

Serum Magnesium Level and CRP as a Predictor of Preterm Labor – A Case Control Study**Suman Buraniya¹, Balveer Singh Gurjar², Shyam Sunder Mittal³, Dalal Rajesh Kumar⁴, Harjeet Singh⁵**¹JR-3, Department of Biochemistry, SMS Medical College, Jaipur, Rajasthan, India²Associate Professor, Department of Biochemistry, SMS Medical College, Jaipur, Rajasthan, India³Senior Demonstrator, Department of Biochemistry, SMS Medical College, Jaipur, Rajasthan, India⁴CMO (NFSG), ESIC, Regional Office, Kolkata, WB, India⁵Sr. Professor, Department of Biochemistry, SMS Medical College, Jaipur, Rajasthan, India

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Abstract:**Background:** Pre-term delivery is estimated to be one of the leading causes of perinatal morbidity and mortality in India, it accounts for nearly 70% of the neonatal mortality and 50% of long-term neurological complications. Hence there is a need for assessing various markers that can diagnose imminent preterm labor.**Material and Methods:** A hospital based observational case control study was performed in the Immunoassay Lab & Central Lab (Department of Biochemistry) and the Department of Obstetrics and Gynaecology at SMS Medical College and attached hospitals, Jaipur among 60 pregnant women presenting to the labor room, out of which 30 were in preterm labor (cases) and 30 were in term labor (control). Serum Magnesium and C-Reactive Protein (CRP) level was measured.**Results:** The mean serum magnesium level in cases was significantly lower as compared to control ($p < 0.01$) and the mean CRP level among cases was 3 was significantly higher compared to control. (< 0.05) The mean maternal age of cases and control was comparable with no significant difference. ($p > 0.05$)**Conclusion:** Low magnesium level and high CRP level in pregnant mother can be used as marker of imminent preterm labor. Hence regular screening of serum magnesium level and serum CRP level is recommended in all pregnant women at risk of developing preterm labor**Keywords:** Preterm Labor, Magnesium, C-Reactive Protein.**DOI:** 10.25258/ijcpr.18.3.281

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Introduction

According to World Health Organization (WHO) Pre-term labor is defined as labor that occurs with regular, and frequent uterine contractions causing progressive cervical changes, between 28 weeks and 37 completed weeks of gestation. [1,2]

The cause of pre-term labor is not yet completely known; in 50% causes it is spontaneous and idiopathic, although several main one among them is premature rupture of membrane (PROM), and others are multiple pregnancy, polyhydramnios, hypertensive disorder of pregnancy, infection, cervical incompetence, antepartum haemorrhage, fetal and uterine anomalies, anaemia, heavy work, smoking etc. it is also related to socioeconomic status and geographic location.⁴ Approximately 45-50% of preterm births are idiopathic, 30% are related to pre-term rupture of membranes (PROM) and another 15-20% is attributed to medically indicated or elective pre-term deliveries. [3,4]

Pre-term birth is a major cause of neonatal mortality, which is estimated to be at least 50% of all neonatal deaths, with the highest rates of health care costs due to hospitalization of woman with pre-term labor and the expenses of long-term care of preterm birth. The incidence in the developed world is 7-12%. [5,6]

An essential element called magnesium plays a role in numerous biological processes throughout pregnancy. It is involved in DNA synthesis, where magnesium acts as a cofactor for DNA polymerization, protein synthesis for enzymatic processes, energy metabolism by the production of ATP, and the regulation of smooth muscle contractility as a calcium channel blocker.[7]

Magnesium is an important intracellular cation in body. it was shown that low magnesium plays a vital role in the premature onset of labor. [8] Serum magnesium levels fall during pregnancy with

gestational age. This decrease of magnesium plays an important role in the physiology of parturition. Decrease magnesium in plasma may be responsible for decrease of same in myometrium leading to initiation of uterine contractions and labor. [9] Hence magnesium level may be a potential biomarker in assessing the probabilities of preterm labor and monitoring its level throughout the pregnancy may be conceivable to lower maternal and neonatal mortality.

C-reactive protein (CRP) is one of the sensitive markers of systemic inflammation and is synthesized by liver in response to infection and tissue injury in body. Maternal serum concentrations of highly sensitive C-reactive protein (hs-CRP) can be studied as a marker of subclinical infection in pregnant women who end up with pre-term labor or premature rupture of membrane. [10]

So, with the objective to estimate and compare the levels of serum magnesium and CRP in patients with preterm labor this study was conducted.

Methodology

A hospital based observational case control study was performed in the Immunoassay Lab & Central Lab (Department of Biochemistry) and the Department of Obstetrics and Gynaecology at SMS Medical College and attached hospitals, Jaipur. Permissions were obtained from the Ethics Committee and the Research Review Board of SMS Medical College and Hospital, Jaipur.

After calculating the sample size to provide 80% study power and a significance level (alpha) of 0.05, based on previous studies showing a correlation coefficient of 0.405 between serum magnesium and CRP levels, 60 pregnant women

presenting to the labor room were selected using simple random sampling. Out of total 30 study participants who were in preterm labor were selected as cases and rest 30 study subject those in term labor were selected as control.

Inclusion criteria for cases included those with preterm onset of labor [between 28 weeks and 37 weeks of gestation], with singleton gestation, in active labor and with intact fetal membranes. Inclusion criteria with control include patients in active labor, with singleton gestation, with term onset of labor [After 37 weeks of gestation] and with intact fetal membranes. Those patients with previous history of recurrent abortions and preterm delivery, onset of labor before 28 weeks, with recurrent UTI, with pre-eclampsia, polyhydramnios, antepartum hemorrhage or any uterine malformations, fetal congenital malformations, intra uterine death, pregnant women with placenta praevia, eclampsia, preeclampsia and patients with autoimmune diseases like rheumatoid arthritis, SLE, patient on any drug affecting serum magnesium level were excluded from the study.

Detail history was taken and serum magnesium and C-Reactive Protein (CRP) of the study population was measured. Data was collected in MS Excel and later analyzed using SPSS version 26. Continuous variables (e.g., serum magnesium and CRP) were expressed as mean \pm standard deviation. Student's t-test was used for comparing means between cases and controls and Pearson correlation coefficient was used for assessing the relationship with statistical significance being set at $p < 0.05$.

Results

Table 1: Comparison of Mean Age of Control and Cases (N=60)

Group	Age (yrs)	p-value
Control Group (n=30)	27.50 \pm 3.1	>0.05
Case Group (n=30)	28.60 \pm 3.3	

As shown in the table 1. the mean maternal age in cases (28.6 \pm 3.3 years) was comparable to controls (27.5 \pm 3.1 years), with no statistically significant difference ($p = 0.062$) showing cases and controls were comparable in terms of age. The majority of the participants belong to the 21–30 year age group in both control group (77%) and case group (63%).

The majority of participants were multigravida in control group 60% (18) and in case group 87% (26). The majority of participants were nullipara 43% (13) in control group and primipara 40% (12) in case group.

Table 2: Comparison of Mean Serum Magnesium and Serum CRP among Control and Cases (N=60)

Parameters	Control (30)	Cases (30)	p-value	Statistical Significance
Mean Serum Magnesium Level (mg/dl)	1.9 \pm 0.40	1.36 \pm 0.25	< 0.01	HS
CRP (mg/dl)	1.13 \pm 0.33	3.17 \pm 0.97	< 0.05	S

As shown in the Table2. when the mean Magnesium level among control and cases was compared it was found that the mean serum magnesium level in cases was 1.36 ± 0.25 mg/dl which was significantly lower as compared to

control in which it was 1.9 ± 0.40 mg/dl.s($p < 0.01$) Similarly the mean CRP level among cases was 3.17 ± 0.97 mg/dl which was significantly higher compared to control in which it was 1.13 ± 0.33 mg/dl . (< 0.05).

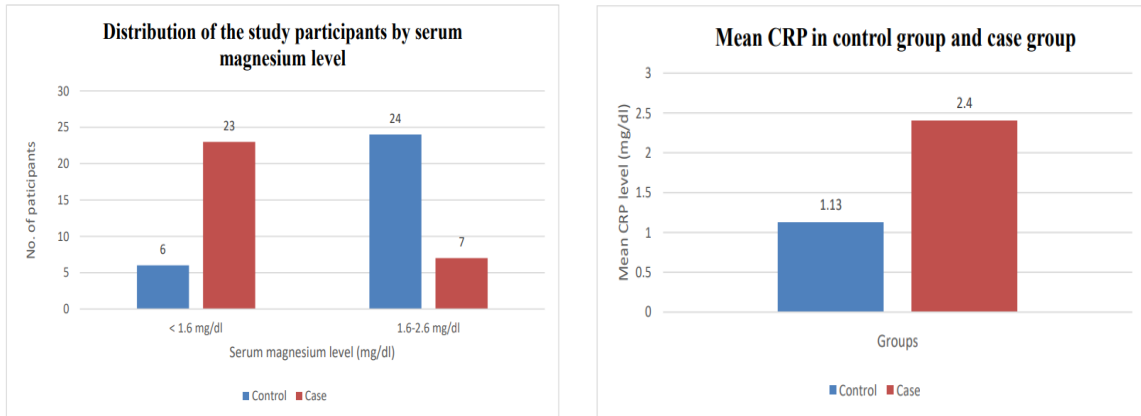


Figure 1: Bar diagram showing mean serum magnesium and CRP level in Control and Cases.

Table 3: Correlation between Gestational Age Vs Magnesium level and CRP level among Controls and Cases.

Parameters	Type of Study Subject	Pearson Coefficient of correlation (r)	p value
Gestational Age and serum Magnesium level	Controls (30)	0.154	0.286
	Cases (30)	0.188	0.191
Gestational Age and serum CRP level	Controls (30)	- 0.261	0.070
	Cases (30)	0.187	0.192

On doing correlation analysis it was found that Serum magnesium level was weakly positively correlated with gestational age both in cases and control, though this relationship was not statistically significant ($p > 0.05$). The serum CRP

level was weakly negatively correlated with gestational age in controls, but it was weakly positively correlated with gestational age in cases and both this relationship being not statistically significant. ($p > 0.05$)

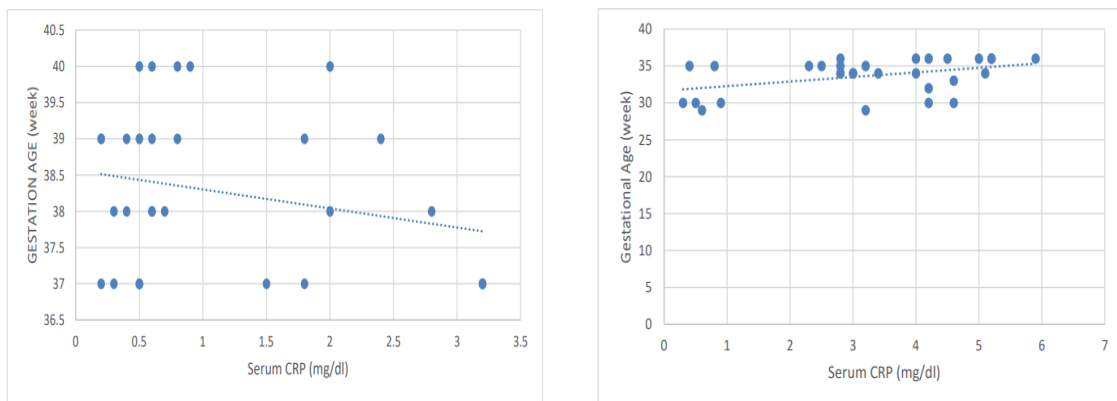


Figure 2: Correlation between gestational age and serum CRP level in controls and cases

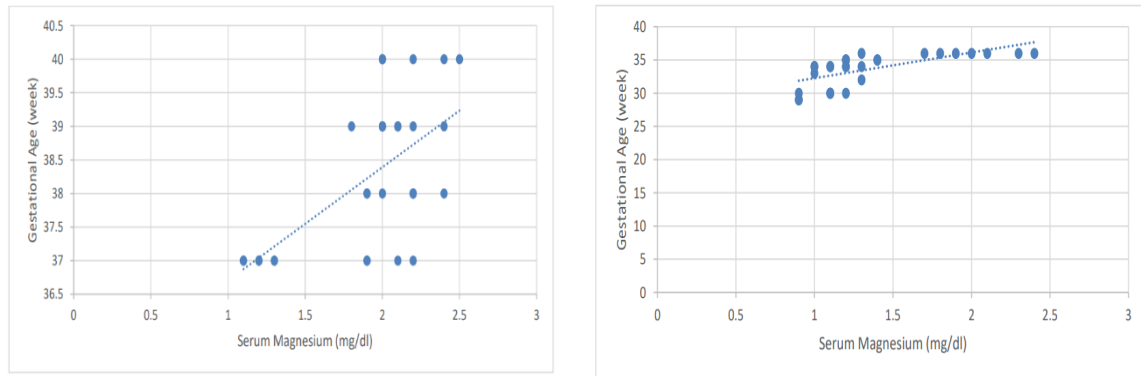


Figure 3: Correlation between gestational age and serum magnesium levels in controls and cases

Even on doing correlation analysis between magnesium and CRP it was found that weak negative but non-significant correlation was found between serum magnesium and CRP levels ($r = -0.227$, $p = 0.060$).

Discussion

The etiopathogenesis of preterm labor is complex and multifactorial. It may result from a wide variety of maternal, fetal, and environmental factors acting singly or in combination. Infections, both overt and subclinical, have been consistently linked with the onset of preterm uterine contractions. Ascending infections from the lower genital tract leads to localized chorioamnionitis, stimulating the release of pro-inflammatory cytokines and prostaglandins that ultimately induce myometrial contractility. [11] Lower Magnesium and higher CRP level are linked to increase myometrial contractility leading to preterm labor. [9,10]

In the present study, the mean maternal age in cases (28.6 ± 3.3 years) was comparable to controls (27.5 ± 3.1 years), with no statistically significant difference ($p = 0.062$) as shown in table 1. This suggests that maternal age did not significantly affect preterm labor risk in this population. Literature regarding maternal age and preterm birth presents mixed findings, Carolan et al. [12] (2013) reported that advanced maternal age was associated with increased risk of preterm delivery, whereas Chen et al. [13] (2007) observed that preterm deliveries were more prevalent in adolescents.

Nikbakht et al. [14] (2020), in their CRP study, found that elevated CRP values were more strongly predictive of preterm labor in women < 29 years, while in women ≥ 30 years, the correlation was weaker, possibly reflecting differences in the underlying etiology of preterm birth (nutritional/infective in younger women vs. medical comorbidities in older women). Kashanian et al. [15] (2013) also noted that CRP levels were significantly higher in younger mothers with preterm delivery, and the strength of association decreased with increasing maternal age. Tsiartas et

al. [16] (2012) demonstrated that very early preterm births (< 32 weeks) with high CRP were disproportionately represented among women below 25 years, suggesting that maternal age modifies both the inflammatory response and risk of very early preterm birth.

Magnesium, act as a cofactor in more than 300 enzymatic reactions. Magnesium regulates diverse physiological processes including protein synthesis, neuromuscular conduction, myocardial excitability, and smooth muscle tone. It regulates neuromuscular transmission, smooth muscle tone, and uterine contractility. [17]

The present study revealed that serum magnesium levels were significantly lower in women with preterm labor (1.36 ± 0.25 mg/dl) compared to controls (1.9 ± 0.40 mg/dl), ($p < 0.01$) (Table 2) strongly suggesting that hypomagnesemia predisposes to preterm labor.

The findings of this study are largely in concordance with global and Indian studies. Gharehbaghi et al. [18] (2019) reported that hypomagnesemia was more prevalent among women who experienced preterm delivery compared to those delivering at term. Rai et al. [19] (2015) also suggested that hypomagnesemia may be used as a biochemical marker for predicting preterm birth.

Jain et al. [20] (2015) and Malas et al. [21] (2018) also stated that hypomagnesaemia is seen in women with preterm labor. Mechanistically, hypomagnesemia during pregnancy reduces the intracellular magnesium content of the myometrium, leading to increased calcium influx and heightened contractility of uterine smooth muscles. In addition, magnesium deficiency is known to exacerbate oxidative stress, increase the release of inflammatory mediators, and promote vasoconstriction, all of which can create a microenvironment favorable for premature initiation of labor.

A weak positive but non-significant correlation was observed between gestational age and serum

magnesium level both in control group and case group ($p > 0.05$), (Table 3) Jenabi et al. [22] (2017) found a positive correlation between maternal magnesium and gestational age, when analysing preterm and term together ($r = 0.3305$), indicating higher magnesium among women delivering at later gestations.

CRP is an acute-phase protein synthesized predominantly in the liver under the influence of pro-inflammatory cytokines, especially interleukin-6 (IL-6). It is a well-recognized biomarker of systemic inflammation and tissue injury. In obstetric practice, CRP is often considered a useful marker for detecting intrauterine infection, subclinical chorioamnionitis, and impending preterm labor. [10]

In the present study, mean serum CRP levels were significantly higher in preterm labor cases (3.17 ± 0.97 mg/dl) compared to controls (1.13 ± 0.33 mg/dl), ($p < 0.05$) (Table 2.) These findings are consistent with those of Nikbakht et al. [14] 104 (2020), who observed a strong association between elevated CRP levels and preterm birth ($p = 0.001$). Foulon et al. [23] 114 (2016) have similarly reported elevated CRP in women with preterm labor and suggested that elevated CRP is a reliable marker of intrauterine inflammation and an important risk indicator for preterm delivery.

Elevated CRP contributes to the inflammatory cascade by promoting leukocyte adhesion, stimulating cytokine release, and activating the complement system. While inflammation is a protective response against infection, uncontrolled inflammatory activity within the fetomaternal unit can trigger premature rupture of membranes, cervical ripening, and initiation of uterine contractions.

A weak negative and non-significant correlation was observed between gestational age and serum CRP level ($r = -0.261$, $p = 0.070$) in controls (Table 3). A weak positive but non-significant correlation was observed between gestational age and serum CRP level ($r = 0.187$, $p = 0.192$) in cases. (Table 3)

Similarly, Sharma et al. [24] (2017) reported significantly elevated CRP levels in women presenting with threatened preterm labor. Foulon et al. [23] (2016) further proposed CRP as a cost-effective biomarker for preterm birth screening, although its specificity is limited.

The present study demonstrated a weak negative but non-significant correlation between serum magnesium and CRP levels ($r = -0.227$, $p = 0.060$). This finding suggests that while both hypomagnesemia and elevated CRP independently contribute to preterm labor, they may not be directly correlated. Interestingly, experimental studies have shown that magnesium deficiency

itself can enhance inflammatory responses. Nielsen et al. [25] (2018) reported that magnesium deficiency is associated with increased acute-phase reactants C-reactive protein and chronic low-grade inflammation.

Screening for hypomagnesemia and elevated CRP may be clinically valuable in identifying high-risk pregnancies. Further large-scale, prospective studies and interventional trials are essential to validate these biomarkers and to develop preventive strategies aimed at reducing preterm birth and improving neonatal outcomes.

Conclusion

Findings of the present study suggest that serum magnesium levels were significantly lower in case group and strong association with occurrence of preterm labor. The study also attempted to assess the significance of serum CRP levels in preterm labor. It was observed that serum CRP levels were significantly higher in case group as compared to control group. Regular screening of serum magnesium level and serum CRP level is recommended in all pregnant women at risk of developing preterm labor.

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