

ORIGINAL ARTICLE

CLINICAL CORRELATION OF MAGNESIUM LEVELS IN SEVERE PRE ECLAMPSIA AND ECLAMPSIA

¹*Dr. Swetha Thotakura and ²Dr A.Malliga

¹Post graduate, Department of Obstetrics and Gynaecology, Rajah Muthiah Medical College and hospital, Annamalai university, Tamilnadu

²Professor, Department of Obstetrics and Gynaecology, Rajah Muthiah Medical college and hospital, Annamalai university,Chidambaram, Tamilnadu

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ABSTRACT

To study the normal levels of magnesium in blood in normal pregnant women and clinical signs of various levels of magnesium. To correlate the clinical signs with various magnesium levels in blood with severity of Pre eclampsia and eclampsia.Design:Retrospective study.Setting:In a single hospital. **Methodology:** The study is to be conducted in Rajah Muthiah Medical Collage and Hospital between the study period October 2012 to October 2014 in department of Obstetrics and Gynecology. Pregnant patients at 20 to 38 weeks of gestational age with single live fetus. The study is prospective comparative evaluation of two groups control and test group. The study was done in 100 patients of which 50 women are severe pregnancy induced hypertension and eclampsia and other 50 patients are normal women. Serum was analyzed for estimation of Magnesium levels in blood.Statistical analysis - Chi square , and student test t. **Results:** The result showed that serum magnesium were significantly decreased (P 0.001) in preeclampsia as compared to normal pregnant women as well as healthy controls. **Conclusion:** This study showed that there is significantly lower level of magnesium in the pre eclamptic pregnant women compared to the normotensive pregnant women. The difference may be due to the variation in the study population and dietary intake. Systemically magnesium lowers blood pressure and alters peripheral vascular resistance. Thus it can be advantageous for pre eclampsia women.

Keywords: Pre eclampsia, eclampsia, magnesium levels

1.INTRODUCTION

Magnesium is the second most abundant intracellular cation and fourth most abundant cation in the body. Magnesium is the important mineral necessary to be present in the body in the right proportions for maintaining the physiological performance at correct levels Hence this study is to determine the normal Magnesium levels and the variations which may trigger hardely associated with hypertensive problems in pregnancy.It plays an important role in maintaining both maternal and fetal health during pregnancy and the deficiency during the fetal stage can result in long term adverse problems. Some of the obvious symptoms of magnesium deficiency include headache, depression and anxiety, high blood pressure and muscle cramps.Pre eclampsia is unpredictable multiorgan disorder unique to human pregnancy.It is associated with significant maternal and fetal morbidity and mortality worldwide.[1]-[3].

Low Magnesium levels decrease the rate of conception because of the fallopian tube spasm , miscarriages and premature delivery because of uterine hyperexcitability. The life-threatening pregnancy complication, preeclampsia is associated with Magnesium deficiency[4]-[6] and same goes for gestational hypertension as well as leg cramps and water retention.

In babies, Magnesium deficiency leads to sudden infant deaths syndrome, IUGR and metabolic disorders. Most studies have reported reduced Magnesium levels in pregnancy and worst levels in preeclampsia. .[4][6][8]

Foods rich in Magnesium include whole grains , cereals, beans,green leafy vegetables, dried fruits,fish, Vitamin D increases Magnesium absorption

Source of Magnesium: Boiled spinach, bran breakfast cereals almonds,cashews

*Corresponding author: Dr. Swetha Thotakura, Post Graduate, Department of Obstetrics and Gynaecology, RMMCH, Chidambaram, India

Assessment of magnesium status

The most commonly used method for Magnesium status is serum magnesium concentration

In Serum Magnesium concentration ,Ultrafiltrable Magnesium, Ionised Magnesium, Intracellular magnesium content, red cells,mononuclear blood cells,skeletal muscle

Physiological tests: 24 hrs urinary excretion of magnesium

Magnesium deficiency and hypomagnesaemia:

Prevalence of hypomagnesaemia varies from 7% to 11%.hypomagnesaemia is <0.7mmol/l

Cause of hypomagnesaemia: redistribution of magnesium, gastrointestinal causes, drugs

Clinical features:

Electrolyte disturbance:

hypokalaemia,hypocalcemia,neuromuscular and central nervous system,cardiovascular: Magnesium deficiency can affect cardiac electrical activity, myocardial contractility and ventricular tone,arrhythmias also common . ecg it will cause depression of ST segment, there will be supraventricular and ventricular arrhythmias . Hypomagnesaemia is present in <10% of patients with mild to moderate heart failure

Hypermagnesaemia:

Prevalence of hypermagnesaemia varies from 5.7% to 9.3%. hypermagnesemia value is >3mmol/l

Causes of hypermagnesaemia: Hypermagnesaemia commonly occurs due to excessive administration of Magnesium salts or Magnesium coated drugs. Magnesium containing medications are commonly used as laxatives, antacids and as rectal enemas

Clinical features of hypermagnesaemia:

Neuromascular: It causes blockage of neuromuscular transmission and depresses the conduction system of the heart and the sympathetic ganglia, clinically one of the earliest effect of Magnesium intoxication is the disappearance of deep tendon reflexes. This is often seen at Magnesium concentration of 2.0 -4.5mmol/l

Cardiovascular: A moderate increase in the serum Magnesium concentration to 2-3 mmol/l result in mild reduction in supine as well as erect blood pressure. Higher concentration of Magnesium may cause hypotension

Review of literature

Joseph black recognized magnesium as an elemental in 1755. It was isolated by Sri Humphry Davy in 1808
Pregnancy cannot be normal unless Magnesium levels are adequate. The concentration of Magnesium in the placental and fetal tissue increases during pregnancy

Magnesium plays a crucial role in fertility , pregnancy and early newborn life many of the problems associated with pregnancy and birth can be resolved with Magnesium supplementation

In 1991 Dr Jean Durlach said primary Magnesium deficiency occurs in fertile women . gestational Magnesium deficiency is able to induce maternal , fetal ,pediatric consequences which might last through out life

Dr Durlach has shown the increased safety of using Magnesium during pregnancy, even worse is the evidence that Magnesium deficiency is involved in the etiology of sudden infant death syndrome

Ascherio and Colleagues have found out that lower serum Magnesium levels are associated with hypertension, coronary heart disease

Magnesium in pregnancy:

Dietary intake of Magnesium is not sufficient to meet the demands of gestation the maternal stores are mobilised and Magnesium deficiency can occur. Although under most circumstances the body maintains plasma Magnesium levels within very narrow limit, the pregnant women tends to develop lower than normal Magnesium levels even in absence of toxemia(Nwe man,1957,Hardy1956)

The first reports of blood levels of Magnesium during pregnancy were in to range of 1.7-2.2mEq/lit

Hirschfelder (1934) first reported a marked low serum Magnesium levels (0.8 mEq/lit) with eclampsia. Among the 8 eclamptic women Haury and Cantarow reported with three serum Magnesium levels of 0.8-1.0mEq/lit and three with levels of 2.7-3.2mEq/lit. Achari et al (1961) reported that 21 eclamptic women had a mean serum Magnesium level of 0.83mEq/lit

Normal pregnancy:magnesium levels the dietary intake of magnesium is not sufficient to meet the demands of gestation, the maternal stores are mobilized and magnesium deficiency can develop.

First reports of blood magnesium levels during pregnancy were in 1923. Krebs and Briggs (1923) reported a range of 1.7-2.2 mEq/liter among 17 women in their 8th to 40th weeks of pregnancy. Bogert and Plass (1923) compared the serum levels of 40 pregnant women at different stages of pregnancy with those of nonpregnant women and found that the average value 2.0 mEq/liter at the outset (which equaled the control average) fell to an average of 1.7 by the end of pregnancy. Watchorn and McCance (1932) found that half of the 12 pregnant women in their series had serum magnesium levels below 1.99 mEq/liter (which was below the values they found in normal nonpregnant subjects), and that the percentage of the total magnesium in the ultrafiltrable fraction was increased was higher especially in the sixth month of gestation (range during pregnancy 1.95-2.78 mEq/liter mean = 2.41.

Extremely low serum magnesium levels (1.0-1.1 mEq/liter) were reported in a small series of cases by Wolff and Jorrand Bourquard (1937) in the second month of pregnancy which increased slightly (to 1.25-1.41 mEq/liter) at the end of gestation. Their control (nonpregnant) mean value was 1.7 mEq/liter. Haury and Cantarow (1942) included four normal

pregnant women in their tabulation of 108 subjects, and reported a range of 1.4-2.1 mEq/liter; most of their normal controls had serum magnesium levels of 1.8-2.4 mEq/liter. Köberlin and Mischel (1958) also reported lower Mg levels in the first trimester than later in pregnancy. A more extensive report by Newman (1957) has shown the range of serum magnesium levels in 27 normal pregnant women to be very wide in each of the trimesters, at delivery, and at 3-5 days and 6 weeks postpartum Newman also reported an unusually wide normal range of serum magnesium (1.34-2.4) in non-pregnant women. The calcium and phosphorus levels also dropped slightly.

Preeclampsia and Eclampsia: Magnesium Levels

In a study 2005 about serum magnesium levels in 40 pre-eclamptic pregnant women and 40 normal pregnant women it was found that serum magnesium concentration in pre-eclamptic pregnant women [0.77±0.08 mmol/l] lower than that in normal pregnant woman [0.85±0.0908mmol/l] this study concluded that hypomagnesemia are the possible etiologies of pre-eclampsia

In a study of 120 patients attending Nehru Hospital, BRD Medical collage, Gorakhpur, comprising of non-pregnant, normal pregnancy and abnormal pregnancy [abortions, preterm labour and pre-eclampsia] cases, serum magnesium level in non-pregnant cases was 2.42±0.132mg/dl while it was 2.0 ±0.212mg /dl, 2.12±0.199mg/dl and 1.89±0.159mg/dl in 1st, 2nd and 3rd trimesters of pregnancy respectively. Serum magnesium in pre-eclampsia was 1.51±0.217mg/dl and in preterm labour it was 1.14±0.185mg/dl. This study concluded that serum magnesium levels is important in high risk pregnancy involving pre-eclamptic abortions and preterm labour. Serum magnesium levels below 1.5 mg/dl certainly predicts poor pregnancy outcome

Pre-eclampsia is a pregnancy induced disorder of unknown origin characterized by vasospasm, elevated blood pressure and increased neuromuscular irritability features common to syndromes of magnesium deficiency

Hypomagnesemia:

Severe hypomagnesemia is usually associated with Magnesium deficiency and the latter decrease in the total content in the body Magnesium. hypomagnesemia occurs due to lack of intestinal absorption or excessive losses in feces, urine or in other body fluids such as biliary fistula during nasogastric suction or prolonged lactation (Balint and Hirschowitz 1961, Booth et al 1963, Savage and Mc Adam 1967)

Severe and prolonged restriction (<1mEq/day) can cause hypomagnesemia and symptomatic Magnesium deficiency (Shills 1969). the diagnosis of Magnesium deficiency is not easy since blood levels of Magnesium does not always reflect the state of body Magnesium, and is the poor guide to degree of Magnesium depletion (Fitzgerald and Fourman 1965) The main clinical manifestation of Magnesium depletion include neuromuscular disturbance and behavioural abnormalities

Causes of hypomagnesemia: decreased intake like protein calorie malnutrition, starvation, prolonged intravenous therapy, decreased intestinal absorption like malabsorption syndrome including nontropical sprue, massive surgical

resection of small intestine, neonatal hypomagnesemia with selective malabsorption of Magnesium

Clinical features of magnesium depletion (Shill 1969): anorexia, nausea, weakness, muscular fibrillation, tremors, ataxia, vertigo, carpopedal spasm, hyperreflexia, depression

Hypermagnesemia:

Elevated levels of plasma Magnesium are seen in patients with acute (Hamburger 1957 Massry et al 1974) and chronic renal failure (Coburn et al 1969, Randall et al 1964)

Signs and symptoms of hypermagnesemia are the result of the pharmacological effects of this ion on nervous and cardiovascular system. Deep tendon reflexes are usually lost when blood Magnesium exceed 6mEq/l. Respiratory paralysis, narcosis, hypotension occurs and abnormal cardiac conduction may occur as blood levels of Magnesium approach 10mEq/l

Maternal mortality: About 210 million women become pregnant every year around the world and every minute one pregnant woman dies.

2. MATERIALS AND METHOD:

The study is to be conducted in Rajah Muthiah Medical College and Hospital between the study period October 2012 – 2014 October in the department of Obstetrics and Gynecology

Pregnant patients at 20 to 38 weeks of gestational age with single live fetus.

The study is prospective comparative evaluation of two groups control and test group

The study was done in 100 patients of which group A 50 women are severe pre-eclampsia and eclampsia and group B 50 patients are normal women

Inclusion criteria:

Single live intrauterine gestation, Multiple pregnancies, vertex presentation, gestational age of 20 to 38 weeks, B.P more than 140/100, Magnesium levels, Eclampsia

Exclusion criteria:

HB <7 gm/dl, Malpresentation, coagulation diseases

Materials:

A demographic and pregnancy sheet and laboratory test were used in this study. The demographic sheet included a few items about the name, surname, contact number, age, parity, gestational age based on LMP and ultrasound, Serum magnesium levels and blood pressure. 5ml of venous blood sample was aspirated from the participants antecubital vein. The sample were sent to laboratory to check the level of magnesium. Serum magnesium was measured by the colorimetric method and use of Xylidil Blue by an auto analyzer.

The data was analyzed using the Students t-test, chi-square test or Fisher exact test when appropriate

3. RESULTS

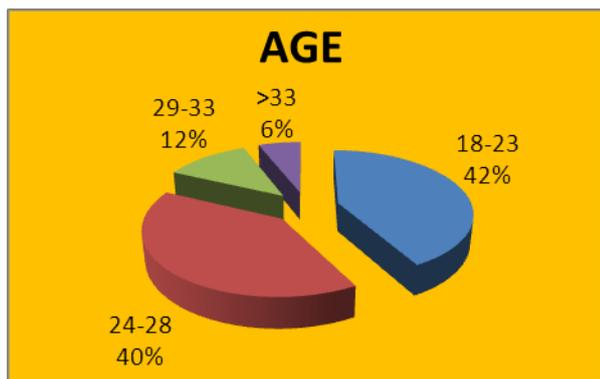
In the present study group A 50 pregnant women who developed group B pre-eclampsia and 50 normal condition

pregnant women were studied for level of magnesium and symptoms associated with variation in magnesium levels

which is lesser than 0.5 hence significant association absorbed between gestational age and presence or absence of pre eclampsia

AGEDISTRIBUTION :-

AGE (in years)	Number of patients	Percentage
18-23	42	42
24-28	40	40
29-33	12	12
>33	6	6
Total	100	100
	MEAN	STANDARD DEVIATION
AGE	24.92	4.47



It is observed that there were 42% of women in the age category 18 to 23years and 40% women in the category 24to28 years. In the age range 29 to 33 years there were 12% of study women and in the age category above 33 years there were only 6% of women

The mean age of study women was 24.92 years with the corresponding standard deviation of 4.47

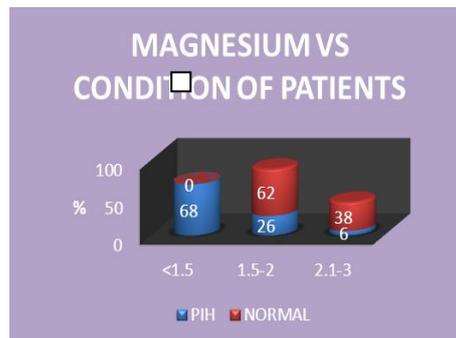
Table 2 Association of gestational age and condition of patients:-

Gestational age	Condition of patients				Total	
	PIH		Normal		Frequency	Percent age
	Frequency	Percentage	Frequency	Percentage		
28-30	4	8	1	2	5	5
32-35	14	28	7	14	21	21
35-40	30	60	33	66	63	63
>40	2	4	9	18	11	11
TOTAL	50	100	50	100	100	100

	Value	Significant ('p' value)
CHI-SQUARE TEST	8.73	0.33

It is observed that in the gestational age category 28 to 30 weeks 8%of the patients developed pre eclampsia. In same gestational age only 2% of the study women are normal without pre eclampsia. In the gestational age range 35 to 40 weeks 60% of women developed pre eclampsia where 66% are normal women, The chi-square test of significance p=0.33

Association of levels of magnesium with condition of the



Mg	Condition of patients				Total	
	PIH		Normal		Frequency	Percentage
	Frequency	Percentage	Frequency	Percentage		
<1.5	34	68	0	0	34	34
1.5-2	13	26	31	62	44	44
2.1-3	3	6	19	38	22	22
TOTAL	50	100	50	100	50	100

	Value	Significant ('p' value)
CHI-SQUARE TEST	53.00	0.001
Mg	Mean	Standard deviation
PIH	1.41	0.36
Normal	2.02	0.14

It inferred that ,68% of women with pih had magnesium levels <1.5 where as there are no women whose was <1.5 in normal women. The majority of the women with normal condition had Ph in the range of 1.5 to 2. The mean magnesium for preeclampsia condition women was 1.14 with corresponding standard deviation of 0.36. The mean magnesium for normal condition women was 2.02 with the corresponding standard deviation of 0.14

The Chi square test of significance was p=0.001 which is less than 0.05 and hence significant association was absorbed between levels of magnesium and condition of pregnant women.

4.DISCUSSION

Preeclampsia is a syndrome characterized by the onset of hypertension and proteinuria after 20 weeks of gestation and affects approximately 5-18% of pregnancies . Preeclampsia is an important disease to screen, as it is common, has significant health outcomes and increases maternal and perinatal morbidity and mortality[1]-[3]. The pathogenesis of placenta dysfunction ,the initiation of systemic vasospasm,ischaemia

and thrombosis that eventually lead to morbidity or mortality in the mother and fetus was poorly understood

women at risk of preeclampsia will enable the identification of high risk of preeclampsia will enable the identification of high risk women who may benefit from enhanced surveillance and prophylaxis. The mean gestational age at presentation for the pre eclampsia was 36.5 weeks and most presented at gestational age of 35 weeks and above. In this study the serum magnesium levels of the control normal pregnant patient was 1.5 - 2.5mmol/l while that of pre eclamptic range from 0.50 to 1.5 mmol/l. The level of serum magnesium are affected by dietary habits, physiological/pathological state, and method of estimation used. In our environment diet rich in magnesium include rice, cassava, beans, soya beans ,beef, vegetables and yam flour.

The major finding in this study is that of significant lower levels of serum magnesium in pre eclamptic patients (0.50 - 1.5)compared to the normal pregnant women(1.5 - 2.5)

Adams and co-workers reported that low cellular magnesium levels in women with pre eclampsia and may contribute to the development of hypertension inn this group of patients.

Also studies have shown decrease in serum magnesium levels has been considered as the cause of pathogenesis of pre eclampsia.

Magnesium deficiency may contribute towards placenta insufficiency and thus to the development of pre-eclampsia as it contribute towards uterine artery spasm, fetal growth retardation and has essential regulatory role in prostaglandin synthesis. It has been suggested that magnesium supplementation during pregnancy can reduce maternal morbidity and improve fetal outcome

Mineral deficiencies like calcium, magnesium, zinc, etc., have been identified to cause significant health problems for women of reproductive age, especially in developing countries due to inadequate dietary intake. The risk of deficiency becomes increased during pregnancy because of increased need of the growing fetus for various nutrients . Changes in levels of these elements could affect pregnancy. One of the problems that may be influenced by nutrient deficiencies is preeclampsia. Recently, more emphasis has been laid on the relationship between maternal serum level of elements and occurrence of preeclampsia . The present study showed that serum magnesium level was significantly reduced in pre-eclampsia mothers compared with the healthy control group. These findings confirmed that hypomagnesaemia may be one of the etiologies of preeclampsia.

5.CONCLUSION

In conclusion, according to the results from our research, the level of magnesium should be considered as a predicting factor of preeclampsia during the first evaluation of pregnancy. A study by Kulier et al. suggested that the intake of magnesium supplements since the beginning of pregnancy may reduce the rate of preeclampsia among pregnant women. Some studies have reported This difference may be due to the variation in the study population and the dietary intake. Systemically, magnesium lowers blood pressure and alters peripheral vascular resistance. Thus, it can be advantageous for pre-eclampsia women.

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