

**EFFECTS ON SERUM MAGNESIUM LEVEL IN ALCOHOLIC & NON  
ALCOHOLIC PATIENTS OF TYPE-II DIABETES MELLITUS**

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***ABSTRACT***

***Background:*** Diabetes mellitus is one of the leading diseases that are engulfing the world fast. According to an estimate, 347million peoples are suffering fromdiabetes mellitus (DM) in Pakistan. Diabetes mallitus leads to hypomagnesemia while alcohol misuse in diabetes mallitus further worsen the condition. Magnesium critically stabilizes different enzymatic reactions, including many ATP generating reactions.

***Aims and objectives:*** The aim and objective of this study was to evaluate the relationship between serum magnesium level and diabetes mellitus in association withalcoholism.

***Methodology:*** The present study was conducted at the Department of Biochemistryin collaboration with the Department of OPD and the Department of Causality (COD). It was a cross-sectional and comparative type of study. One hundred and ten

(110) participants were included to participate in this study. Seventy (70) were in the control group

and 40 were in the test group. The study was conducted according to a specific inclusion and exclusion criteria. Roche C311 auto analyzer was utilized to analyze the serum magnesium level.

**Results:** The results obtained were incorporated in a specific designed Performa. The data was analyzed by SPSS version 23. It was concluded that in patients suffering from diabetes mellitus and are consuming alcohol have more chances of developing Hypomagnesaemia than those diabetic patients do not use alcohol (P value 0.000). The study found that frequency of drinking is also closely associated with development of Hypomagnesaemia (P value 0.002). Recommendation was sent to LUHMS.

**Conclusion:** It was concluded that that there is a direct association between diabetes mellitus and low serum magnesium level and this association become far greater in patients who are regular user of alcohol.

**Keywords:** Diabetes Mellitus, Hypomagnesaemia and Alcohol

### **Introduction:**

Diabetes mellitus represents a syndrome with disordered metabolism and an inappropriate hyperglycemia due to either absolute deficiency of insulin secretion or a reduction of its biological effectiveness or both<sup>1</sup>

The increasing epidemic proportions of type 2 diabetes (T2D)<sup>6</sup> have been attributed to ~1.3 million deaths in 2008 globally, and an estimated 347 million people worldwide have been affected<sup>2</sup> Pakistan having data of 7.6 to 11% of adult diabetes mellitus cases in adults<sup>3</sup> The burden of type-II diabetes mellitus as a major cause of premature illness and death is mostly a result of the relevant risk of cardiovascular diseases and micro vascular complications.<sup>4</sup> Alcohol is one of the most widely consumed beverages in non-Muslim communities, and hence investigating whether alcohol consumption is associated with the risk of chronic diseases has important public health implications.<sup>5</sup> Alcohol influences glucose metabolism in several ways in diabetic patients as well as in non- diabetic patients. Since alcohol inhibits both gluconeogenesis and glycogenolysis<sup>6</sup> Magnesium is the eighth common element in the crust of earth, fourth most abundant cation in

human body and second abundant intracellular cation. It may exist as protein bound, complexed or in free form. It is a cofactor in more than 300 enzymatic reactions. Magnesium critically stabilizes enzymes, including many ATP generating reactions.<sup>7</sup>

It increases activity of insulin to control blood sugar level. Magnesium is involved on multiple levels in insulin secretion, binding and activity.<sup>8</sup> Cellular magnesium deficiency can alter the membrane bound sodium-potassium-ATPase enzyme which is involved in the maintenance of gradients of sodium and potassium and in glucose transport.<sup>9</sup>

Normal serum magnesium levels are between 1.46 and 2.68 mg/dL. Hypomagnesemia is an electrolyte disturbance caused when there is a low level of serum magnesium (less than 1.46 mg/dL) in the blood.<sup>10</sup>

In diabetics there is a direct relationship between serum magnesium level and cellular glucose disposal that is independent of insulin secretion. This change in glucose disposal has been shown to be related to increased sensitivity of the tissues to insulin in the presence of adequate magnesium levels.<sup>11</sup> The Hypomagnesemia that is found in type 2 diabetes mellitus is usually because of a disproportionate loss of magnesium from the kidney, with lesser intake and more loss.<sup>12</sup> Most of the people take less amount of magnesium as recommended by doctors. They recommend more than 300 mg of magnesium per day. If they intake less than 250mg/day, eventually will suffer from Hypomagnesemia.<sup>13</sup>

About 2.5 to 25% of the population is suffering from magnesium deficiency. The reference level in serum is 75mmol. Deficiency of magnesium leads to metabolic, cardiovascular, and central nervous system disorders. The clinical presentation includes body weakness, vomiting, and abdominal pain.<sup>14</sup> the basic supplement of magnesium that comes into the body is through the dietary route.<sup>15</sup>

Diabetes mellitus leads to hypomagnesemia and Hypomagnesemia leads to development of complications of DM.<sup>16</sup> Magnesium acts against the inflammatory changes in the vessels, and Hypomagnesemia produces cardiovascular abnormalities.<sup>17</sup> Magnesium enhances the sensitivity of tissue receptors to insulin.<sup>18</sup> Deficiency of magnesium is also positively correlated with the rapid progression of pre-diabetes to diabetes.<sup>19</sup> Hypomagnesemia has a triple side effect in producing

diabetes mellitus. First, it decreases the peripheral sensitivity to insulin; second, it increases the secretion of glucagon hormone from the alpha cells; and third, it decreases the secretion of insulin in response to hyperglycemia.<sup>20</sup>

According to serum magnesium concentration, hypomagnesemia is isolated into three classes. Normal serum level ranges between 1.7mg/dl to 2mg/dl. In mild Hypomagnesemia serum level is between 1.5mg/dl to 1.7mg/dl, moderate Hypomagnesemia is between 1.6 mg/dl to 1g/dl, and severe below 1mg/dl.<sup>21</sup> Hypomagnesemia is closely associated with renal disease. Excessive loss of magnesium leads to Hypomagnesemia, which causes the production of diabetes mellitus type2 disease.<sup>22</sup>

The mechanism of action and role of magnesium in the production of diabetes mellitus is very vital. Insulin acts through the 2<sup>nd</sup> messenger system by binding to a tyrosine kinase enzyme. This binding initiates multiple chemical reactions, facilitating the transport of glucose across the cell membrane. Magnesium activates the sodium-potassium ATPase pump, which is involved in the transport of electrolytes across the cell membrane.<sup>23</sup> The role of Hypomagnesemia in diabetes mellitus is debatable throughout the world. In serum, magnesium occurs in two forms; one ionized form, which is 70%, and the other bound to proteins, which is 30%. Hypomagnesemia is relatively more common in type2 diabetes patients Hypomagnesemia is 10 times more frequent in diabetes mellitus type2. Diabetes mellitus produces kidney damage, leading to microalbuminuria resulting in Hypomagnesemia.<sup>24</sup> By increasing the supplements of magnesium through dietary sources, then the conversion of pre-diabetes into diabetes and the complications of diabetes mellitus type 2 can be reduced.<sup>25</sup> many researchers believe that the dietary supplement of magnesium improves the control of blood sugar level in the long term, especially in patients suffering from diabetes mellitus type 2.<sup>26</sup> The Serum magnesium level decreases in alcohol dependence syndrome (ADS). It is due to decrease intake of magnesium and decrease consumption due to gastric and liver disorders, from which these users suffer most.<sup>27</sup> Hypomagnesemia is caused by increased urinary excretion of magnesium and chronic diarrhea.<sup>28</sup>

## ***MATERIAL & METHOD***

This study was conducted by the Department of Biochemistry with collaboration of the Diagnostic Research Laboratory and Diabetic OPD and emergency department LUH Hyderabad. The duration of the study was within six months after approval of synopsis. It was a comparative cross-sectional study. Sampling was convenient non-Probability type of sampling. Total one hundred and ten (110) diagnosed cases of type-II Diabetes Mellitus were selected from diabetic OPD and emergency department of LUMHS Jamshoro/Hyderabad. They were divided into two groups. Control group comprised of 70 diagnosed cases of non-alcoholic type-II diabetes mellitus and Test group comprised of 40 diagnosed cases of type-II diabetes mellitus with alcoholism.

### ***Including criteria***

In the including criteria only male diagnosed diabetic patients were selected who were an age range of 45-65 years. In the control group nonalcoholic patients while in the test group only alcoholic diabetic type 2 patients were selected. Alcoholic patients were recruited from both Muslim and non-Muslim communities who were having history of alcohol intake at least from last one year. Only those patients were selected who do not have any present or past history related to any sign and symptoms of diabetic neuropathy, retinopathy and nephropathy. All participants were of similar socioeconomic status. The range criteria for HbA1c% levels was between 8.0% to 10.0%

### ***Exclusion Criteria***

The subjects having following parameters were excluded from this research study. Alcoholic and non-alcoholic patients of Type-I diabetes mellitus. Alcoholic diabetic patient with history of alcohol taking below one year. Age below 45 years or above 65 years. Any present or past history related to any sign and symptoms of diabetic neuropathy, retinopathy and nephropathy. The difference between socioeconomic statuses of patients like some belong very poor class some belong middle class or some belong upper socioeconomic class. HbA1c% level below 8.0% or above 10.0%

### ***Sample Collection***

The patients included in this study were explained about the purpose of research and the procedure regarding the collection of sample. All the physical parameters were recorded including blood pressure, temperature and other complications regarding diabetes mellitus. The participants filled a consent form. The seven ml of blood was drawn from each patient included in study by venipuncture using plastic disposable syringes under aseptic measures. Two ml of blood was collected in screw-cap bottle containing anti-coagulant, EDTA for estimation of HbA1cpercentage; remaining blood was centrifuged for separation of serum within two hours of blood collection, glucose determination was done immediately by glucose oxidase method. Remaining serum was transferred to clean and dried bottles having rubber caps and stored at - 20<sup>0</sup>C for serum magnesium analysis. Before analysis sample was allowed to attained room temperature.

#### ***Analytic Method***

Serum magnesium level & HbA1cpercentage was analyzed by Roche C311 auto analyzer available at Diagnostic & Research Laboratory LUMHS Jamshoro/Hyderabad

#### ***Data Collection Procedure***

For this study, we registered clinical data and other relevant details of each participant by filling a Performa or questionnaire.

#### ***Data Analysis Procedure***

The Data analysis procedure was performed using the Statistical package for social sciences (SPSS) version 23. All the variables were categorical in nature. Frequency variable were calculated using frequency option. Cross tabulation was performed using descriptive statistics to compare different variables. p values were obtained by applying chi-square test. P-values less than 0.005 were set as significant.

#### ***Ethical Consideration***

The study was conducted strictly under the ethical rules after approval from ethical committee of

LUMHS Jamshoro. There was no conflict of interest

## **RESULTS**

Table 1 explains frequency of drinking, age and duration of alcohol use. There were 110 participants. Forty 40 participants were in the alcoholic group. Twenty-seven (24.5%) were using drink once a week, 7 (6.4%) were having drink twice a week. Six (5.5%) were using drink more than twice a week while 70 (63.6%) were non-alcoholic. Participants who were between 45-55 years' age group were 63 (57.3%) while the participants who were between 56-65 age group were 47 (42.5%). The participants who were drinkers for 1-5 years were 14 (12.7%), between 5-10 years were 17 (15.5%), between 10-20 years were 9(8.2%) and who were nonalcoholic were 70 (63.6%).

Table 2 describes the magnesium outcome in control and test group. In the control group 58 (82.9%) were having normal serum magnesium level while 12 (17.1%) were suffering from Hypomagnesia. In the test group, 22(55%) were having normal serum magnesium level while 18 (45%) were suffering from Hypomagnesia. The P value was 0.002, which indicate highly significant association. The P value was 0.002, which is highly significant.

In the severity of serum magnesium level 81 (73.6%) were having normal serum magnesium levels, 16 (14.5%) having mild level of deficiency, 6 (5.5%) were having a moderate level of deficiency, while 7 (6.4%) were suffering from a severe level of deficiency.

Table 3 describes the association of drinking frequency, duration of alcohol use and HbA1C to serum magnesium level. The participants who were taking drink once a week, 18 (66.7%) were of normal serum level, 9 (33.3%) were suffering from hypomagnesemia, out of 7 (100%) 5 (71.4%) were suffering from hypomagnesemia in participants who were using alcohol twice a week while in participants who were using alcohol more than twice a week, 4 (66.7%) were suffering from hypomagnesemia. The P value was 0.001.

The participants who were drinkers for 5 years, 3 (21.4%) were suffering from Hypomagnesemia, for 10 years 8 (47.1%), for 20 years 7 (77.8%) were suffering from Hypomagnesemia, while in case of nonalcoholic group 12 (17.1%) were suffering from Hypomagnesemia. The P value was 0.001,

which was highly significant.

In the association of HbA1C and serum magnesium level out of total 110 participants, Seventy-six (78.4%) participants who were having serum HbA1c level between 6.7-7.7 had normal serum level while 21 (21.6%) showing Hypomagnesemia. 4(36.4%) who had serum level between 7.7-8.7 showed normal serum level while 7 (63.6%) were showing Hypomagnesemia. In patients above 8.7 criteria 0 (0%) were of normal serum level while 2 (100%) were of hypomagnesemia. The P value was 0.001

**Table 1: Distribution of patients according to frequency of diabetic alcoholic and diabetic non-alcoholic, duration of alcohol use and drinking, of alcohol use in weeks**

(n = 110)

Variable	Frequency	Percentage
<b>Non- alcoholic diabetic (Control)</b>	70	63.6%
<b>Alcoholic        diabetic (Case)</b>	40	36.4%
<b>AGE GROUP</b>		
<b>45-55 years'</b>	<b>63</b>	<b>(57.3%)</b>
<b>56-65 years</b>	<b>47</b>	<b>(42.5%).</b>
<b>Duration of alcohol use</b>		
<b>Up to 5 years</b>	14	12.7%
<b>6 to 10 years</b>	17	15.5%
<b>11 to 20 years</b>	9	8.2%
<b>Non-alcoholic</b>	70	63.6%



Frequency of times for Alcohol use		
Once a week	27	24.5%
Twice a week	7	6.4%
More than twice a week	6	5.5%
Non-alcoholic	70	63.6%

*Table 2: Distribution of study participants according to status of normal serum magnesium and hypomagnesemia levels and severity of magnesium level in diabetic alcoholic (case) and diabetic non-alcoholic (control) patients*

(n = 110)

Status of participants	Serum magnesium level		Total	P-Value
	Normal serum Magnesium level	Hypomagnesemia		
Non-Alcoholic (control)	58(82.9%)	12(17.1%)	70(100.0%)	0.002
Alcoholic (case)	22(55.0%)	18(45.0%)	40(100.0%)	
Severity of magnesium level				
	Normal (1.8 to 2.2 mg/dl)	Mild (1.5 to 1.8 mg/dl)	Moderate (1 to 1.4 mg/dl)	Severe (<1 mg/dl)
Non-alcoholic (control)	60(85.7%)	5(7.1%)	2(2.9%)	3(4.3%)
Alcoholic (case)	60(85.7%)	5(7.1%)	2(2.9%)	3(4.3%)

**Table 3: Distribution of study participants according to drinking frequency of alcohol use HbA1C and duration of alcohol use in normal magnesium and hypo magnesium levels**

(n = 110)

Drinking Frequency	Serum Magnesium level		Total	P-Value
	Normal serum Magnesium level	Hypomagnesemia		
Once a week	18(66.7%)	9(33.3%)	27(100.0%)	0.001
Twice a week	2(28.6%)	5(71.4%)	7(100.0%)	
More than twice a week	2(33.3%)	4(66.7%)	6(100.0%)	
Non-Alcoholic	58(82.9%)	12(17.1%)	70(100.0%)	
<b>HbA1C</b>				
6.7 to 7.7	76(78.4%)	21(21.6%)	97(82.2%)	0.001
7.8 to 8.7	4(36.4%)	7(63.6%)	11(10.0%)	
Above 8.7	0	2(100.0%)	2(1.8%)	
<b>Duration of alcohol use</b>				
Up to 5 years	11(78.6%)	3(21.4%)	14(100%)	0.001
6 to 10 years	9(52.9%)	8(47.1%)	17(100%)	
11 to 20 years	2(22.2%)	7(77.8%)	9(100%)	
Non-alcoholic	58(82.9%)	12(17.1%)	70(100%)	

**DISCUSSION**

Diabetes mellitus is one of the most common non-communicable diseases throughout the world. as the population is increasing and socio-economic conditions are deteriorating, incidence of diabetes mellitus is increasing. There are various types of diabetes mellitus including type 1 and type 2 diabetes and these types are produced by different etiologies.

The prevalence of hypomagnesemia among chronic alcoholics was estimated at ~30% (Liamis, 2000; Swaminathan, 2003; Baj et al., 2020) or higher. (Grochowski et al., 2019; Maguire et al., 2022) However, a study of 60 alcoholic men could not confirm a statistically significant reduction in Mg levels, with Mg levels reported to be within the normal range irrespective of the duration of alcohol consumption and abstinence. (Ayirimeethal et al., 2019) In a study of 129 alcohol-dependent individuals, 84 had normal, 37 had decreased, and 8 had excessive blood magnesium concentrations. (Stasiukinene, Pilvinis and Reingardene, 2004) According to a recent systematic review, (Flora O. Vanoni *et al.*, 2021) no study has thus far investigated the management of Mg depletion in chronic alcohol-use disorders.

Research is going throughout the world to diagnose the factors which are causing this disease to spread so rapidly. The present study was designed to detect the role of magnesium and alcohol in producing diabetes mellitus. this was a retrospective comparative type of study. To conduct this study only male participants were selected because in Pakistani society female are reluctant to participate in a study which is concerned about alcoholism. participants were grouped according to age, duration of alcohol use and serum magnesium level. A strong relationship was found between diabetes mellitus and Hypomagnesemia. It was also noted that this association become stronger when the alcohol factor is included.

The result of this study was compared to the result of studies worldwide. The study conducted by Stefanie N in in 2021 concluded that there is a reduce chances of diabetes mellitus in patients who are regular drinkers. This study is in contrast to present study which describe a higher chances of developing diabetes mellitus. The difference in result is most probably because the study of Stefanie N was conducted on female patients only who were suffering from gestational diabetes mellitus. Patrice A in 2013 studied relationship between alcoholism and glycemic control. The result was similar to present study, which also deduced the same result. The most probable reason behind the phenomena is that drinkers do not pay attention to treatment and prevention. In a study conducted by wanders F in 2020 it was discovered that there is a close link between diabetes mellitus and Hypomagnesemia. He detected that 9% of the participants suffering from diabetes mellitus were suffering from Hypomagnesemia. These results are very similar to the present study, which discovered Hypomagnesemia in 12% of participants suffering from diabetes mellitus, and 18% participants who were alcohol drinkers. The major difference was in alcohol drinkers, which also signifies the additional Burdon of Hypomagnesemia, produced due to the alcohol. The present study concludes that severity of diabetes mellitus and poor control of glycemic level also increases the level of Hypomagnesemia. It is more common and more severe in patients who are controlling their glycemic level than those who were controlling it to normal or nearby normal range. These results were in quite in accordance to the study conducted by Ruchi Pala Diya in 2021. The severity of poor glycemic control leads to more drastic Hypomagnesemia because of urinary

tract infection and loss of magnesium through the urine.

### ***CONCLUSION***

It was concluded after the study that there is a direct association between diabetes mellitus and low serum magnesium level and these chances become far greater in patients who are regular user of alcohol. The diabetic patients who were suffering from diabetes mellitus showed greater degree of Hypomnesia. The incidence of Hypomagnesemia increases as there is increase in duration and amount of alcohol increase

### ***RECOMMENDATIONS***

After the study, the recommendation will be sent to relevant authorities and health authorities about the result of the study. It was concluded that either Hypomagnesemia is produced by diabetes mellitus or it leads to development of diabetes mellitus. It is advised that during the treatment of diabetes mellitus magnesium supplements should be given.

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