tive patients. Furthermore, we found no evidence of increased iron overload in patients with more prominent inflammatory changes.

HCV infection is an independent risk factor for liver fibrosis.[10] Nevertheless, fibrosis progression was unrelated to the presence of HCV RNA in a recent study.[2] In our study as well, HCV antibody and HCV RNA positive patients did not significantly differ from seronegative patients in fibrosis score.

In conclusion, liver disease is common in TM patients and severe hepatic iron overload is still observed in approximately 40% of them. In this context, increased implementation of the direct assessment of liver iron content to monitor hemosiderosis is of special importance in order to individualize chelation therapy. In parallel, the maximum possible efforts must be concentrated on improving compliance to chelation therapy.

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Disorders of iron Metabolism

Hemoglobinopathies, body iron stores and gestational diabetes mellitus

Higher iron stores, reflected by an elevated ferritin concentration and elevated transferrin saturation, can affect glucose intolerance during pregnancy. We determined the incidence of gestational diabetes mellitus in patients with heterozygous form of hemoglobinopathies and in a healthy control group.

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The association between β thalassemia major and intermedia and an increased risk of diabetes mellitus (DM) has been shown by various studies.[1-3] Glucose intolerance correlated significantly with the number of transfusions received by subjects with β thalassemia major.[1] Interestingly, patients with heterozygous sickle cell anemia had higher values of glycosylated hemoglobin than did homozygous patients.[4]

In a retrospective case-control study at the Department of Obstetrics, University Hospital Zurich we compared the incidence of gestational diabetes (GDM) in a set of pregnancies among women heterozygous for various hemoglobinopathies and in a normal, matched control group. The matching criteria were the known diabetes risk factors, i.e. maternal age, parity, ethnicity, weight and body mass index. Between 1998 and 2001 we identified 29 patients presenting heterozygous hemoglobinopathies and anemia. Hematologic work-up, including high performance liquid chromatography (HPLC), plasma iron status and erythrocyte indices, showed the presence of α thalassemia trait in 2, hemoglobinopathy E in 2, β thalassemia in 20 and sickle cell trait in 5 pregnancies. Before measuring plasma ferritin concentration, any inflammation was excluded. Treatment of anemia in the patients with a hemoglobin concentration less than 9.0 g/dL was individualized on the basis of hematologic parameters and iron status, and consisted of recombinant human erythropoietin (rhEPO; 10,000 U) with or without parenteral iron (iron-III-saccharate 100 mg).[5] Screening for GDM and the determination of iron status were conducted before therapy. Screening tests for genetic hemochromatosis were not done. All patients and controls were examined for GDM between 24 and 28 weeks of gestation as proposed by Perucchini *et al.*[6]

The incidence of diabetes mellitus was 20.7% (6/29) in the study group versus 0% in the control group (Fisher's exact test; p=0.0009). When all cases with impaired glucose tolerance were included the incidence was 31% (9/29) in the study group vs. 6.9% (4/58) in the control group (Fisher's exact test; p=0.008). The demographic data and iron status of the study and the control group are listed in Table 1. The median ferritin values were statistically different in the patients with GDM in the study group (76 vs. 35 ng/mL; Mann-Whitney test, p=0.004). There is little information on the relation between heterozygous forms of hemoglobinopathies and the impairment of glucose regulation. Only one study has examined the association between heterozygous α thalassemia trait

Table 1. Maternal demographic data and body iron status in the study and control groups.

	Study group (n=29)	Control group (n=58)	P value
Age (years)	29.48±6.20	29.29±5.35	NS
Weight (kg)			
Booking	55.79±7.87	57.72±8.00	NS
Pre-delivery	70.55±10.71	70.46±11.06	NS
Height (cm)	158.76±7.17	161.27±6.12	NS
BMI (kg/m^2)			
Booking	22.10±2.62	22.20±2.61	NS
Third trimester	27.96±3.73	27.04±3.93	NS
Hb (g/dL)			
Booking	10.01±1.70	11.78±1.05	0.000
Third trimester	10.21±1.22	11.74±0.92	0.000
Parity	2.31±2.05	2.10±1.41	NS
Ferritin (ng/mL)	53 [10 - 261]	10 [4 - 121]	0.0000
Iron (µmol/L)	19.37±10.62	10.37±5.65	0.0060
Transferrin (µmol/L)	35.04±8.81	45.17±8.71	0.0011
Transferrin saturation (%)	30.54±23.95	12.14±7.39	0.0006

and GDM.[7] A higher incidence of GDM was found in patients suffering from α thalassemia trait than in a control group.[7] Lao *et al*. suggest that iron excess might not be the explanation of the high prevalence of GDM in women with α thalassemia trait, because pancreatic alpha cell overactivity with increased glucagon response has also been shown in thalassemic patients with impaired glucose tolerance.[7] However, two recent new prospective case-control studies confirmed the association between stores of iron and the incidence of diabetes.[8,9] These studies showed that higher iron stores are associated with an increased risk of type 2 diabetes in healthy populations, independently of known diabetes risk factors. Our results confirmed this hypothesis. In our study the median ferritin concentration and the mean transferrin saturation in the study group were significantly higher than in the control group. In the study group, the median ferritin values were statistically different in patients with GDM (p=0.004). Despite the higher incidence of GDM in the study group, there were no differences in the incidence of obstetrical complications or perinatal outcome.

Our results support the hypothesized association between heterozygous forms of hemoglobinopathies with higher iron stores and the impairment of carbohydrate regulation.[10] The increased risk of GDM could have a substantial impact on preconception counseling and the antenatal management of patients with heterozygous forms of hemoglobinopathies. Further studies are needed to clarify the origin of the impaired glucose regulation in patients heterozygous for hemoglobinopathies. It would be useful to apply higher iron stores as a diabetes risk factor and to compare the incidence of diabetes mellitus between two groups with heterozygous forms of hemoglobinopathies with high and low ferritin concentrations and transferrin saturation. If this identifies an increased incidence of GDM in patients with elevated ferritin concentrations and transferrin saturation, one may suspect that the higher body iron store is the main factor in impaired glucose regulation.

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Chronic Myeloid Leukemia

e6a2 *BCR/ABL1* fusion with cryptic der(9)t(9;22) deletions in a patient with chronic myeloid leukemia

This is the first report of e6a2 and e1a2 *BCR/ABL1* positive chronic myeloid leukemia (CML) with cryptic deletions of the 5'ABL1 and 3'BCR in separate clones which differ in genomic regions of the deleted der(9). Both deletions were detected throughout monitoring. Imatinib mesylate stabilized this CML with rare genetic aberrations for a relatively long time.

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A 37-year old man, was admitted to the Haematology Unit, Perugia General Hospital because of persistent fever, scotoma, and sternal pain. A peripheral blood count showed anemia (hemoglobin 10.9 g/dL), and leukocytosis (WBC 38×10^9/L). The blood film showed