



C-reactive protein in early months of pregnancy as a screening test for gestational diabetes mellitus developing in later months of pregnancy

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OBJECTIVE(S) : To study whether positive test for C-reactive protein in early months of pregnancy can be used as a screening test for gestational diabetes mellitus developing in later months of pregnancy.

METHOD(S): C-reactive protein was tested by latex-agglutination semi-quantitative method in early months of pregnancy in 91 women. Gestational diabetes mellitus was diagnosed by 3 hour glucose tolerance test, if recommended after performing the glucose challenge test between 24-28 weeks of pregnancy. Statistical analysis was done with Z statistic.

RESULTS: Among the 91 women 27 were C-reactive protein test positive, out of whom four developed gestational diabetes (14.8%). Among the 64 women that were C-reactive protein negative, seven developed gestational diabetes (10.9%). This was not statistically significant.

CONCLUSION(S): C-reactive protein in early months as an inflammatory marker is not a dependable screening test for gestational diabetes developing in later months of pregnancy.

Key words : C-reactive protein, gestational diabetes mellitus

Introduction

Gestational diabetes mellitus (GDM) is defined as the new onset or new diagnosis of glucose intolerance during pregnancy and its incidence varies from 3-12% depending on the population studied. This estimate may increase in future given the alarming increase in the rate of obesity and type 2 diabetes mellitus in younger generations. GDM is an important medical complication in pregnancy and has significant impact on perinatal and maternal morbidity and mortality.

There is increasing evidence that an ongoing cytokine induced acute phase response (sometimes called low grade inflammation, but part of a widespread activation of the innate immune system, is closely involved in the pathogenesis of type 2 diabetes mellitus (DM)¹.

Although GDM and type 2 DM share certain pathophysiological mechanisms, few studies have examined the relation between inflammation and risk of GDM. The present study aims to find out the presence of C-reactive protein (CRP) as an inflammatory marker in early months of pregnancy as a screening test for GDM development in later months of pregnancy.

Methods

One hundred pregnant women reporting for antenatal care in the first trimester were tested for presence of CRP in blood, in addition to the standard antenatal tests. Nine women were lost to follow-up and the records of only 91 women were finally available. These women were followed up in the antenatal clinic and underwent glucose challenge test (GCT) with 50 g of glucose between 24 and 28 weeks of gestation, and the standard 3 hour glucose tolerance test (GTT) was done if the value of plasma glucose in GCT exceeded 140 mgm%. GDM was diagnosed as per the modified criteria of Carpenter and Coustan².

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CRP was tested by the latex agglutination semiquantitative test kit (Humatex CRP, Human Gesellschaft fur Biochemica and Diagnostica mbH, Germany). This test kit is standardized to detect CRP concentrations of approximately 6 mg/L or higher in undiluted serum samples (positive test).

Exclusion criteria were –

1. Known diabetics
2. History of GDM in past pregnancy
3. Other associated endocrine diseases like, thyroid disease or adrenal disease
4. Women taking corticosteroid therapy

Sixty-five percent of the women were primigravidas. The youngest woman was 22 years old and the oldest 41 years. Lowest body mass index (BMI) was 15 kg/m² and the highest 30 kg/m².

Table 1. Demographic characteristics of the two groups of women studied.

Characteristic	CRP positive (n=27)		CRP negative (n=64)	
	Developed GDM	Did not develop GDM	Developed GDM	Did not develop GDM
Average age (years)	28.5	27.5	31.4	27.9
Average BMI (kg/m ²)	26	25.3	25.7	24.2

GDM – Gestational diabetes mellitus.

Results

Table 1 shows the demographic characteristics of the two groups of women, those that tested CRP positive and those that tested negative.

Out of 91 women, 27 were found to have positive CRP test and 4 of them (14.8%) developed GDM later. Similarly, 7 out of the 64 (10.9%) CRP negative group developed GDM.

Discussion

CRP is an acute phase reactant and its elevation is a nonspecific host response to infection, inflammation, and tissue injury. Healthy individuals maintain very low concentration of CRP and a normal CRP value is of negative predictive value ³. CRP is easily measured by semiquantitative latex agglutination test which is cheap and can be easily applied in a developing country. Highly sensitive methods are also available but they are expensive.

GDM identifies a population of women at high risk for subsequent development of type 2 DM and represents an early stage in the natural history of the disease. King et al ⁴ found an association between glycemic control and systemic inflammation in people with established diabetes.

The present study shows that GDM develops in 14.8% of CRP positive women and in 10.9% of CRP negative women. Based on this data and developing the Z statistic for testing individual proportions in the two groups, it is found that the calculated value of Z under the hypothesis H⁰ (P₁=50%) was -3.92. Going by the tabulated Z value at 1% level of significance i.e. -2.33, the hypothesis is rejected. Hence the difference between the two proportions is insignificant and so the significance of CRP positivity as a screening test for GDM cannot be confirmed. Also, testing the CRP negative cases by the same statistic on H⁰ (P₂=50%) at 1% level of significance, the observed value is -6.26 which is way beyond the tabulated value of -2.33. Hence, CRP negative cannot be taken as a dependable screening test.

Thus the present study shows that the maternal inflammatory response as detected by elevated CRP level is not different in women prone to GDM before the onset of clinical symptoms, from that in women with uncomplicated pregnancies. Hence inflammatory reaction in the maternal system may not be an important factor in the development of GDM in later months of pregnancy.

Failure to find any significant correlation between elevated CRP and GDM may be because maternal inflammatory response is not exaggerated before the clinical detection of GDM or CRP is not part of the inflammatory response that might exist or the present testing method may not be sensitive enough to detect the low grade but clinically significant inflammation.

The present study was done using latex agglutination test. Schalla et al ⁵ found that the results of latex agglutination test and quantitative radial immunodiffusion assays have strong positive correlations. Again, using high sensitive testing for CRP, Retnakaran et al ⁶ found that CRP was not related to an increased risk of developing GDM. They found that CRP was strongly correlated with prepregnancy obesity, which may be a factor in increasing the risk of GDM. However, our findings (Table 2) are not in agreement with this.

Conclusion

C-reactive protein during early pregnancy cannot be used as a screening test to predict development of gestational diabetes later during pregnancy.

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