Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 1, 2021, Pages. 4070 - 4076

Received 15 December 2020; Accepted 05 January 2021.

Study of Serum Magnesium Levels in Patients of Cirrhosis of Liver

Mansi Patel[1], Sachin Agrawal[2], Sunil Kumar[3], Sourya Acharya[4], Shilpa Bawankule[5]

[1]Resident, Medicine Department, JLN Medical College, DMIMS Medical College

[2]Professor, Medicine Department, JLN Medical College, DMIMS Medical College

[3]Professor, Medicine Department, JLN Medical College, DMIMS Medical College

[4]Professor, Medicine Department, JLN Medical College, DMIMS Medical College

[5]Professor, Medicine Department, JLN Medical College, DMIMS Medical College

Email: [1]mansipatel95@gmail.com[2]dragrawal82@gmail.com, sunilkumarmed@gmail.com, [4]souryaacharya74@gmail.com, [5]drshilpagaidhane@gmail.com

Corresponding author's name and address: Mansi Patel

Corresponding author's email id-mansipatel95@gmail.com

Contact number of the corresponding author:9429735534

Type of Article- Original Article

Conflict of Interest: None

Funding: Nil.

Abstract:

Background :

Magnesium, in addition to potassium, is one of the irons which are inorganic found in the human body and one of the common intracellular ions. Acute liver dis orders are associated with elevated serum levels of magnesium, which is equal to serum level s of bilirubin. But withchronic liver disease and cirrhosis patient, only few studies are available.Deficiency of magnesium isvery common in the general population and prevalence of it in the patients of cirrhosis is even more. Difference between the serum levels of magnesium and total body content is weak because most of the magnesium is intracellular. Therefore,We hereby have planned this study to assess magnesium levels in patients of cirrhosis in different phases of disease.

Objective: To correlate the serumlevels of magnesium with various aetiology of cirrhosis, to correlate serum magnesium levels with severity of cirrhosis and to the various complications of cirrhosis.

Method: The Prospective cross-sectional study will be conducted in medicine department, atAVBRH, a tertiary care teaching hospital in the rural area of Wardha District. We will prospectively enroll all consecutive patients > 18 years of age regardless of gender or ethnicity who undergo clinical, biochemical and radio diagnostic testing forcirrhosis

Expected Outcome: The study estimates the serum levels of magnesium in patient of cirrhotic liver disease and as previous studies which is been conducted outside India, have observed low serum magnesium levels, we expect the same with our study.

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 1, 2021, Pages. 4070 - 4076

Received 15 December 2020; Accepted 05 January 2021.

Keywords: Serum magnesium, cirrhosis of liver, phases of disease.

INTRODUCTION:

Liver cirrhosis is a worldwide health problem.[1]It is the end stage of liver fibrosis characterized by nodule formation. Cirrhosis means scaring of liver in end stage of disease which are hepatitisandthe chronic alcoholism.[2,3] Any time liver is damaged, it attempts to heal itself whether due to sickness, lar ge alcohol intake or another cause.[4,5] Scaring forms in suchthe process. More and more of the scar tissue develops as cirrhosis progresses, rendering it difficult for liver to function it is so called decompensated cirrhosis. Advanced cirrhosis is life-threatening. Most commonly causes of liver cirrhosis are alcoholism and hepatitis B or C. Epidemiology of cirrhosis of liver varies between gender, geographical distribution and ethnic groups.[6,7]

Liver cirrhosis of the liver is that the final stage of chronic liver diseases, which may cause portal hypertension-related complications and liver failure. In a very remunerated state, the cirrhotic patient maintains a close to traditional solution and acid–base standing, however this delicate balance may be discontinuous by malady progression, infection, dietary indiscretion/deprivation, or medicine intervention. It's clinically necessary to predict the first mortality in patients of liver cirrhosis. The information is beneficial to alert the physicians, patients and patient's relatives who is at a high risk of early death. Though this issue has been mentioned by varied studies2, the main focus of few studies has been on the role balancing in predicting the various results in liver cirrhosis

Many mineral metabolism disorders are represented in relation with hepatic diseases, however, their etiology, complication is nevertheless to be known. Several components play necessary roles within the living human as elements of metalloproteins and metalloenzymes further as catalyst cofactors3. As the metabolism of those compounds mainly happens in liver, therefore studies of minerals in liver disorders are of much importance in recent years. However, the factors related to liver diseases and mineral metabolism are still unclear. Since hepatic pathology and cirrhosis of the liver cause purposeful deterioration of liver tissue, modifications within the levels of necessary minerals could play a vital part in the pathological process of hepatic fibrosis4.

Magnesium's role as a cofactor in the enzyme- coenzyme system is well known in the body's various metabolic reactions.[8] The stability of DNA, RNA and binding of mRNA to rib osomes is needed. Magnesium forms the substrate with ATP and is involved in all reactions i n which ATP takes part, such as the use of glucose, protein, fat, metabolism of nucleic acid a nd synthesis of nucleotides.[9]The ATP-dependent sodium and potassium pump system associated with the membrane is also concerned. It plays an essential part in the homeostasis of the cell. In a healthy person, natural serummagnesium levels are 1.7 to 2.3mg/dl. Studies are available to associate serum magnesium levels with chronic and acute liver diseas e, but the levels of cirrhosis were not definitive in establishing a definite relationship.

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 1, 2021, Pages. 4070 - 4076

Received 15 December 2020; Accepted 05 January 2021.

Magnesium is the significant part of the human body and other mammals whose function is st ill a matter of study in liver cirrhosis and its complications. In patients with liver cirrhosis, the re are contradictory reports about their serum concentrations. About 300 enzymatic reactions including energy metabolism and protein and nucleic acid synthesis are associated with magn esium[10,11.]

Magnesium is also involved in the synthesis of immunoglobulin, adherence to immune cells, cytolysis dependent on antibodies, adherence to T helper B cells and additional responses. In serum there is just 0.3 percent of total body magnesium

Although it is possible to obtain the role of minerals in liver diseases with relevant intelligent knowledge, the relation between mineral alteration and hepatic fibrosis development is not ap parent.

In addition, little or no evidence can be obtained of changes in the minerals within the cirrhoti c liver. The currentstudy supposedto find serumlevels of magnesium in the patients of cirrhosis of liver and its levels in various levels of disease. There are no such studies been carried out in the current scenario. Magnesium should be prescribed in cirrhosis patients in view of reducing neuromuscular and neuropsychiatry manifestations.Magnesium's use as a drug of treatment in asthma, myocardial infarction, and pre-eclampsia is also discussed and being proven. Although the function of minerals in liver diseases can be obtained with relevant intelligent information, the connection between mineral modification and the production of hepatic fibrosis is not obvious. Moreover, little to no evidence on shifts in the minerals inside the cirrhotic liver can be collected. Therefore, an assessment of the serum levels of magnesium in liver cirrhosis was performed in the current report.

Aim: To study correlation of serum magnesium levels in patients of cirrhosis of liver.

Objectives: To correlate the serum magnesium levels with various aetiologyof cirrhosis, to correlate serum magnesium levels with severity of the cirrhosis and to relate the serum magnesium levels with various complications cirrhosis.

Material: The study will be held in the Medicine department at AVBRH, a tertiary care teaching hospital in the rural area of district Wardha. The study will be undertaken after approval from institute ethical committee (applied for).We will prospectively enroll all consecutive patients > 18 years of age regardless of gender or ethnicity who undergo clinical, biochemical and radio diagnostic testing forcirrhosis at AVBRH, Sawangi. Written informed consent will be obtained from all participants.

Inclusion criteria: After written inform consent all the patients of more than 18 years of age who will be screened clinically for liver disease, relevant biochemical analysis will be done and after confirmed cirrhosis on ultrasound study, patients will be taken up for the study,

Exclusion criteria: Patients with known case of systemic hypertension, patients with Kidney disease and raised serum creatinine, patient with coronary artery disease, patient with type 2 diabetes mellitus, patients with osteoporosis and patients not willing to give informed consent.

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 1, 2021, Pages. 4070 - 4076

Received 15 December 2020; Accepted 05 January 2021.

Duration

The duration of study will be 2.5 years (November 2020 to April 2022)

Methods

The study will be carried out in the Medicine Department, AVBRH,sawangimeghe, Wardha during July to 2022 aftergetting Institutional Ethics committee permission, and written informed consent from all participants. Patients fulfilling inclusion and exclusion criteria will be enrolled into the study. Total 200 subjects will be selected and divided into two groups. Each person will undergo the following procedure:

History taking: Including age, gender, comorbidities like diabetes mellitus, systemic hypertension, coronary artery disease, chronic kidney disease (serum creatinine levels more then 1.

H/O alcohol intake/ Drug abuse/ Blood transfusions/ Dialysis will be asked in subjects.

Biochemical testing for liver function test, kidney function test and blood sugar levels will be done and clinical examination as per format given below will be done.

Laboratory investigations: Peripheral venous blood specimens Will be collected on admission for measuring of: Complete blood count (CBC) and differential leucocytic count. Serum levels of magnesium will be calculated by the spectrophotometer at 530 nm. (Wavelength range: 500-550 nm) using the calmagite method.

Sample collection: Adequate venous blood samples will be withdrawn and collected into the plain bulb and centrifuged immediately for serum specimen that will be stored frozen at a temperature -20 °C under complete aseptic technique.

The theory of method depends on creation of the color complex in the alkaline medium betwe en magnesium ions and the calmagite. EGTA (ethylene glycol tetra acetic acid) decreases the calcium interference, KCN (potassium cyanide) decreases heavy metal interference, and surfactants minimize protein and lipid interference.The method involves incubating just 10 ml of serum with 1000 ml of the

reagent at room temperature for five minutes and colour represents the concentration of magn esium in serum. Serum levels of magnesium will be calculated with the following formula: absorbance of Sample /absorbance of standard × 2 = magnesium meq/l

Males / Females 1.4 - 1.9 meq/L or 0.7 - 0.94 mmol/L

USG Abdomen Pelvis: Findings for liver and kidney diseases will be looked for in the scan and on basis of that patients will be confirmed to enroll for cases or controls or whether to be excluded

Group I will include 100 diagnosed cases with liver cirrhosis. The subjects will in the age group of more then 18 years male and female. Group II will include 100 healthy control subjects. The age limits of this group will also be more then 18 years in both male and female.

In the inclusion criteria patients will be further divided into 3 classes:

- According to etiology
- According to complications

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 1, 2021, Pages. 4070 - 4076

Received 15 December 2020; Accepted 05 January 2021.

- According to severity

For the severity patients will be classified with the CHILD PUGH Scoring:

Bilirubin (Total)	<2 mg/dL (<34.2 µ mol/L)	+1
	2-3 mg/dL (34.2-51.3 µmol/L)	+2
>3 mg/dL (>51.3 µmol/L)		+3
Albumin	>3.5 g/dL (>35 g/L)	+1
	2.8-3.5 g/dL (28-35 g/L)	+2
<2.8 g/dL (<28 g/L)		+3
INR	<1.7	+1
	1.7-2.2	+2
>2.2		+3
Ascites	Absent	+1
	Slight	+2
	Moderate	+3
Encephalopathy	No Encephalopathy	+1
	Grade 1-2	+2
	Grade 3-4	+3

Classification: of Child-Pugh:

Class A:	Five to six points	Mild Disease
Class B:	Seven to nine points	Moderate Disease
Class C:	Ten to fifteen points	Severe Disease

Study will be followed with the patient and healthy individuals for a period of there hospital stay and till the day of discharge. The first reading of serum magnesium levels will be put in case and control and will be taken up for study.

After the end of 1.5 years total numbers of cases and controls will be analysed using the formula of p value.

Sample size:

Sample Size: $\frac{Z\alpha^2 * (p)*(1-p)}{c^2}$

Where:

Z= Z value (1.96 for 95% confidence level)

P= percentage of picking a choice, expressed as decimal

This was found to be 80% for the present study which was expressed as 0.80

C= confidence interval, expressed as decimal

So, the sample size was calculated as per formula

$=\frac{(1.96)^2 x\ 0.8\ x\ 0.2}{(0.05)^2}$

This study will include 100 patients with cirrhosis and 100 of healthy individuals, thus total of 200 patient.

Received 15 December 2020; Accepted 05 January 2021.

DISCUSSION:

Many studies have been proven that mg deficiency is associated with the alcoholic fatty liver disease because the correlation of hypomagnesaemia with alcoholism has been known for a very long time[12,13] Several mechanismrelated with the alcoholism contributed to magnesium deficiency, that includes urinary Mg wastage, poor nutrition, GI losses, phosphate deficiency, Metabolic acidosis, deficiency of vitamin D and free fatty acidaemia related to alcohol withdrawal[12]. We found that, low Mg levels were not only in presented in patients with alcoholic disease but also in non-alcoholic disease tooproves that the alcohol cannot be only cause of hypomagnesaemia in the patients with fatty liver and that in the latter patients also other factors participate in pathogenesis of hypomagnesaemia. Koivisto et al.,[14] described hypomagnesaemia in the patients with cirrhosis. Chronic intake of alcohol may beone of the cause factor for deficiency of magnesium. Hypomagnesemia was noted to be in 30% of admissions in hospital with the alcohol abuse and in 85% of the admissions for delirium tremors. [15.] Studies have shown Mg alterations have beenmost commonlyseen in the critically ill elderly patients, as in this study, who have a higher prevalence of hypomagnesemia.[16]

CONCLUSION:

In conclusion, our study will show lower magnesium concentrations associated with anrise in cirrhosis severity. Therefore,magnesium could be added among the nutrients that are given particular consideration in the management of cirrhosis in view of preventing magnesium deficiency and can be used as a sensitive indicator of liver cirrhosis. A routine assessment of magnesium in liver cirrhosis patients may be effective in treatment protocol and to decrease progression of the disease and avoid significant derangements in the health status

REFERENCE:

[1] Prasad AS, Oberleas D. Trace elements in human health and disease. 1976.
[2] Bhandari: Trace elements in human health and disease, Quart. Med, review 72.261-90 (March1983).
[3] Elin RJ. Magnesium metabolism in health and disease. Disease-a-month. 1988 Apr 1;34(4):166-218.
[4] Harper HA, Granner DK, Martin DW, Mayes PA, Rodwell VW. Harper's review of biochemistry. 1985..
[5] Hannas: Syndrome of magnesium deficiency in man. Lancet. 3057-68 (Feb. 1960).
[6] Rude RK, Singer FR. Magnesium deficiency and excess. Annual review of medicine. 1981 Feb;32(1):245-59.
[7] Rodríguez-Roisin R, Krowka MJ, Hervé P, Fallon MB. “Pulmonary-Hepatic vascular Disorders (PHD)”. EurRespir J.; 24 (5) : 861– 880 (2004)
[8] Bhandari: Trace elements in human health and disease, Quart. Med, review 72.261-90 (March1983). 3. Disease a Month: Magnesium metabolism in health and disease. 205-56 Vol. 2(April 1988).
[9] Henry JB., Clinical Diagnosis and Management, 17th ed., W.B. Saunder Co. Philadelphia,157 (1984)
[10] Weisinger JR, Bellorin Front E. “Magnesium and phosphorus”. Lancet; 352: 391-396. (1998)
[11] Elin RJ. Magnesium metabolism in health and disease. Disease-a-month. 1988 Apr 1;34(4):166-218.
[12] Rink EB. Magnesium deficiency in alcoholism. Alcoholism: Clinical and Experimental Research. 1986 Nov;10(6):590-4.
[13] Shane SR, Flink EB. Magnesium deficiency in alcohol addiction and withdrawal. Magnes Trace Elem. 92: 263-268. (1991).

Received 15 December 2020; Accepted 05 January 2021.

[14] Koivisto M, Valta P, Hockerstedt K, Lindgren L. Magnesium depletion in chronic terminal liver cirrhosis. Clin Transplant. 16: 325-328 (2002).

[15] 15. Kumar S, Honmode A, Jain S, Bhagat V. Does magnesium matter in patients of Medical Intensive Care Unit: A study in rural Central India. Ind J Crit Care Med: Peer-Reviewed, Official Publication Indian Soc Critical Care Med. 2015;19(7):379.

[16] Kumar S, et al., Impact of serum magnesium levels in critically ill elderly patientsdA study in a rural teaching hospital, Journal of Clinical Gerontology & Geriatrics (2016), http://dx.doi.org/10.1016/j.jcgg.2016.04.002