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Magnesium Associated Complications in Pregnant Women

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Abstract: This observational study was conducted in the department of Physiology LUMHS Jamshoro with collaboration of G U IV Liaquat university Hospital Jamshoro. The inclusion criteria of the study were pregnant women with 20-35 years of age, primigravida, had 2nd and 3rd trimester of pregnancy and willing for follow-up. The informed consent was taken from all participants participated in the study and the grouping was made according to serum magnesium level, trimester of pregnancy and age of women and the various complications were observed. The blood sample collected for serum Mg++ level and other routine tests and sent to laboratory for analysis. The data was analyzed in SPSS version 11.00. Total of 150 patients were selected in this study, the Group I of 75 (50%) were those pregnant women who had low serum magnesium (Hypomagnesemia) level less than 1.5mg/dl with mean + SD 1.16 + 0.22 while Group II of. 75 (50%) were those having magnesium level within normal range from 1.8-2.9mg/dl with mean + SD 1.94 + 0.30 ($P \leq 0.001$). The toxemia of pregnancy observed significantly high in group I as compared to group II ($P = 0.003$). The pre term labour was significantly high in Group I 40% versus 18.7% for Group II ($P = 0.007$) and no significant difference was observed with age ($P = 0.85$). The intra uterine growth restriction (IUGR) also significantly higher in group I as compared to group II 41.3% versus 6.7% (P value ≤ 0.001). The IUGR was also more significant in higher age group 52.0% versus 10.0% ($P \leq 0.001$). The leg cramps was noted that history of leg cramps were significantly higher in Group I 46.7% versus 26.7% Group II ($P = 0.01$) and the incidence of leg cramps was significantly higher in older age group 80.0% versus younger age group 15.0%. ($P \leq 0.001$).

Key words: Hypomagnesaemia · Magnesium · Pregnancy · Toxemia Of Pregnancy · Pre Term Labour · Intra Uterine Growth Restriction (IUGR) · Leg Cramps

INTRODUCTION

Magnesium has a very important role and function in life and is one of the familiar metals that, in minute amounts, is necessary for body's proper metabolism to occur. It normally occurs at low concentrations and is known as a trace metal. Its bioavailability may change due to aging and its deficiency among the elderly is also well documented, especially among the institutionalized and people with pathologies [1]. Signs and symptoms of magnesium deficiency include: fatigue, confusion, irritability, weakness and hypertension, loss of appetite, insomnia, nausea, vomiting, diarrhea, defect in nerve conduction and muscle contraction. The magnesium plays important roles in the structure and the function of the human body. The adult human body contains about 25 grams of magnesium. Over 60% of all the magnesium in the body is found in the skeleton, about 27% in muscle, while 6 to 7% is found in other cells and less than 1% is found outside cells. Magnesium is involved in more than 300 essential metabolic reactions [2].

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Magnesium plays an important role in pregnancy for the formation of new tissues (maternal and fetal). Pregnant women require higher magnesium intake than the normal non-pregnant women of same age [3, 4].

Serum *magnesium* levels decline during pregnancy, because of increased demand and increase renal excretion of magnesium and inadequate water intake has been concluded that pregnancy is actually a state of extra cellular magnesium depletion. Mg^{++} deficiency in pregnant women compared with non-pregnant women, they found that both total and ionized magnesium were significantly lower during normal pregnancy [5].

Mg^{++} deficiency during pregnancy can induce not only maternal and fetal nutritional problem but also consequences that might lost in offspring throughout life. Since magnesium has an inhibitory role on myometrial contractions, it dilates blood vessels, improve cerebral blood flow. Attention has been paid to the role of magnesium deficiency in causing preterm labour, IUGR, hypertension. Hypomagnesemia leads to neuromuscular hyper-excitability resulting in muscle cramp and uterine hyper-activity [6].

Magnesium has an established element for fetal well-being. Its deficiency during pregnancy has been reported to be associated with pre-eclampsia, small for gestational age (IUGR) and preterm labour [7], leg cramps [8]. Magnesium supplementation during pregnancy may improve fetal and maternal outcome by decreasing incidence of preterm Labour, for preventation and control of seizure (convulsions) [9] and reduce incidence of maternal and neonatal hospital admissions [10].

Therefore by considering these facts in mind the present study was conducted at a tertiary care teaching hospital to observe the effects of serum magnesium level on pregnancy associated complications.

MATERIAL AND METHODS

This observational study was conducted in the department of Physiology LUMHS Jamshoro with collaboration of G U IV Liaquat university Hospital Jamshoro from January 2008 to December 2008. The pregnant women visiting gynaecology out patient department (OPD) were studies with inclusion criteria; women with 20-35 years of age, primigravida, had 2nd and 3rd trimester of pregnancy and willing for follow-up. The exclusion criteria of the study were; multipraous women, 1st trimester of pregnancy, history of hypertension (essential), known diabetics, anemia (moderate and severe), tuberculosis, cardiac disease, multiple pregnancy (Twin, Triplet), hyper emesis gravidarium not responding to treatment, history of congenital malformation in family, congenital malformation in current pregnancy as diagnosed by ultra sound, history of smoking or any drug abuse, molar pregnancy, less than 20 years and more than 35 years of age, patients with acute pancreatitis and had a history of alcoholism, patients with history of diarrhea, vomiting and nasogastric suction, gastrointestinal fistulas and ostomies, patients on Diuretics, antimicrobials (Amphotericin B, aminoglycosides, pentamidine, capreomycin, viomycin and foscarnet), chemotherapeutic agents (cisplatin), immunosuppressants (tacrolimus and cyclosporine) and proton-pump inhibitors. The informed consent was taken from all paticipants participated in the study and the grouping was made according to serum magnesium level, trimester of pregnancy and age of women. The data were collected on the preformed questionnaire. The questionnaire comprised of sections to elicit the information regarding the general bio-data of the patient as well as specific information. The section of specific information comprised of patients weight gain during pregnancy, blood pressure recording, edema, abdominal examination, ultrasound finding and serum magnesium level. After taking detailed history, clinical examination and ultrasound examination, blood sample collected for serum Mg++ level and other routine tests and sent to laboratory for analysis. After collection and centrifuging the sample, serum was obtained. Serum Mg++ was estimated by an end-point colorimetric method by Cobas Mira Roche Diagnostic System Analyzer. The method is based on the reaction of magnesium with xylidyl blue in alkaline solution containing GEDTA (Glycol ether diamine tetra acetic acid)to mask the calcium in the sample. Briefly, 50 µL of each serum sample were added to 400 µL of buffer 1 (Tris-hydroxymethyl) aminomethane/6-aminocapronic acid, pH 11.25, 500 mmol/L and GEDTA 90 µmol/L). Then, buffer 2 containing xylidyl blue 0.28 mmol/L was added. In alkaline solution Mg++ forms a purple complex with xylidil blue, a diazonium salt. The data was evaluated in statistical program SPSS version 11.0. The student t test (Independent sample t test) was applied to compare the means (2-tailed) among the numerical variables i.e. serum magnesium, age (in years) and blood pressure. The Fisher's exact test was used among the categorical parameters such as outcome, preterm labour, IUGR, Leg cramps, trimester of pregnancy and age group to compare them with dependent variable and calculated their frequency and percentages at 95% confidence interval. The p-value $\leq$ 0.05 was considered as statistically significant.

Table 1:Toxemia of pregnancy (pre eclampsia/ eclampsia)

	Serum Magnesium (n = 150)		
	Hypo n = 75	Normal n = 75	P value
Outcome:			
Toxemia	25(33.3%)	9(12.0%)	0.003
Normal	50(66.7%)	66(88.0%)	

Table 2: Toxemia of Pregnancy according to age group

	Age in Group (n = 150)		
	21-30 n = 100	31-35 n = 50	P value
Outcome:			
Toxemia	20(20.0%)	14(28.0%)	0.30
Normal	80(80.0%)	36(72.0%)	

Table 3: Premature (preterm Labour) according to serum magnesium level

	Serum Magnesium (n = 150)		
	Hypo n = 75	Normal n = 75	P value
Preterm Labour:			
Preterm	30(40.0%)	14(18.7%)	0.007
Full term	45(60.0%)	61(81.3%)	

Table 4: Preterm labour according to age group

	Age in Group (n = 150)		
	21-30 n = 100	31-35 n = 50	P value
Preterm Labour:			
Preterm	30(30.0%)	14(28.0%)	0.85
Full term	70(70.0%)	36(72.0%)	

Table 5: IUGR (Intra Uterine Growth Restriction) according to serum magnesium level

	Serum Magnesium (n = 150)		
	Hypo n = 75	Normal n = 75	P value
IUGR:			
IUGR	31(41.3%)	5(6.7%)	< 0.001
Normal	44(58.7%)	70(93.3%)	

Table 6: IUGR (Intra Uterine Growth Restriction) according to age group

	Age in Group (n = 150)		
	21 - 30 n = 100 (%)	31-35 n = 50 (%)	P value
IUGR:			
IUGR	10(10.0%)	26(52.0%)	< 0.001
Normal	90(90.0%)	24(48.0%)	

Table 7: Leg Cramps according to serum magnesium level

	Serum Magnesium (n = 150)		
	Hypo n = 75	Normal n = 75	P value
Leg cramp:			
Positive	35(46.7%)	20(26.7%)	0.01
Negative	40(53.3%)	55(73.3%)	

Table 8:Leg Cramps according to age group

	Age in Group (n = 150)		
	21 - 30 n = 100	31-35 n = 50	P value
Leg cramp:			
Positive	15(15.0%)	40(80.0%)	< 0.001
Negative	85(85.0%)	10(20.0%)	

RESULTS

Total 150 patients were selected in this study from the period of January 2008 to December 2008. Group I of 75 (50%) were those pregnant women who had low serum magnesium (Hypomagnesemia) level less than 1.5mg/dl with mean ± SD 1.16 ± 0.22 while Group II of. 75 (50%) were those having magnesium level within normal range from 1.8-2.9mg/dl with mean ± SD 1.94 ± 0.30 ($P \leq 0.001$).

The Toxemia of Pregnancy: Observed significantly high in group I as compared to group II (P = 0.003) as shown in Table 1 and 2.

The Pre Term Labour: The incidence of this was significantly high in Group I 40% versus 18.7% for Group II (P = 0.007) as shown in Table 3 and no significant difference was observed with age (P = 0.85) as shown in Table 4.

The Intra Uterine Growth Restriction (IUGR): Also significantly higher in group I as compared to group II 41.3% versus 6.7% (P value $\leq$0.001). The IUGR was also (Table No. 5) more significant in higher age group 52.0% versus 10.0% ($P \leq 0.001$) as shown in (Table 6)

The Leg cramps: it was noted that history of leg cramps were significantly higher in Group I 46.7% versus 26.7% Group II (P = 0.01) as shown in Table 7. The incidence of leg cramps was significantly higher in older age group 80.0% versus younger age group 15.0%. ($P \leq 0.001$) as shown in Table 8.

DISCUSSION

In pregnancy, with the need to provide nutrition for the baby too, these mothers often become more deficient and this can impact not only on their health, but that of their babies too [11].

Intra-uterine growth restriction was found to be an important complication of low magnesium level in pregnant women as 36 patients had IUGR and was more

marked in older age group and the same has been cited by Naila O.E. Barbosa, [12] who observed that IUGR may be due to imbalance in magnesium homeostasis. Magnesium supplementation resulted in statistically significant decrease in the number of low birth weight babies a fact observed by Haider and Bhutta [13].

Low magnesium level is a risk factor for preterm labour as magnesium has an inhibitory role on myometrial contraction, [14] Hypomagnesemia leads to neuromuscular hyper excitability resulting in muscle cramp and uterine hyper excitability as cited by Skajaa [15].

In this study 44(30%) patients with low magnesium level also had preterm labour which is quite significant number and match with study of Skajaa. [15] Serum magnesium level of 1.4mg /dL or less may be a marker for true preterm labour. A study with the same results was conducted by Kamal [16] in department of Clinical Biochemistry Indra Gandhi Institute of Medical Science observed that magnesium depletion markedly occurs in pregnancy and oral magnesium treatment from 25th week of gestation is associated with a low frequency of preterm and other complications]. Magnesium sulphate could effectively prevent preterm birth as cited by one group of investigators [17].

Similar study conducted by Mittendorf [18] reported that magnesium sulphate successfully prevent pre term labour in more than 92% of subjects prefer oral supplements. Preterm labour can result in neurological deficit in neonates which can be an additional mental stress for parents and therefore magnesium supplements during pregnancy can be a protective tool.

Toxemia of pregnancy was another important complication observed in this study. Epidemiological evidence suggests that magnesium may play an important role in regulating blood pressure. Diet that provide plenty of fruits and vegetables which are good source of potassium and magnesium are associated with low blood pressure. Lowered plasma Mg^{++} concentration in pregnancy may contribute to the development of hypertension in pregnancy. Thirty three percent patients having low magnesium level developed toxemia of pregnancy where as with normal magnesium only 9(12%) developed toxemia which suggests that magnesium may have role in the development of toxemia of pregnancy.

More than half of the pregnant women (55%) with hypomagnesemia during pregnancy developed leg cramps in this study which compares favorably with a study published in 1995 showed that pregnant women benefit from oral magnesium supplementation [19].

The magnesium deficiency in pregnant women is an important risk factor for the complications which, can be prevented by timely detection and proper management.

CONCLUSION

This data supported that magnesium has an important role for safe maternal and fetal outcome. Magnesium supplementation is important for prevention of pregnancy associated complications.

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