

## CLINICAL LABORATORY VALUES DURING DIABETIC PREGNANCIES

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**Background:** Physiological pregnancy can affect routine laboratory tests, e.g., the erythrocyte sedimentation rate increases above the reference range for healthy non-pregnant adults and little is known about whether diabetes and pregnancy together can cause additional changes that require monitoring of blood-tests. **Objective:** The purpose of this study was to investigate changes in clinical chemistry and haematological laboratory test results during pregnancies of type 1 diabetics and to compare the results with changes during normal pregnancies. **Methods:** We studied 25 type 1 diabetic women with standard clinical chemistry and haematological blood-tests during pregnancy. **Results:** Haemoglobin, haematocrit, and erythrocyte number decreased until the 3<sup>rd</sup> trimester and leucocytes and platelets did not change significantly. The erythrocyte sedimentation rate increased by over 200%. Protein and albumin decreased until the 3<sup>rd</sup> trimester to below the reference range. Urea did not change, creatinine decreased and uric acid increased within the reference range. AST and ALT remained within the reference range. Alkaline phosphatase and leucine aminopeptidase increased until above the reference range. Cholesterol and triglycerides increased until the third trimester above results from normal pregnancies. **Conclusion:** A wide range of biochemistry and haematology laboratory values changed during diabetic pregnancy comparable to physiological pregnancies. No additional routine laboratory-testing during diabetic pregnancies compared with physiological pregnancies is required.

**Key words:** Type 1 diabetes, pregnancy, laboratory values, haematological, clinical biochemistry.

### INTRODUCTION

Despite considerable technological advances and increased knowledge, pre-existing maternal diabetes is still associated with increased risks for woman and baby. Pregnancy outcomes in women with pre-existing diabetes are correlated with the level of blood glucose before and during pregnancy.<sup>1,2</sup> Apart from blood glucose level also other parameters such as glycosylated haemoglobin, cholesterol and triglycerides can be increased by the metabolic state of diabetes and contribute to the development of complications.<sup>3,4</sup>

Physiological pregnancy can affect a number of routine clinical laboratory blood tests such as the erythrocyte sedimentation rate (ESR) with a 2-3 times increase above the reference range.<sup>5-7</sup> Blood leucocytes can increase to up to 16,000/ $\mu\text{l}$ <sup>5-7</sup> and the alkaline phosphatase can increase to up to 2-3 times above the upper limit of normal.<sup>8-11</sup> Blood tests such as leucocytes, ESR, and alkaline phosphatase are frequently used in the clinical care of diabetic patients and little is known about whether diabetes during pregnancy causes additional changes and requires particular laboratory testing and monitoring.<sup>1-2</sup>

The purpose of this study was to monitor the course of clinical chemistry and haematological laboratory blood test results during pregnancies of type 1 diabetic patients, and to compare the results with changes during physiological pregnancies.

### MATERIAL AND METHODS

We conducted the study at University Clinic Tübingen, Department of Endocrinology and Clinical Chemistry, a tertiary care centre. After obtaining

internal approval for the study 28 pregnancies of 25 Type 1 diabetic patients were investigated as outpatients for one year with monthly clinical chemistry and haematological blood tests.

The inclusion criteria were Type 1 diabetic pregnancy and all White-classes for complications. The exclusion criteria were gestational diabetes, incomplete medical records, and type 2 diabetes.

The following clinical blood tests were performed according to standard methods:

Erythrocyte sedimentation rate (ESR), complete blood count, erythrocyte indices, haematocrit, creatinine, urea nitrogen, uric acid, bilirubin, total protein, albumin, protein electrophoresis, cholesterol, triglycerides, glutamic oxalacetic transaminase (GOT, AST), glutamic pyruvate transaminase (GPT, ALT), glutamic-lactate-dehydrogenase (GLDH), lactic dehydrogenase (LDH), alkaline phosphatase (AP),  $\gamma$ -glutamyl transferase ( $\gamma$ -GT), leucine aminopeptidase (LAP), cholinesterase (Che), glucose (non-fasting), glycosylated haemoglobin (Hb A1), potassium, sodium, calcium, chloride, phosphate and iron.

The data were divided into 31 days periods during pregnancy, time periods before and after pregnancy and were summarized with mean and standard error of the mean (SEM). The data were compared with physiological pregnancies from previously published studies.<sup>6-14</sup> The statistical program SPSS 3.0 (Chicago, Illinois, US) was used for the multivariate analysis of variance.

### RESULTS

#### Diabetic women and pregnancies:

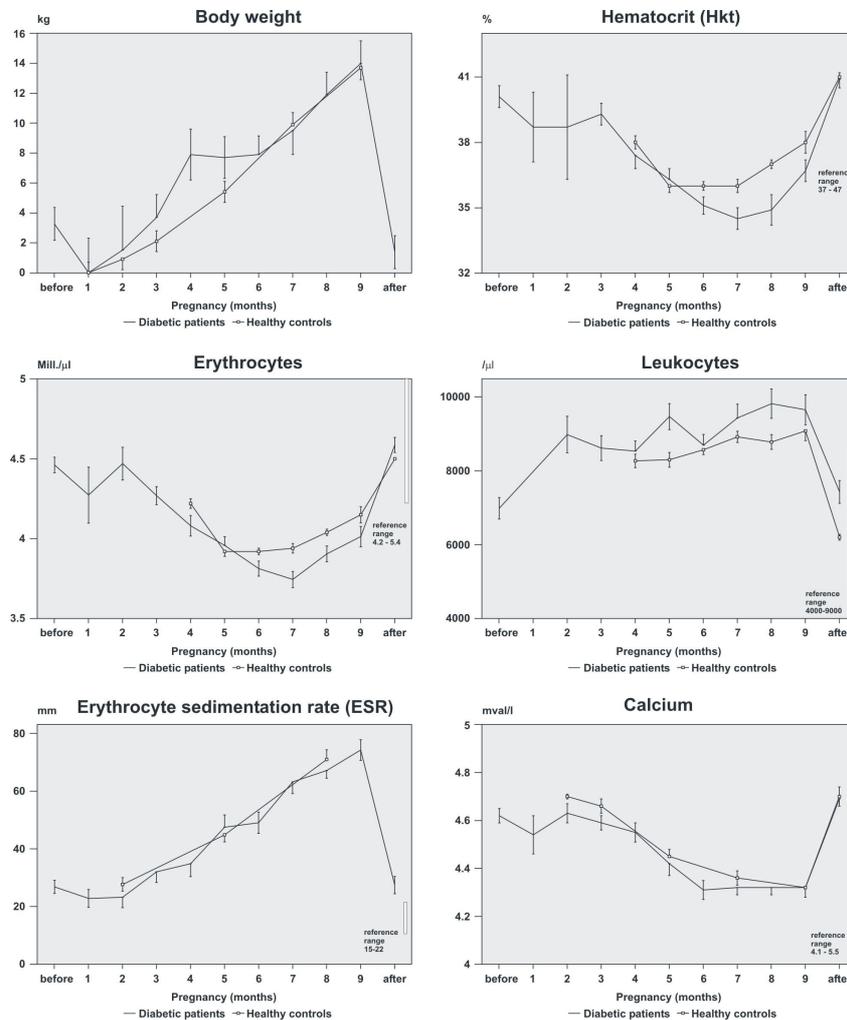
The diabetic women had a mean age of 28 $\pm$ 4 years (mean $\pm$ SEM) with a mean age at diagnosis of 20 years

(1-37 years range). The mean BMI (body mass index) was  $22.7 \pm 2.5$  (mean  $\pm$  SEM), insulin therapy was ICT (intensive conventional therapy) in 20 (71%) and CSII (continuous subcutaneous insulin) in 8 (29%) patients. Sixteen (57%) diabetic patients were classified as White B, 6 (21%) as C, 4 (14%) as D, and 2 (7%) as White R.

**Laboratory studies**

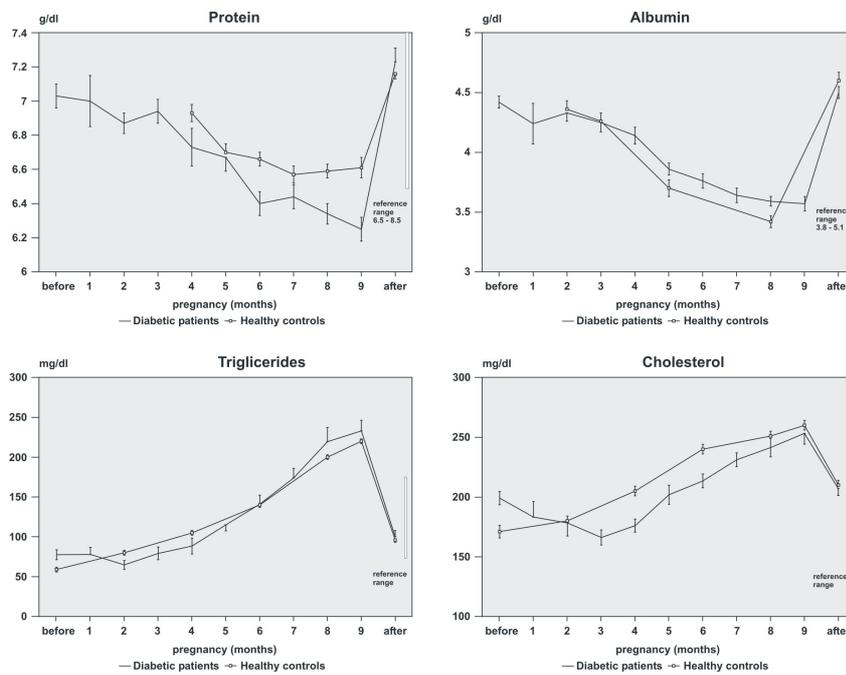
Haemoglobin, haematocrit, and erythrocyte number decreased with lowest values during the third trimester. Leucocytes (Figure-1) and platelets (data not shown) showed no significant changes. The ESR increased by over 200% above the reference range (Figure-1). Electrolytes did not change except for a decrease of calcium within the reference range (Figure-1). Protein and albumin decreased until the third trimester to below the reference range (Figure-2). Urea nitrogen

did not change, creatinine decreased and uric acid increased within the reference range (data not shown). Cholesterol and triglyceride increased until the third trimester slightly above the reference range (Figure-2). AST and ALT remained within the reference range. Alkaline phosphatase and leucine aminopeptidase increased until the third trimester and were elevated above the reference range (>150%). The postprandial blood glucose concentration and glycosylated haemoglobin (Hb A1) results were elevated compared to physiological pregnancies (data not shown).



**Figure-1: Pregnant type 1 diabetic women studied with monthly testing of body weight, haematocrit (Hkt), erythrocytes, leukocytes, erythrocyte sedimentation rate (ESR) and calcium in peripheral blood.**

Results were recorded before, during, and after pregnancy (mean  $\pm$  SEM). Results for physiological pregnancies from healthy controls: body weight,<sup>26</sup> haematocrit (Hkt),<sup>12</sup> erythrocytes,<sup>12</sup> leukocytes,<sup>12</sup> erythrocyte sedimentation rate (ESR)<sup>27</sup> and calcium.<sup>28</sup>



**Figure-2: Pregnant type 1 diabetic women studied with monthly testing of protein, albumin, triglyceride, and cholesterol in peripheral blood.**

Results were recorded before, during, and after pregnancy (mean  $\pm$  SEM). Results for physiological pregnancies from healthy controls: protein,<sup>12</sup> albumin,<sup>28</sup> triglyceride,<sup>29</sup> and cholesterol.<sup>29</sup>

## DISCUSSION

The majority of the investigated laboratory blood tests during pregnancy did not demonstrate clinically significant differences between diabetic pregnancies and physiological pregnancies. Only postprandial blood glucose-concentrations and glycosylated haemoglobin (Hb A1) were elevated compared to physiological pregnancies.<sup>3,15-19</sup>

During physiological pregnancies the mean daily glucose concentration decreases from 80 mg/dl before pregnancy to 69 mg/dl during the 38<sup>th</sup> week.<sup>7</sup> During diabetic pregnancies most studies have observed elevated glucose blood concentrations above 120 mg/dl and greater fluctuations with lower fasting values than during physiological pregnancies.<sup>14,18,20-22</sup>

During diabetic pregnancies most investigators have reported higher percentages of glycosylated haemoglobin (Hb A1) compared with physiological pregnancies and only minor overall changes during the course of pregnancy.<sup>17,18,23-25</sup>

The increase in blood of erythrocyte sedimentation rate (ESR), alkaline phosphatase, and triglycerides by over 200% and the decrease of haematocrit (Hkt) by 10% were the most notable findings during diabetic pregnancies, and the changes were comparable to the changes during physiological pregnancies.<sup>5-7,9,11,12</sup> For the clinician familiarity with these changes can be useful when caring for pregnant

patients, e.g., with rheumatological disorders where monitoring of erythrocyte sedimentation rate is required or when investigating abnormalities of the liver with alkaline phosphatase or testing of other enzymes, which all can be affected by liver disease as well as pregnancy.

## CONCLUSION

In summary, changes of a wide range of biochemistry and haematology blood test results were observed during diabetic pregnancy equivalent to physiological pregnancies. No additional routine laboratory testing during diabetic pregnancies compared with physiological pregnancies is required.

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