia that grows only in arid areas of southern Arabia and in parts of Somalia, Sudan, and Ethiopia. The gum oozes out, hardening in lumps. These lumps are then gathered and stored in mountain caves for 6 months to dry. Combined together, or with other spices such as cinnamon, cassia, and iris, they create a myriad of scents. The aim of this study is to determine whether exposure to environmental incense may contribute, as trigger factors, for occurrence of asthma among Qatari asthmatic children. The Research Ethics Committee of Hamad General Hospital, Hamad Medical Corporation, approved this study. It was conducted between September to November 2005, following a retrospective case control study design. An interview questionnaire was applied at the Pediatrics Outpatient Clinics of Hamad General Hospital (a tertiary care center in the State of Qatar) on families of asthmatic (cases) and non-asthmatic children (control). According to a consecutive sampling technique, 100 asthmatic Qatari children (55 boys and 45 girls) were included in this study. A total of 100 healthy children were selected as controls. The clinical diagnosis was based on the Expert Panel of the National Asthma Education and Prevention. Both study groups were investigated for the past exposure of interest (Arabian incense) in addition to family history of asthma, allergic rhinitis, and atopic eczema. Asthmatic children comprised 55 boys and 45 girls (mean age ± SD: 4.31 ± 3.48 years), while healthy controls comprised 50 boys and 50 girls (mean age ± SD 4.37 ± 3.65 years. Their age ranged from 2-12 years. Table 1 shows that asthmatic mothers or siblings constitute significant risk factors for bronchial asthma among Qatari children (p=0.026, p=0.045, and p=0.014). The present study showed that atopic families are more exposed to the Arab Gulf incense with statistical difference in the impact of potential risk factor in asthma attack. Whether this reflects a high allergenicity of Arabian Gulf incense is uncertain. Further studies are needed in order to determine which part of ingredients is directly associated with airwayhyper-responsiveness or considered as an irritant to airways. Both in the State of Qatar and Kuwait, the implication of exposure to different types of incense as a trigger for asthma symptoms has been reported as a potential risk factor.

Table 1 - Comparison between cases and control as regard to the family history of asthma, allergic rhinitis, and atopic eczema.

<table>
<thead>
<tr>
<th>Family history</th>
<th>Cases (n=100)</th>
<th>Control (n=100)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mother</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asthma</td>
<td>20</td>
<td>9</td>
<td>0.027</td>
</tr>
<tr>
<td>Allergic rhinitis</td>
<td>17</td>
<td>13</td>
<td>0.627</td>
</tr>
<tr>
<td>Atopic eczema</td>
<td>11</td>
<td>6</td>
<td>0.205</td>
</tr>
<tr>
<td>Father</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asthma</td>
<td>9</td>
<td>3</td>
<td>0.074</td>
</tr>
<tr>
<td>Allergic rhinitis</td>
<td>10</td>
<td>9</td>
<td>0.809</td>
</tr>
<tr>
<td>Atopic eczema</td>
<td>5</td>
<td>1</td>
<td>0.097</td>
</tr>
<tr>
<td>Sibling</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Asthma</td>
<td>52</td>
<td>11</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Allergic rhinitis</td>
<td>7</td>
<td>5</td>
<td>0.552</td>
</tr>
<tr>
<td>Atopic eczema</td>
<td>6</td>
<td>5</td>
<td>0.756</td>
</tr>
</tbody>
</table>

In conclusion, exposure to potential indoor environmental Arabian incense can be commonly incriminated exposures. Moreover, asthmatic mother or sibling constitutes significant risk factors for bronchial asthma among Qatari children. It is recommended to avoid exposure to identified factors triggering bronchial asthma among children.

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References

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 stores 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. In normal pregnancy, maternal serum ferritin level decreases with advancing gestation, even when iron supplementation has been given antenatally. Lao et al 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/m², has shown that those who developed impaired glucose tolerance during pregnancy, had significantly increased Hb concentrations compared with BMI-matched groups. 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, 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 (pBMI) (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
maternal weight gain during pregnancy. The p BMI was 23.1±3.5 kg/m² for diabetic group and 22.8±3.1 kg/m² 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 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

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

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>GDM (n=56)</th>
<th>Controls (n=56)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gravida</td>
<td>2.45±1.45</td>
<td>1.93±1.16</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Age (years)</td>
<td>29.96±3.9</td>
<td>26.63±5.51</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Weight gain in pregnancy (kg)</td>
<td>13.75±3.2</td>
<td>12.54±2.46</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Gestational age (week)</td>
<td>38.13±1.65</td>
<td>39.04±1.43</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>APGAR 5-minute</td>
<td>8.77±0.46</td>
<td>8.95±0.22</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Serum ferritin (ng/mL)</td>
<td>17.17±13.35</td>
<td>16.23±15.28</td>
<td>NS</td>
</tr>
<tr>
<td>Mean cell volume (fl)</td>
<td>90.2±5.0</td>
<td>89.3±4.7</td>
<td>NS</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>34.6±3.2</td>
<td>34.1±2.9</td>
<td>NS</td>
</tr>
<tr>
<td>Transferrin (µmol/L)</td>
<td>63.5±18.8</td>
<td>61.4±16.6</td>
<td>NS</td>
</tr>
<tr>
<td>Insulin (µIU/mL)</td>
<td>10.92±4.48</td>
<td>9.13±3.75</td>
<td>NS</td>
</tr>
</tbody>
</table>

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

Figure 1 - Correlation between ferritin and hemoglobin values for control group.
Maternal serum ferritin and hemoglobin values in patients with gestational DM

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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