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ORIGINAL ARTICLE

MATERNAL SERUM C-REACTIVE PROTEIN CONCENTRATION IN EARLY PREGNANCY AND SUBSEQUENT RISK OF PRETERM DELIVERY

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ABSTRACT: A prospective study was conducted in the department of Obstetrics and Gynaecology, Susheela Tiwari Memorial Hospital, Haldwani, from September 2012 to September 2013. **OBJECTIVES:** Its aim & objective was to study the relationship between maternal Serum C-Reactive Protein concentration in Early Pregnancy and subsequent Risk of Preterm Delivery. **MATERIAL & METHODS:** Women eligible for inclusion in the present study were those who initiated prenatal care prior to 20 wks gestation, were 18 years of age or older and planned to carry the pregnancy to term. Women excluded from the study were those with previous history of preterm delivery, pregnancy induced hypertension or those with gestational diabetes mellitus. Of the total 106 women who participated in the study, 6 were excluded (those who experienced an abortion or fetal demise prior to 28 weeks of gestation and those with multi-fetal pregnancies). Thus, a cohort of 100 women remained for analysis. Gestational age was based on the last menstrual period and confirmed by USG conducted prior to 20 weeks gestation. Maternal blood samples were collected at 12-14 weeks gestation. Serum CRP concentrations were measured by an ultra-sensitive competitive immunoassay. We categorized preterm delivery cases according to gestational age at delivery as very preterm delivery (≤34 weeks gestation) and moderate preterm delivery (between 34 and 37 weeks). **RESULTS:** We observed increased risk of preterm delivery among women with CRP concentrations ≥ 7.5 mg/l as compared with women whose concentrations were < 2.0 mg/l. We noted little evidence of an association between maternal serum CRP concentrations& moderate preterm delivery. However, elevated CRP concentrations were associated with an increased risk of very preterm delivery. **CONCLUSIONS:** From this study, we concluded that determination of CRP status using serum collected in early pregnancy served to clarify the temporal relationship between elevated maternal serum CRP concentrations and subsequent risk of preterm delivery i. e., elevated CRP concentration in early pregnancy is associated with an increased risk of Preterm delivery. But there were some limitations of the study as only single measurement of serum CRP was done & the relatively small number of subjects available for subgroup analyses. Keywords: CRP, early pregnancy, preterm delivery. Maternal Serum C-Reactive Protein Concentration in Early Pregnancy and Subsequent Risk of Preterm Delivery.

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INTRODUCTION: Preterm delivery is defined as delivery prior to the completion of 37 weeks gestation. It is an important determinant of neonatal and infant morbidity and mortality. Intrauterine infections may contribute to 40–50 percent of all preterm births.[1] Systemic maternal infections lead to increased inflammatory cytokine levels, which in turn stimulate prostaglandin production.[2,3] This process can lead to the induction of uterine contractions and cervical ripening culminating in preterm parturition.[4,5,6] C-reactive protein (CRP) is an acute phase reactant protein i.e., a sensitive marker of

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systemic inflammation.[7,8,9] Synthesized in hepatocytes in response to proinflammatory cytokines like IL-6 and TNF-α like in infection & tissue injury. CRP help in diagnosing subclinical infection in preterm labor.[10,11] Increased CRP during gestation have been linked to adverse pregnancy outcomes.[12]

This study examined the association between maternal plasma CRP levels in early pregnancy and risk of subsequent preterm delivery among singleton pregnant women. H. vilsom et al, in 2002, were among the first group of investigators to report that elevated concentrations of CRP in maternal serum during early pregnancy were associated with a 2-fold increased risk of preterm delivery.[13,14]

This early finding has been corroborated by some, though not all investigators. Because of the conflicting reports, we assessed the relation between maternal serum CRP concentrations in early pregnancy and the risk of subsequent preterm delivery among a cohort of singleton pregnant women.

MATERIAL & METHODS: Women eligible for inclusion in the present study were those who initiated prenatal care prior to 20 wks gestation, were 18 years of age or older and planned to carry the pregnancy to term. Women excluded from the study were those with previous history of preterm delivery, pregnancy induced hypertension or those with gestational diabetes mellitus. Of the total 106 women who participated in the study, 6 were excluded (Those who experienced an abortion or fetal demise prior to 28 weeks of gestation and those with multi-fetal pregnancies). Thus, a cohort of 100 women remained for analysis. Gestational age was based on the last menstrual period and confirmed by USG conducted prior to 20 weeks gestation. Maternal blood samples were collected at 12-14 weeks gestation. Serum CRP concentrations were measured by an ultra-sensitive competitive immunoassay. We categorized preterm delivery cases according to gestational age at delivery as very preterm delivery (≤34 weeks gestation) and moderate preterm delivery (between 34 and 37 weeks).

RESULTS:

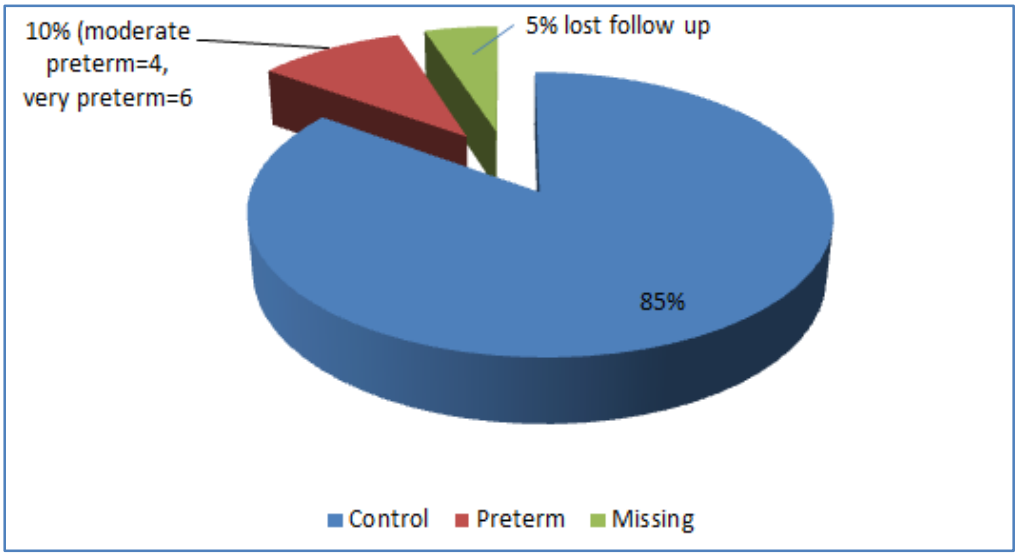

Fig. 1: Distribution of patients enrolled for study

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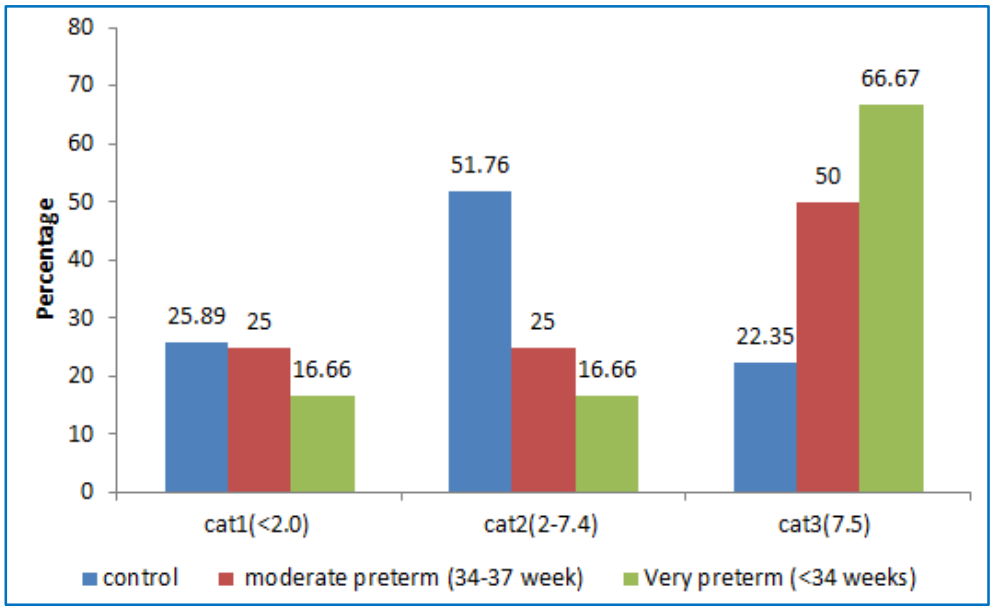

Fig. 2: Distribution of controls & preterm cases in different categories according to CRP levels

We observed increased risk of preterm delivery among women with CRP concentrations ≥7.5mg/l as compared with women whose concentrations were < 2.0 mg/l. We noted little evidence of an association between maternal serum CRP concentrations & moderate preterm delivery. However, elevated CRP concentrations were associated with an increased risk of very preterm delivery. In control vs moderate preterm group, p= 0.348 (Fischer's Exact test) while in control vs very preterm group, p=0.085 (Fischer's Exact test).

DISCUSSION: We observed increased risk of preterm delivery among women with CRP concentrations ≥7.5 mg/l as compared with women whose concentrations were < 2.0 mg/l. We noted little evidence of an association between maternal serum CRP concentrations& moderate preterm delivery. However, elevated CRP concentrations were associated with an increased risk of very preterm delivery. Our results are largely consistent with reports by Hvilsom et al. The authors reported that women with CRP concentrations the ≥85th percentile (i.e., ≥7.6 mg/l) experienced a 2-fold increased risk of preterm delivery compared with women who had lower CRP concentrations. Pitiphat et al also examined the association between CRP concentrations and preterm delivery risk in a nested case-control study. The authors reported that CRP concentrations ≥ 8 mg/l were associated with a more than doubling in risk of preterm delivery.

CONCLUSIONS: From this study, we concluded that determination of CRP status using serum collected in early pregnancy served to clarify the temporal relationship between elevated maternal serum CRP concentrations and subsequent risk of preterm delivery i.e., elevated CRP concentration in early pregnancy is associated with an increased risk of Preterm delivery. But there were some limitations of the study as only single measurement of serum CRP was done & the relatively small

number of subjects available for subgroup analyses. In the present study, we found that elevations in maternal serum CRP concentrations in early pregnancy are positively associated with preterm delivery risk. Hence, C-reactive protein, a marker of systemic inflammation, may be involved in the pathogenesis of preterm delivery.

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