Original Research Article

High incidences of low serum magnesium in pre-eclampsia and eclampsia than in normal pregnancy

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ABSTRACT

Background: Hypertension is one of the most frequently encountered medical disorder in obstetrics practice and remain a major cause of maternal, fetal and neonatal morbidity and mortality. Objectives was to find out the high incidences of low serum magnesium in pre-eclampsia and eclampsia than in normal pregnancy.
Methods: All consenting 50 cases of normal pregnant women and 50 women with pre-eclampsia attending antenatal clinic for checkup of ≥20 weeks who fulfills the inclusion and exclusion criteria were included in the study. Serum magnesium was measured by Calmagite method.
Results: Out of 100 primigravidae 50 cases of pre-eclampsia women were in the age group of 18-30 years and the mean serum magnesium was 1.156±0.328. In contrast out of 50 cases of pregnant women were in the age group of 18-30 years and the mean serum magnesium was 1.907±0.321. The difference between the mean serum magnesium level in pre-eclampsia and normal pregnant women cases were statistically significant (p=0.0016). The study presented below it is clear that there are numerous factors that contribute to the causality of pre-eclampsia and from our analysis it was clear that the serum magnesium levels show an irregular pattern of fluctuations in cases suffering from pre-eclampsia and can be attributed to numerous physiological causes.
Conclusions: Our study shows a significant reduction of serum magnesium levels in pre-eclampsia cases compared to normal pregnant women and occurrence of both maternal and neonatal complications with the serum magnesium levels decreased.

Keywords: Eclampsia, Pre-eclampsia, Proteinuria, Serum magnesium

INTRODUCTION

Pregnancy is a normal physiological process with profound adaptations at the anatomical and biochemical levels that assist in nurturing and survival of the fetus. These adaptive changes are clearly distinct from non-pregnant state.[1] Hypertensive diseases in pregnancy is an universal problem complicating 10% of all pregnancies that cause the most detrimental effects to the mother and baby.[2] Accounts for 40000 maternal death annually thereby contributing significantly to maternal and perinatal morbidity and mortality.[3] Preeclampsia is an idiopathic multisystem disorder complicating 6-8% of all pregnancies.[4] The pathophysiology of preeclampsia is the development of abnormal placental vasculature early in pregnancy resulting in decreased relative placental perfusion, hypoxemia, ischemia in turn leading to release of antiangiogenic factors into the maternal circulation altering the endothelial functions resulting in hypertension and other manifestations.[5] Measurement in early pregnancy or during pregnancy of a variety of biological, biochemical and biophysical markers implicated in pathophysiology of pre-eclampsia has been proposed to predict its development. Studies suggest a pivotal role of micro and macronutrients supplementation in pregnancy and in prevention of some pregnancy

related complications.[3] Magnesium is the second most prevalent intracellular cation of which 60% is complexed with calcium in bone.[7] Magnesium acts as a cofactor for many enzymes, is a peripheral vasodilator and improves glucose tolerance. It has significant effects on cardiac excitability and vascular tone, contractility and reactivity. It is a membrane stabilizer.[1,8] Research focuses on prevention rather than treatment.[2] Based on the physiology of these ions in cellular, neuronal metabolisms and functions and their role in maintaining the normal vasculature suggest that calcium and magnesium may have a role in the etiology of preeclampsia.[4,8] It is therefore imperative to evaluate the levels of these ions in pregnant women with the aim of providing data that could be useful in the prevention and management of preeclampsia and eclampsia through magnesium supplementation during antenatal period especially in a developing country like ours where there is a poor nutrition. Hypomagnesemia related to preeclampsia supports the hypothesis that alteration in the total serum magnesium levels may be involved in possible etiologies of preeclampsia.[10] Advice to rest at home is not recommended as an intervention for the primary prevention of pre-eclampsia and hypertensive disorders of pregnancy in women considered to be at risk of developing those conditions.[13] Previous and family history of preeclampsia, dietary related chronic diseases (obesity, diabetes mellitus and essential hypertension), being primigravida and increasing maternal age are risk factors that increased the risk of development of preeclampsia. Proper antenatal care and prompt management of dietary related chronic diseases are important in the early detection and management of preeclampsia.[14] With this basis, the study is done at our tertiary care institute in the rural set up to assess the association of these elements that is magnesium in the etiopathogenesis of preeclampsia.

Aim of the study

Aim of the study was to assess and correlate the significance of maternal serum calcium and magnesium levels in the etiology of preeclampsia as compared to normal pregnant women

Hence in future it can be used as a predictor or screening tool for development/arrest of progression of preeclampsia and its complications, thus reducing maternal and perinatal morbidity and mortality by early supplementation of calcium and magnesium during pregnancy

METHODS

It is a prospective observational study performed on consenting 50 normal pregnant women and 50 preeclamptic women attending antenatal clinic in the department of obstetrics and gynaecology for antenatal checkup of ≥20 weeks who fulfills inclusion and exclusion criteria.

The study carried out at South Dumdum municipal hospital, Dumdum, Nager Bazar, Kolkata-700074. The study was conducted from December 2018 to September 2019.

Selection criteria of the patients

Study performed on consenting 50 normal pregnant women and 50 preeclamptic women attending antenatal clinic in the department of obstetrics and gynaecology for antenatal checkup of ≥20 weeks who fulfills the inclusion and exclusion criteria.

Inclusion criteria

Control group: Singleton pregnant women of ≥20 weeks irrespective of the parity. Lower socio-economic class strata and normotensive pregnant woman.

Study group: Primi gravida pregnant women of ≥20 weeks. Lower strata. Blood pressure >140/90 mmHg on two occasion 6 hours apart. Urine albumin ≥1+ by dipstick method or 300 mg in 24 hours urine sample, pedal edema. Patient with or without convulsions were included in the study.

Exclusion criteria

Medical conditions like chronic hypertension, renal disease, cardiovascular disease, liver disease, diabetes mellitus and other endocrine disorders. Pregnancy with multiple gestation, hydatidiform mole and other secondary causes of hypertension, malignancy and hematological disorders. Women who smoke, consume alcohol and any drug consumption. Women treated with antiepileptic drugs and patients with autoimmune diseases were excluded from the study.

Gestational age will be based on reliable last menstrual period or first trimester ultrasound examination or both. Informed consent is obtained from each subject before recruiting for the study. Patient's medical records will be reviewed for maternal demographic characteristics and any antepartum complications. Detailed family and medical history are taken. Thorough general physical examination is done in all subjects. Systolic and diastolic blood pressure is carefully recorded by the same observer in sitting position with the arm at the level of the heart and rechecked. An appropriately sized cuff is used and the device should be at the heart level of patient. Korotkoff phase V should be used to designate DBP. Systemic and obstetric examination is done. Urine analysis of all subjects is done to note the extent of proteinuria by dipstick method or by presence of 300mg of albumin in 24 hours urine sample.

About 4 ml of venous blood is collected from antecubital vein under aseptic precautions using sterile needle and syringe into a clean and dry centrifuge tubes. Care will be taken to prevent venostasis during sample collection. It is

allowed to clot for 8-10 minutes and then serum is separated by centrifugation at 3000 revolutions per minute for 5 minutes within 30 minutes of sample collection. If there is a delay in analysis, then the samples are stored +2 to +8 C with icepacks till further analysis. Serum magnesium is measured by Calmagite method.

Serum magnesium estimation

Normal range of serum magnesium is 1.3-2.5 mEq/L.

Methodology: Calmagite method used for this study.

Principle: Magnesium combines with Calmagite in an alkaline medium to form a red colored complex. Interference of calcium and proteins is eliminated by the addition of specific chelating agents and detergents. Intensity of the color formed is directly proportional to the amount of magnesium present in the sample.

Procedure: Wavelength/filter: 510 nm (Hg 546 nm)/green.

Temperature: Room temperature.

Calculation: Magnesium in mEq/L=(Abs. T/Abs. S)×2

SI conversion factor: 2 mEq/L=1 mmol/L=2.44 mg/dl

Ethical approval

When patient came for the antenatal checkup in the antenatal clinic data were taken and serum magnesium percentage recorded. As no treatment was given to the patients and when patient came with complications in the hospital and repeat serum magnesium estimation done. So, no ethical approval needed.

Statical tool used for analysis of data

The R project for statical computing used for analysis of the study.

RESULTS

This is a comparative prospective study consisting of 100 preeclamptic women (cases) and 100 normal pregnant women (controls), done to study the levels of serum magnesium levels in both the groups.

BMI analysis

Report based on BMI analysis: From the above descriptive analysis, we can infer that the BMI group of 22-24 amongst the pregnant women suffering from eclampsia is our target audience as they have a high concentration of the respective case amongst them.

Table 1: Descriptive analysis of BMI.

Normal patients				Eclampsia patients			
BMI (kg/m²)	Frequency	Rate of change	Relative frequency	BMI (kg/m²)	Frequency	Rate of change	Relative frequency
12-14	0	0.06	0	18-20	0	0.08	0
14-16	3	0.02	0.06	20.22	4	0.22	0.08
16-18	4	0.04	0.08	22-24	15	-0.16	0.3
18-20	6	0.1	0.12	24-26	7	0.04	0.14
20-22	11	-0.14	0.22	26-28	9	-0.06	0.18
22-24	4	0.08	0.08	28-30	6	-0.02	0.12
24-26	8	-0.08	0.16	30-32	5	-0.06	0.1
26-28	4	-0.04	0.08	32-34	2	-0.04	0.04
28-30	2	0.08	0.04	34-36	0	0	0
30-32	6	-0.08	0.12	36-38	0	0.04	0
Above 31	2	0.96	0.04	Above 38	2	0.96	0.04

Blood pressure analysis

Report based on blood pressure analysis: We also know that the normal blood pressure of a human being is 120/80 (Systole/diastole), which leads us to the conclusion that on an average, eclampsia cases tend to have a high blood pressure during pregnancy than the normal cases. The minimum and the maximum systolic blood pressure of the eclampsia cases can reach as low as

130 and as high as 180. This makes it as very sensitive area to be monitored, when discovered with such a case. On the other hands we can also infer that the minimum systolic pressure for the normal cases can reach as low as 70, which is concerning. It is also clear, that the dispersion observed in our data is quite high as the standard deviation of the systolic and diastolic pressure for both the cases is high. This leads us to conclusion that the blood pressure of both the cases is quite erratic in nature. This is also clear from Table 2 and 3.

Table 2: Univariate analysis of blood pressure (Normal cases).

Normal cases	Mean	Standard deviation	Minimum	Maximum
Blood pressure (Systole)	100.36	14.82243198	70	130
Blood pressure (Diastole)	59.36	10.15343513	40	80

Table 3: Univariate analysis of blood pressure (Eclampsia cases).

Eclampsia cases	Mean	Standard deviation	Minimum	Maximum
Blood pressure (Systole)	153.02	12.24993128	130	180
Blood pressure (Diastole)	93.98	10.22938828	73	120

From the descriptive analysis carried out above it is clear that the serum magnesium levels are lower in the eclampsia cases when compared with the normal cases. From Table 4, it is clear that the serum magnesium levels show an erratic movement in eclampsia cases. It is clear that the serum magnesium levels are lower and vary in an erratic fashion in eclampsia cases than in the normal cases.

Serum albumin analysis

Report based on serum albumin analysis

From the analysis carried out from Table 5, it is clear that the serum albumin levels remain within the natural levels for normal cases where as the serum albumin levels for the eclampsia cases remain below the natural level on an average. Moreover, the serum albumin levels show an erratic behavior in eclampsia cases.

Analysis of serum urea

Report based on serum urea analysis

As per study, serum urea levels should lie between 10-50 mg/dL in normal cases. Hence from the descriptive analysis carried out above it seems that both the normal and eclampsia cases have their serum urea levels within the normal range. It is clearly evident from the fact that all the measures of central tendency (Mean, median, mode) lie within ten to fifty mg/dL for both the distributions. But if we look closely, we can see a slight variation in the two distributions. If we closely examine the distribution of the Eclampsia cases, we can see that the dispersion is quite higher than that of the normal cases. This is clearly visible if we look at the standard deviation of the former (18.70 mg/dL) and compare it with the latter (3.20 mg/dL). A similar observation can also be made if we compare the range of both the distributions. This clearly imply that the serum urea concentration shows an erratic behavior in case of eclampsia cases. This can be further validated if we take a look at the maximum and the minimum values of distributions. The maximum value of serum urea can reach high as 86 mg/dL whereas situation is quite different in case of normal cases, it's 18 mg/dL.

Table 4: Descriptive analysis of serum magnesium.

Parameters	Normal cases	Eclampsia cases
Mean	1.9072	1.156
Standard error	0.045471714	0.046437142
Median	1.9	1.2
Mode	1.9	1.2
Standard deviation	0.32153357	0.328360181
Sample variance	0.103383837	0.107820408
Kurtosis	7.580591427	0.41921398
Skewness	-2.06341707	0.656683722
Range	1.73	1.4
Minimum	0.67	0.6
Maximum	2.4	2
Sum	95.36	57.8
Count	50	50
Confidence level (95.0%)	0.091378828	0.093318929

Table 5: Descriptive analysis of serum albumin.

Parameters	Normal case	Eclampsia cases
Mean	3.7648	2.586
Standard error	0.038876298	0.07526877
Median	3.8	2.4
Mode	3.8	2.1
Standard deviation	0.274896938	0.53223058
Sample variance	0.075568327	0.28326939
Kurtosis	0.109675688	-1.3085442
Skewness	0.363838242	0.28681821
Range	1.1	1.7
Minimum	3.2	1.8
Maximum	4.3	3.5
Sum	188.24	129.3
Count	50	50
Confidence level (95.0%)	0.078124844	0.15125825

Table 6: Descriptive analysis of serum urea.

Parameters	Normal cases	Eclampsia cases
Mean	13.84	43.84
Standard error	0.45117534	2.64349182
Median	14	42
Mode	18	42
Standard deviation	3.19029139	18.6923099
Sample variance	10.1779592	349.402449
Kurtosis	-1.410073	-0.5454671
Skewness	-0.0997824	0.56173905
Range	9	70
Minimum	9	16
Maximum	18	86
Sum	692	2192
Count	50	50
Confidence level (95.0%)	0.90667077	5.31229559

Comparative analysis of linear trend between auxiliary parameters and serum magnesium
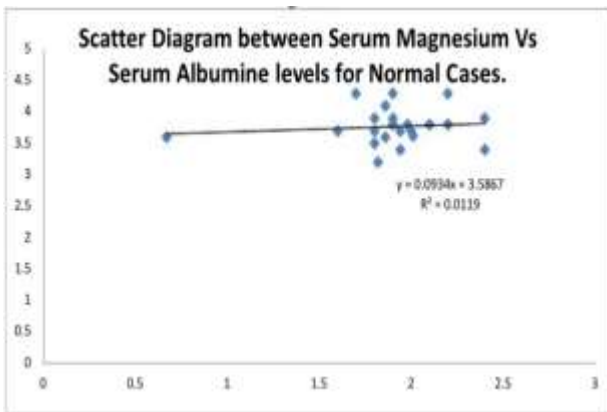
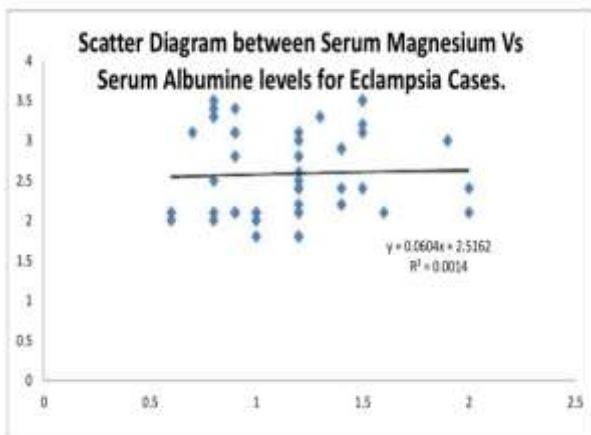**Figure 1: Scatter diagram between serum magnesium versus serum albumin levels for normal cases.**

Figure 2: Scatter diagram between serum magnesium versus serum albumin levels for eclampsia cases.
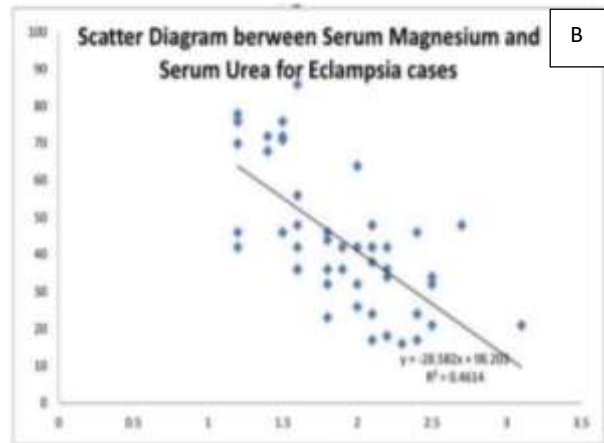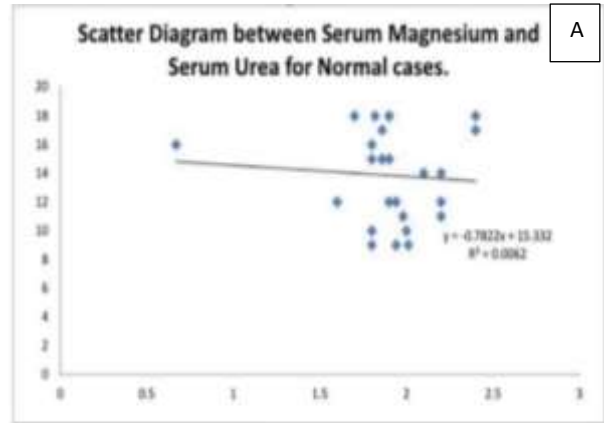

Figure 3 (A and B): Scatter diagram between serum magnesium and serum urea.

Report based on linear trend analysis

From the above linear trend analysis, it is clear that serum magnesium has a lower degree of linear association with the other serum parameters in the blood. It seems that the serum magnesium has no direct linear relationship with the other parameters, which in turn implies that they have no one correspondence. But on the other hand, from figure 25 we can clearly see that the serum urea has a high degree of linear association with serum magnesium levels. The coefficient of correlation between them being 0.461. This clearly indicates that they probably have a one correspondence between them which needs to be further investigated.

DISCUSSION

The patients suffering from eclampsia has the highest concentration of BMI in the group 22-24. Eclampsia patients tend to have a higher systolic (130-180) and diastolic (73-120) blood pressure. The pathophysiology of preeclampsia is the development of abnormal placental vasculature early in pregnancy resulting in decreased relative placental perfusion, hypoxemia, ischemia in turn leading to release of antiangiogenic factors into the maternal circulation altering the endothelial functions resulting in hypertension and other manifestations.[5]

Patient suffering from eclampsia tend to have higher bilirubin levels. The average serum creatinine levels in eclampsia cases are 1.56 mg/dL which show higher serum creatinine level. Eclampsia cases shown the SGOT levels fluctuate beyond the normal range. This will serve as good indicator for the presence of eclampsia in women. Cases suffering from eclampsia show a high degree of fluctuation in their SGPT levels as compared to the normal cases. Eclampsia cases tend to have a relatively high serum urea concentration than the normal cases. Serum albumin level for the eclampsia cases is lower and below the normal level. Eclampsia cases show the serum globulin level are considerably lower when compared with the normal cases. The mean serum magnesium level in case of normal cases is 1.907 mg/dL and in eclampsia cases is 1.156 mg/dL. Serum magnesium levels are lower and vary in an erratic fashion in eclampsia cases than in the normal cases.[4,8] Serum calcium, magnesium and zinc can be considered as factors having a role in the etiopathogenesis of the disease and as severity indicators in pre-eclamptic women.[11] These factors and the underlying evidence base can be used to assess risk at booking so that a suitable surveillance routine to detect pre-eclampsia can be planned for the rest of the pregnancy.[15] Serum urea has a high degree of linear association with serum magnesium levels. The coefficient of correlation between them being 0.461.

Limitations

Medical conditions like previous history of chronic hypertension, renal disease, cardiovascular disease, liver disease, diabetes mellitus and other endocrine disorders. Pregnancy with multiple gestation, hydatidiform mole and other secondary causes of hypertension, malignancy and hematological disorders. Women who smoke, consume alcohol and any drug consumption. Women treated with antiepileptic drugs. Autoimmune diseases can be limitation for the study.

CONCLUSION

Hypertensive disorders complicate 5 to 10% of all pregnancies, and together they are one member of the deadly triad along with hemorrhage and infection that contributes greatly to maternal morbidity and mortality. Of these disorders, the preeclampsia syndrome, either alone or superimposed on chronic hypertension, is the most dangerous. Hypertensive disorders of pregnancy are one of the major causes of maternal and fetal morbidity and mortality. It forms a member of the deadly triad, along with hemorrhage and infection. Yet as long as its etiopathogenesis is unclear, prophylaxis will be uncertain. Though the prevention is difficult, maternal and fetal morbidity and mortality can be reduced to a greater extent by early recognition and timely management. Pregnancy is associated with physiological decrease in the concentration of elements like calcium and magnesium which is further aggravated in conditions like

preeclampsia. As the severity of preeclampsia increases, more and more reduction in the levels of magnesium is seen in maternal blood. In our study, a reduction of serum magnesium levels is seen in preeclampsia and eclampsia cases compared to normal pregnant women. It was also established in this study that the magnesium in patients with severe preeclampsia and eclampsia were less compared to the normal patients. In this study, both maternal and neonatal complications were more in preeclampsia cases where the serum magnesium levels are decreased. These findings support the hypothesis that hypomagnesaemia is possible etiology of preeclampsia and help in establishing strategies for prevention and reduction of severity of the disease. Needs further studies to find out whether estimation of magnesium at an early gestation age can be used as a predictive marker for early diagnosis of preeclampsia and supplementation with these nutrients in early pregnancy can be a preventive tool in preeclampsia.

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