



COMPARATIVE ANALYSIS OF SERUM MAGNESIUM & ZINC LEVELS AND THEIR ASSOCIATIONS WITH PRETERM LABOUR

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ABSTRACT

Background: Preterm is defined as babies born alive before 37 weeks of pregnancy, it occurs when there is a regular contraction of uterus which results in opening of cervix after 20 weeks and before 37 weeks of gestation. preterm labour is spontaneous but it can also be due to a biochemical changes in body functions at the cellular level of trace elements such as magnesium and zinc. The main objective of this study is to find the association of hypomagnesaemia and low zinc levels in preterm delivered women and to compare the maternal serum magnesium and zinc levels between Preterm and Term delivered mothers. **Methods:** A Comparative study was done in the Department of Biochemistry, Andhra Medical College, Visakhapatnam. A total of 126 women who were admitted to the labour room at Department of Obstetrics and gynaecology, King George Hospital, Visakhapatnam were selected for this study. All the subjects were divided into two groups as Preterm Consists of 63 women with spontaneous preterm labour delivered between 28- 37 weeks and Term Consists of 63 Women with Term labour after 37 weeks. **Results:** Women with Preterm labour had a significantly low serum magnesium level with a mean serum magnesium level of 1.8 mg/dl with SD of 0.38 whereas the patients with Term labour had a mean serum magnesium level of 2.09 mg/dl with SD of 0.50 and also low zinc levels in Preterm labour with mean zinc levels of 51.28 µg/dl with SD 10.9 whereas patients with Term labour had mean serum zinc levels of 56.5 µg/dl with SD 9.7. The difference of serum magnesium and zinc levels observed between the study population and control population is independent of factors like maternal age, parity, gestational age, Blood pressure and socioeconomic status. In this study there is non significant weak correlation was found between Demographic data and parametric data. **Conclusions:** Serum magnesium and zinc levels can be used as predictors for preterm labour. Spontaneous preterm delivery can be avoided by early assessment of maternal magnesium and zinc status and also by simple oral supplementation of magnesium and zinc which might provide an easy and inexpensive means to decrease the problems related to preterm labour. There is a further scope for research on serum magnesium and zinc levels based on gestational age.

KEYWORDS

Serum zinc, Serum Magnesium, Preterm labour, Term labour

INTRODUCTION

Preterm is defined as babies born alive before 37 weeks of pregnancy it occurs when there is a regular contraction of uterus which results in opening of cervix after 20 weeks and before 37 weeks of gestation¹. There are 3 subtypes of Preterm delivery based on gestational age: Extremely Preterm¹ = Less than 28 weeks Very Preterm = 28 to 32 weeks

Moderate to late Preterm = 32 to 37 Weeks

Every year worldwide, an estimated 15.5 million babies are born preterm and their number is rising exponentially². Preterm births complications are the leading cause of mortality in children less than 5 years of age, responsible for approximately 1.2 million deaths every year. Incidence of preterm labour in India is 10% leading to 70% of perinatal deaths. Late preterm births (34-36 weeks) account for about 73% of all preterm births while the early preterm births (<32 weeks) comprise 2% of all births and remained constant over the last two decades. Three-fourth of these preterm deaths could be prevented with current cost effective methods and interventions²⁻³.

The exact causes of preterm labour are not known completely, in 50% cases it is mostly spontaneous and idiopathic, although there are several risk factors have been identified. The main among them is premature rupture of membranes (PROM) which account for up to 30% and another 15-20% is secondary to conditions like multiple pregnancies, polyhydramnios, infections, uterine anomalies, cervical incompetence, antepartum hemorrhage, hypertensive disorder of pregnancy, anemia, smoking, fetal anomalies and IUD, etc⁴. It is also related to socioeconomic status and geographic location. Beside these etiologies, preterm labor is also due to a biochemical changes in body functions at the cellular level of trace elements such as magnesium and zinc³⁰. A modifiable factor to reduce preterm baby and fetal growth retardation is maternal nutritional status. The trace elements that have been linked to adverse pregnancy outcomes are copper, zinc, calcium, magnesium etc. Some studies concluded that copper deficiency was correlated with preterm delivery with premature rupture of membranes and fetal nervous system damage²⁶. Zinc has an important role in late pregnancy in preventing fetal growth restriction, congenital malformations, and fetal death. Magnesium deficiency was shown to

cause gestational hypertension and aggravate postpartum haemorrhage²⁷.

Magnesium is 2nd most intracellular abundant cation with number of vital physiological and biochemical roles; intracellular ionized magnesium is calcium channel blocker and its function is relaxation of muscles after muscular contraction¹². Low magnesium levels leads to neuromuscular hyper excitability resulting cramps in muscles and thus uterine musculature hyperactivity which leads to dilatation of cervix. Thus the inhibitory effect of magnesium on preterm labour contractions is attributed to antagonism of calcium mediated uterine contractions leading to preterm delivery^{5,6,7}.

Zinc is an outstanding trace elements for its multiple biological functions its requirement is increased in pregnancy to promote fetal growth, placental and maternal tissues and also necessary for DNA synthesis, replication and transcription by helping developmental process of fetus²⁹. Abnormal fetal growth like intrauterine growth retardation and malformation is reported to be associated with low zinc levels in maternal serum²⁶. Inadequate availability of maternal zinc to fetus is plausible etiological factor in fetal or placental growth failure thus there is higher incidence of premature delivery, inefficient and prolonged labour with atonic uterine bleeding and spontaneous labour²⁸.

This study was aimed to evaluate the status of zinc and magnesium in preterm labour women and their role as biochemical markers for early prediction and prevention of preterm labour.

MATERIALS & METHODS

Study Design

A Comparative study was done in the Department of Biochemistry, Andhra Medical College, Visakhapatnam from February 2021 to April 2022.

Study Population

A total of 126 patients between the age group 18 – 35 years, who were admitted to the labour room at Department of Obstetrics and gynaecology, King George Hospital, Visakhapatnam were selected for

this study. All the subjects were divided into two groups as Preterm Consists of 63 women with spontaneous preterm labour delivered between 28- 37 weeks and Term Consists of 63 Women with spontaneous labour after 37 weeks.

Inclusion Criteria

- Pregnant women with single gestation.
- Pregnant women with preterm onset of labour between 28-36 weeks of gestation.
- Pregnant women who is in active labour.
- Pregnant women with intact fetal membranes
- Those who provided informed consent

Exclusion Criteria

- Patients with previous history of recurrent abortions and preterm labour
- Patients with recurrent Urinary tract infections.
- Patients with preeclampsia, antepartum hemorrhage, cervical incompetence or any other uterine malformations.
- Pregnant women who had any medical, surgical or gynecological problems.
- Fetal congenital malformations, intra uterine death.
- Patient who decline to give consent.

Sample Collection And Determination Of Serum Magnesium And Zinc

Samples were collected under strict aseptic conditions. 5ml of venous blood was collected from the antecubital vein of each participant into an EDTA and red top vacutainer and to clot spontaneously. Samples were transported carefully and then centrifuged for 10mins at 3000 rpm. Sample analysis was done for serum magnesium and serum zinc immediately whenever possible and they are stored at 2°-8° c in case of any delay for further analysis. The reference value for normal serum magnesium level is 1.6-2.6 mg/dl and for serum zinc level is 51-77µg/dl in pregnant individuals. Routine investigations like CBC, HIV/HBsAg/VDRL/ CUE (Urine sugar, Albumin, pus cells, casts) are done.

Serum Magnesium by Direct method- Color complex formation with Xylidyl blue at pH 11.4 the color produced is measured bichromatically at 520nm and is proportional to the magnesium concentration.

Serum Zinc by Nitro PAPS Method- Zinc in alkaline medium reacts with Nitro-PAPS at pH 11.4 to form a colored complex. Intensity of color is directly proportional to the concentration of zinc present in sample.

Statistical Analysis:

All the findings were recorded and tabulated in excel sheets and analysed statistically.

Parametric results on continuous measurements are presented as Mean $\pm$ SD and results on categorical measurements are presented as Number (%). Student t-test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (Inter group analysis). Chi-square/Fisher exact test has been used to find the significance of study parameters on categorical variables in a group. The statistical software SPSS 21.0 version 3.2.2 was used for analysis of data, Microsoft word and Excel has been used to generate tables and graphs.

RESULTS

A total of 126 participants were included in this study and they were divided into two groups as Preterm and Term delivered mothers with 63 in each group.

In this study, majority of the patients belong to the age group between 20-30 years in both the groups. The mean age group among preterm mothers is 24.20 $\pm$ 3.9 and the mean age group among Term mothers is 25.1 $\pm$ 4.05, percentage distributions of age shown in Table 1. The youngest patient included in the study is 19 years and the eldest is 35 years.

Table 1:- Age Distribution In Study Groups

Age in years	Preterm n=63	Term n=63
<20	03 (5%)	05 (7%)
20-30	54 (87%)	52 (83%)
>30	06 (8%)	06 (10%)
Mean $\pm$ SD	24.20 $\pm$ 3.9	25.1 $\pm$ 4.05

p value- 0.20, not significant

The Mean $\pm$ SD of period of gestation in Preterm mothers is 31.1 $\pm$ 3.4 weeks and in Term mothers is 38.5 $\pm$ 0.36 in weeks, the % distribution is shown in Table 2&3

Table No-2: Pog Distribution Among Preterm Delivered Mothers

POG (weeks)	Preterm (n=63)
28-32	40 (63%)
33-34	12 (20%)
35-36	11 (17%)
Mean $\pm$ SD	31.1 $\pm$ 3.4

Table No-3: Pog Distribution Among Term Delivered Mothers

POG (weeks)	Term (n=63)
37-38	29 (46%)
39-40	26 (41%)
41-42	08 (13%)
Mean $\pm$ SD	38.5 $\pm$ 0.36

Majority of pregnant women in both study groups are primi gravida with 51% and 49% in Preterm and Term mothers respectively. The % distribution of Gravida is shown in Table 4

Table 4:- % Gravida Distribution

Gravida	Preterm (n=63)	Term (n=63)
1	33 (51%)	31 (49%)
2	27 (27%)	19 (30%)
3	13 (13%)	9 (14%)
4	5 (9%)	4 (7%)

p value- 0.56, not significant

The Mean $\pm$ SD of Systolic/Diastolic blood pressure in Preterm mothers is 130 $\pm$ 18 /84 $\pm$ 14 mmHg respectively and in Term mothers is 120 $\pm$ 14 /80 $\pm$ 10 mmHg and p value is 0.44, not significant.

Table no 5 shows the % distribution of socioeconomic status among study groups

Table 5:- % distribution of socioeconomic status between study groups is

Socioeconomic status	Preterm n=63	Term n=63
Lower middle	30 (46%)	27 (40%)
Upper lower	27 (43%)	25 (41%)
Upper middle	6 (11%)	11 (19%)

p value is 0.25, not significant

The Mean $\pm$ SD of serum magnesium in Preterm mothers is 1.80 $\pm$ 0.38 mg/dl and in Term mothers is 2.09 $\pm$ 0.50 in mg/dl. The % and mean distribution of serum magnesium in study groups is shown in Table 6 & 7

Table 6:- % Distribution Of S.Mg²⁺ Between Study Groups Is

S.Mg ²⁺ (mg/dl)	Preterm (n=63)	Term (n=63)
<1.8	34 (54%)	20 (32%)
1.9-2.5	29 (46%)	43 (68%)
Mean $\pm$ SD	1.80 $\pm$ 0.38	2.09 $\pm$ 0.50

p value < 0.05, significant

Table 7:- Mean Distribution Of S.Mg²⁺ Between Study Groups Is

S.Mg ²⁺ (mg/dl)	Preterm Mean $\pm$ SD	Term Mean $\pm$ SD
<1.8	1.57 $\pm$ 0.21	1.7 $\pm$ 0.21
1.9-2.5	2.1 $\pm$ 0.27	2.36 $\pm$ 0.32

The Mean $\pm$ SD of serum zinc in Preterm mothers is 51.28 $\pm$ 10.9 µg/dl and in Term mothers is 56.5 $\pm$ 9.7 µg/dl.

The % and mean distribution of serum zinc in study groups is shown in Table 8 & 9

Table 8:- % Distribution Of S. Zn²⁺ Between Study Groups Is

S.Zn ²⁺ (µg/dl)	Preterm (n=63)	Term (n=63)
51-77	25 (39%)	39 (61%)
<50	38 (61%)	24 (39%)
Mean $\pm$ SD	51.28 $\pm$ 10.9	56.5 $\pm$ 9.7

p value=0.012 (< 0.05), significant

Table 9:-mean Distribution Of S. Zn²⁺ Between Study Groups Is

S.Zn ²⁺ (µg/dl)	Preterm Mean $\pm$ SD	Term Mean $\pm$ SD
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51-77	62.56 ± 7.04	62.5 ± 7.53
<50	43.86 ± 5.16	46.8 ± 2.57

Correlation analysis was performed to determine the relationship between parametric data (Mg,Zn) and demographic data like age, gravida, blood pressure and period of gestation. A non significant negative correlation is found between the parametric and demographic data

Table 10:- Correlation Analysis Between Metals And Demographic Data In Term Gestation

Variables	Magnesium		Zinc	
	r	p	r	p
Age	-0.14	0.23	-0.23	0.06
POG	-0.14	0.27	-0.004	0.97
SBP	-0.03	0.81	0.197	0.87
DBP	-0.05	0.96	-0.001	0.98
Gravida	-0.02	0.87	-0.15	0.23

Table 11:- Correlation Analysis Between Metals And Demographic Data In Preterm Gestation

Variables	Magnesium		Zinc	
	r	p	r	p
Age	0.19	0.13	-0.07	0.58
POG	-0.18	0.15	0.05	0.67
SBP	-0.05	0.69	0.12	0.31
DBP	-0.13	0.27	0.15	0.22
Gravida	-0.01	0.93	0.06	0.63

Karl pearson correlation

Receiver Operating Curve (ROC)

Finally, receiver operating characteristic (ROC) curve analyses were conducted to estimate the value of Zn and Mg status as biomarkers for knowing the status of Preterm delivery (Fig. 1 and 2).

Figure 1 shows Receiver operating characteristics (ROC) curves of Zinc and Magnesium in relation to diagnosis in preterm labour. Figure 2 shows the multiple regression model based Zn and Mg outperformed any other combination of variables via stepwise AIC selection. The final model, based on these two parameters, yielded the highest AUC of 73.6 %.

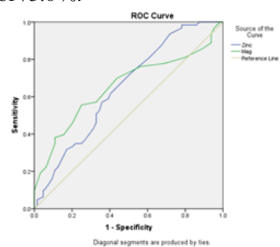


Fig 1

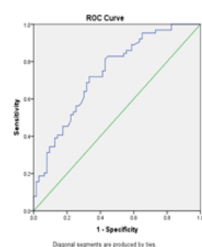


Fig 2

Area Under the Curve					
Test Result Variable(s)	Area	Std Error	Asymptotic Sig	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
Zinc	.646	.049	.005	.551	.742
Mg	.655	.050	.003	.557	.752
Zinc+Mg		0.736	.000	.650	.822

DISCUSSION

The results obtained were compared between the two study groups.

Age: In this study majority are between the age group 20-30. The mean age of Term women is 25.1 ± 4.0, and of preterm delivered women is 24.2 ± 3.9 p-value is 0.2 (>0.05), indicates that there is no statistical significance in the age between the study groups. Results of the present study are in accordance with the study conducted by Kamal et al¹⁵, Malathi et al¹⁶ and Shahid et al¹⁷.

Period of Gestation: The Mean ± SD of period of gestation in Term is 38.5 ± 0.36 in weeks and in Preterm is 31.1 ± 3.4 in weeks. In Preterm 63% of women are at 28-32 weeks of gestation and in Term 46% belong to 37-38 weeks of gestation.

Gravida: Majority of pregnant women in both study groups are primi gravida with 51% and 49% in Preterm and Term respectively. The

value is 0.56 done by using Fischer exact test and when parity is compared The p value is > 0.05 and is statistically not significant in both groups This is in accordance with the study Malathi et al¹⁶, Kamal et al¹⁵ and Arian et al¹⁸ where p values are 0.46 and 0.50 respectively.

Blood Pressure: The Mean ± SD Systolic Blood pressure and Diastolic blood pressure in Preterm is 130 ± 18 / 84 ± 14 mmHg respectively and in Term is 120 ± 14 / 80 ± 10 mmHg. There is a no statistical significance with p value > 0.05 in the systolic BP and diastolic BP between the study groups. This is similar to previous other studies like Begum H et al¹⁹, Shafali et al²⁰ but in contrast to Jones et al²¹ and Skudder et al²² the result is statistically significant between 2 groups.

Serum Magnesium: In this study 54% of patients in Preterm and only 32% of patients in Term has serum magnesium levels <1.8. This shows that relative risk of low magnesium levels in preterm delivered pregnant women is 1.7 times more than the term delivered women. The Mean ± SD of serum magnesium in Term is 2.09 ± 0.50 in mg/dl, in Preterm is 1.80 ± 0.38 in mg/dl. The serum magnesium levels between the study groups are statistically significant with p value <0.001. The results obtained are similar to various studies like Shahid et al¹⁷, kamal et al¹⁵, shifali et al²⁰, malathi et al¹⁶ with p value statistically significant. Comparison with previous study is shown in Table no 8.

Table No 12:- Comparison With Previous Studies

References	S.Mg (mg/dl)	p value
Shahid et al ¹⁷	1.8±0.3	<0.001
Kurzel et al ²³	1.60±0.46	<0.005
Pushpo D et al ²⁴	1.67±0.23	<0.001
Wojcieka et al ²⁵	1.63±0.05	<0.001
Begum H et al ¹⁹	1.7±0.3	<0.001
Malathi et al ¹⁶	1.59±0.8	<0.001
Present study	1.80± 0.38	<0.001

Serum Zinc: In this study 61% of mothers who are preterm delivered have zinc levels < 50 µg/dl with mean ± SD 43.86 ± 5.16, only 39% mothers have serum zinc levels between 51-77 µg/dl with mean ± SD 62.56 ± 7.04.

In Term delivered mothers 61% have serum zinc levels between 51-77 µg/dl with mean ± SD 62.5 ± 7.53 and only 39% mothers have serum zinc < 50 µg/dl with mean ± SD 46.8 ± 2.57, by comparing the serum zinc levels between preterm and term delivery, it indicates that serum zinc levels are low in preterm delivered compared to term delivered mothers with p value 0.012 (<0.05) which is statistically significant.

The results obtained are in accordance with Masuda et al²⁸ with mean ± SD is 62.70 ± 7.18 and 33.30 ± 11.00 in term and preterm delivery respectively, Similarly Huwang et al²⁹ conducted a study on maternal zinc status and pregnancy outcome in which results are statistically significant.

Karl pearson correlation analysis performed between demographic data and parametric data (Mg,Zn), non significant weak correlation obtained with p value >0.005.

Finally, ROC analysis performed using logistic regression model, there is significant Area Under Curve with 73.6% when both Mg and Zinc combined. This indicates that there is High Sensitivity and Specificity of Magnesium and zinc levels, Thus these parameters can be used as biomarkers for predicting the Preterm delivery.

CONCLUSION

Preterm labour is spontaneous, multi factorial and idiopathic in nature with varying outcomes affecting new born in terms of mortality and morbidity.

The present study is carried out to establish a comparison between preterm and term labour in terms of maternal biochemical parameters like serum zinc and magnesium. All these parameters are assessed in 126 pregnant women with preterm labour and term labour.

There is no significant difference with age, parity and blood pressure among the two study groups.

There is a significant change in the mean of serum magnesium and serum zinc in patients with preterm labour and term labour.

By studying these parameters which gives us the idea about low level of maternal serum zinc and magnesium is associated with adverse pregnancy outcomes, including preterm labour and low birth weight.

Hypomagnesaemia and zinc deficiency may be used as predictors of preterm labour.

Some predictive tests for preterm births are used but they have poor sensitivities and are very expensive. Estimation of magnesium and zinc is relatively cheap.

To conclude that the present study gives us knowledge about that these biochemical parameters have some association with preterm delivery. However since the size of the study group is small, it needs to be studied further with larger groups.

They may also serve as predictors of the preterm labour if they are studied in maternal serum from early pregnancy at regular intervals and thus may help in prevention of maternal and foetal morbidity and mortality.

Magnesium and zinc supplementation may be considered in patients with low serum magnesium and zinc levels to prevent preterm delivery.

Hence supplementation of oral magnesium and zinc can be considered in high risk pregnancies as it may prevent spontaneous deliveries and preterm labour and thus helps in preventing low birth weight.

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Conflict of Interest: None declared

Ethical Approval: the study was approved by the Institutional Ethics Committee

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