



## EVALUATION OF SERUM MAGNESIUM LEVEL IN PREDIABETIC SUBJECTS IN INDIAN POPULATION

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### ABSTRACT

Diabetes mellitus (DM), commonly referred to as diabetes, is a group of metabolic disorders in which there are high blood sugar levels over a prolonged period. Pre-diabetes is the precursor stage before diabetes mellitus in which not all of the symptoms required to diagnose diabetes are present, but blood sugar is abnormally high. This stage is often referred to as the "grey area". Hypomagnesaemia may be considered as one of the aggravating factors for insulin resistance. The kidneys lose their ability to maintain magnesium levels during periods of uncontrolled hyperglycaemia which may then result in lower blood levels of magnesium. Our study was aimed to assess and compare the serum magnesium level in pre-diabetic subjects and healthy controls. The present study is a case control study, conducted on 150 pre-diabetic subjects. Subjects were selected from MOPD of Jawahar Lal Nehru Medical College and Associated Group of Hospitals, Ajmer. Age and sex matched healthy controls (n = 50) were selected from MOPD of Jawahar Lal Nehru Medical College and Associated Group of Hospitals, Ajmer. The present study is approved by Institutional Ethical Committee. Serum magnesium level was found to be lower in pre-diabetic subjects. Serum magnesium can be used as a biomarker for the early detection of pre-diabetic subjects in the general population to prevent the morbidity and mortality which are associated with diabetes mellitus. Therefore, in these pre-diabetic subjects if hypomagnesaemia is detected, magnesium supplementation can be a useful for improving the metabolic status in these subjects.

**KEYWORDS:** Diabetes Mellitus (DM), Cardiovascular Disease (CVD), Magnesium (Mg), Glucose Tolerance Test (GTT), Impaired Fasting Glucose (IFG), Body Mass Index (BMI)

Diabetes mellitus is now considered a giant killer disease of the 21<sup>st</sup> century with its vicious prongs in the South-East Asian countries, specially India, which is rightly said to be the "Diabetes Capital" of the world (Wild *et al.*, 2004). In Indian population, 61.3 million people had diabetes in 2011, which is expected to reach 101.2 million by 2030 (International Diabetes Federation) now placing India at second position in world diabetic prevalence (Anjana *et al.*, 2011). Diabetes mellitus (DM), commonly referred to as diabetes, is a group of metabolic disorders in which there are high blood sugar levels over a prolonged period ("About diabetes", WHO 2014). Pre-diabetes is a component of the metabolic syndrome and is characterized by elevated blood sugar levels that fall below the threshold to diagnose diabetes mellitus. It usually does not cause symptoms but people with pre-diabetes often have obesity (especially abdominal or visceral obesity), dyslipidemia and hypertension (American Diabetes Association, 2017). Pre-diabetes is the precursor stage before diabetes mellitus in which not all of the symptoms required to diagnose diabetes are present, but blood sugar is abnormally high. This stage is often referred to as the "grey area" ("Prediabetes"). Pre-diabetes typically has no distinct signs or symptoms

except the sole sign of high blood sugar. Patients should monitor for signs and symptoms of type 2 diabetes mellitus such as increased thirst, increased urination, and feeling tired ("Diabetes: 'Prediabetes'", 2009).

Impaired fasting glycemia or impaired fasting glucose (IFG) refers to a condition in which the fasting blood glucose is elevated above what is considered normal levels but is not high enough to be classified as diabetes mellitus. It is considered a pre-diabetic state, associated with insulin resistance and increased risk of cardiovascular pathology, although of lesser risk than impaired glucose tolerance (IGT). IFG sometimes progresses to type 2 diabetes mellitus (Nichols *et al.*, 2007). Fasting blood glucose levels are in a continuum within a given population, with higher fasting glucose levels corresponding to a higher risk for complications caused by the high glucose levels. Some patients with impaired fasting glucose also may be diagnosed with impaired glucose tolerance, but many have normal responses to a glucose tolerance test. Fasting glucose is helpful in identifying pre-diabetes when positive but has a risk of false negatives.

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Approximately 11% of people with pre-diabetes who receive no treatment or intervention will develop type 2 diabetes every year (Knowler *et al.*, 2002). A recent study reported that 77.2 million populations in India fall in pre-diabetic group or the risk group (Anjana *et al.*, 2011). Magnesium plays an important role in carbohydrate metabolism. It may influence the release and activity of insulin, the hormone that helps to control blood glucose levels. Low blood levels of magnesium are frequently seen in individuals with type-2 diabetes (Kobrin and Goldfarb, 1990) (Mishra *et al.*, 2012). Mg is found in many foods, especially whole grains, legumes, green leafy vegetables and nuts. According to previous researches, Mg intake may be negatively correlated with several chronic diseases, such as metabolic syndrome, diabetes, hypertension and cardiovascular disease (Delva, 2003) (Elmarakby and Sullivan, 2012) (Mima, 2013) (Schulze *et al.*, 2007) (Touyz, 2003).

## MATERIALS AND METHODS

The present study is a case control study, conducted on 150 pre-diabetic subjects. Pre-diabetic Subjects were selected from MOPD of Jawaharlal Nehru Medical College and Associated Group of Hospitals, Ajmer. Age and sex matched healthy controls (n = 50) were selected from MOPD of Jawaharlal Nehru Medical College and Associated Group of Hospitals, Ajmer. The results of pre-diabetic subjects were compared with healthy controls (n=50). The present study is approved by Institutional Ethical Committee.

### For Control Group

Healthy individuals age and sex matched with Fasting serum glucose level <110mg/dl & two hour serum glucose level <140mg/dl.

### Inclusion Criteria for Study Group

1. Fasting serum glucose level 110 – 125mg/dl (IFG).
2. Two hour serum glucose level after ingestion 75g of glucose 140 to 199 mg/dl.

### Exclusion Criteria for Study Group

1. Fasting serum glucose greater than or equal to 126 mg/dl.
2. Two hour serum glucose level greater than or equal to 200 mg/dl during an oral glucose tolerance test.
3. Patients with classic symptoms of hyperglycemia, random serum glucose greater than or equal to 200 mg/dl.

4. Patients diabetes mellitus, hypothyroidism, cardiovascular disease, cerebrovascular disease, renal disease, smokers and alcoholics.

Blood samples were collected after an overnight fast (12-14hrs) and after two hour post prandial under aseptic conditions from all the study participants. All samples were centrifuged and analyzed for blood sugar and serum magnesium. The blood sugar was measured by enzymatic GOD-POD end point method. Magnesium was measured by Colorimetric Xylidyl blue method.

## STATISTICAL ANALYSIS

All data were analyzed by SPSS-13 version. P< 0.01 were considered as significant.

## RESULTS

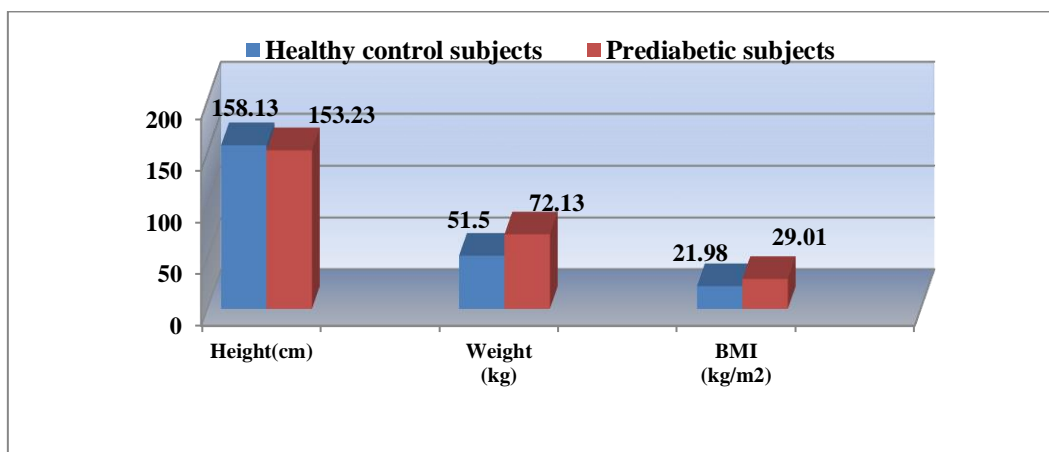
The study included 150 pre-diabetic subjects and 50 healthy control subjects. The results are summarized in tables and figures. Among the 150 pre-diabetic subjects, 40 (26.66%) were males and 110 (73.33%) were females. Out of the 50 healthy subjects, 15 (30%) were males and 35 (70%) were females. There was no significant difference in the sex distribution between the pre-diabetic subjects and healthy controls. The sex distribution of the study population is depicted in table 1. The physical characteristics and anthropometric measures were presented in table 1. The difference between both groups was found that the Mean±SD of weight and the BMI were more in pre-diabetic subjects than controls and difference was statistically significant (p<0.001) while the mean age and sex matched were not significant (p>0.005), it also shows (table 1 & figure 1) that the mean height was less than controls and the difference was significant. The table 2 & figure 2 show the Mean±SD of blood sugar and serum magnesium level. The table 2 & figure 2 show Mean±SD of Fasting Serum Glucose level (116.5±4.61 v/s 98.87±9.8) mg/dl and two hour Post Prandial Serum Glucose level (165.26±16.2 v/s 126.06±15.6) mg/dl in pre-diabetic subjects compared to healthy controls were significantly (P<0.0001) raised. Also table 2 & figure 2 shows that the Mean ± SD of Serum Magnesium level was less in pre-diabetic subjects (1.72±0.09mg/dl) than healthy controls (2.19±0.24 mg/dl) and difference was statistically highly significant (P<0.0001). Pre-diabetic subjects have lower serum magnesium levels (<1.9 mg/dl).

**Table 1: Anthropometric Parameters of Healthy Control Subjects V/S Pre-diabetic Subjects**

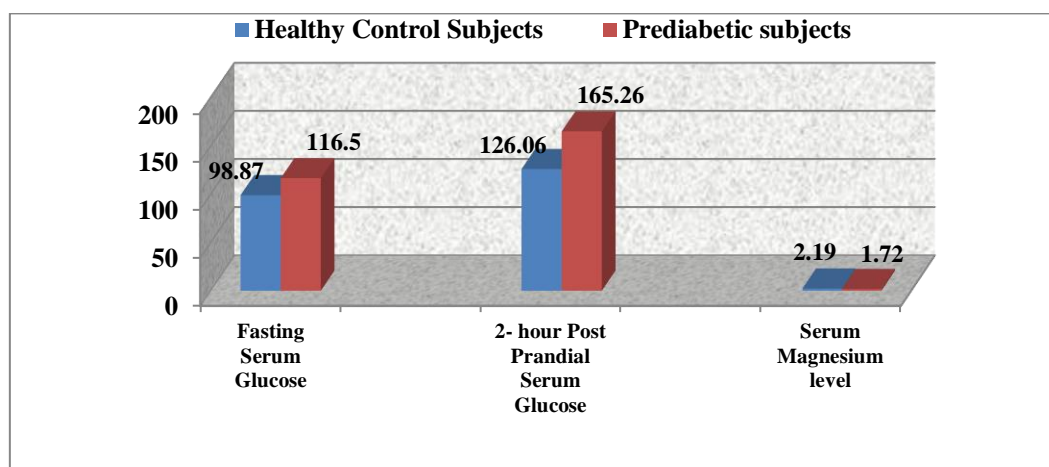
Anthropometric Parameters	Healthy control subjects (n=50) Mean ± SD	Pre-diabetic subjects (n=150) Mean ± SD	P-Value
Age(yr.)	48.51±8.44	49.42±9.01	>0.005
Sex distribution			
Female (%)	35 (70%)	110 (73.33%)	(NS)
Male (%)	15 (30%)	40 (26.66%)	(NS)
Height(cm)	158.13±0.05	153.23±4.4	<0.001(HS)
Weight (kg)	51.5±4.9	72.13±4.5	<0.001(HS)
BMI (kg/m <sup>2</sup> )	21.98±5.03	29.01±3.01	<0.001(HS)

**Table 2: Biochemical Parameters of Healthy Control Subjects v/s Pre-diabetic Subjects**

Biochemical Parameters	Healthy Control Subjects (n=50) Mean ±SD	Pre-diabetic subjects (n=150) Mean ±SD	P-Value
Fasting Serum Glucose (mg/dl)	98.87±9.8	116.5±4.61	<0.0001
2- hour Post Prandial Serum Glucose (mg/dl)	126.06±15.6	165.26±16.2	<0.0001
Serum Magnesium level(mg/dl)	2.19±0.24	1.72±0.09	<0.0001



**Figure 1: Comparison of Anthropometric Parameters of Healthy Control Subjects V/S Pre-diabetic Subjects**



**Figure 2: Comparison of Biochemical Parameters of Healthy Control Subjects V/S Pre-diabetic Subjects**

## DISCUSSION

Diabetes is a group of metabolic disease characterized by hyperglycemia and metabolic changes which could be the result of insufficiency or defect in insulin secretion, insulin action or both (Castell, 2010) (Diabetes Care, 2013). The risk factor for pre-diabetes and diabetes are stress and depression, (Al-Amer et al., 2011) (Rotella and Mannucci, 2013) chronic underlying disease and inflammation, (Delva, 2003) (Mima, 2013) obesity, low physical activity, sedentary lifestyle and environmental factors (Neeland *et al.*, 2012) (Van Dam *et al.*, 2002). Pre-diabetes is a condition in which the blood glucose level is above normal but below the diagnostic threshold for diabetes mellitus (Alberti et al., 2006).

In the present study, the BMI were more in pre-diabetic subjects than controls and difference was statistically significant ( $p < 0.001$ ). Our findings are in concordance with A. Nwafor et al. (2015) which also showed that BMI was significantly associated with high blood glucose level (Nwafor *et al.*, 2015).

In the present study we have observed that the level of fasting serum glucose level was elevated in pre-diabetic subjects as compared to the healthy control subjects. It is concordance with the previous study which also states that mean value of fasting serum glucose level was significantly ( $P < 0.0001$ ) higher in pre-diabetic subjects compared to healthy control subjects (Taif et al., 2011).

Mean activity of two hour post prandial serum glucose level was significantly higher in pre-diabetic subjects than healthy control subjects. Our study are in agreement with Mitra *et al.* (2017) who also found a statistically significant increase in two hour post prandial serum glucose level in prediabetics.

In the present study we have observed that the level of serum magnesium was lower in pre-diabetic subjects as compared to the healthy control subjects. It is in concordance with the previous studies which also states that the serum magnesium was lower in pre-diabetic subjects (He *et al.*, 2006) ("Prediabetes").

Our finding are in agreement with previous studies which state that the mean activity of serum magnesium was significantly lower in pre-diabetic subjects compared to the healthy control subjects ( $p < 0.0001$ ) It has been suggested that magnesium regulates cellular glucose metabolism directly because it serves as an important co-factor for various enzymes and acts as a second messenger for insulin (Aikawa, 1981)

(Paolisso *et al.*, 1992). The kidneys lose their ability to maintain magnesium levels during periods of uncontrolled hyperglycaemia which may then result in lower blood levels of magnesium (Hua *et al.*, 1995).

## CONCLUSION

Serum magnesium level was found to be lower in pre-diabetic subjects and can be used as a biomarker for the early detection of pre-diabetic subjects in the general population to prevent the morbidity and mortality which are associated with diabetes mellitus. Therefore, in pre-diabetic subjects if hypomagnesaemia is detected, magnesium supplementation can be a useful for improving the metabolic status in these subjects.

## REFERENCES

- American Diabetes Association (January 2017). "2. Classification and diagnosis of diabetes". *Diabetes Care*. 40 (Suppl 1): S11–S24.
- "About diabetes". World Health Organization. Archived from the original on 31 March 2014. Retrieved 4 April 2014.
- Alberti K.G., Zimmet P. and Shaw J., 2006. Metabolic syndrome-a world-wide definition. A consensus statement from the international diabetes federation. *Diabet. Med.*, **23**: 469-80.
- Anjana R.M., Pradeepa R. and Deepa M., 2011. Prevalence of diabetes and prediabetes (impaired fasting glucose and/or impaired glucose tolerance) in urban and rural India: phase I results of the Indian Council of Medical Research-India Diabetes (ICMR-INDIAB) study: *Diabetologia*, **54**(12): 3022-7.
- Al-Amer R.M., Sobeh M.M., Zayed A.A. and Al-Domi H.A., 2011. Depression among adults with diabetes in Jordan: risk factors and relationship to blood sugar control. *J. Diabetes Complications*, **25**(4): 247-52.
- Aikawa J.K., 1981. *Magnesium: Its Biological Significance*. Boca Raton, FL: CRC Press.
- Chi P.W., Cheng T.Y.D., Shan P.T., Hui L.H. and Shu L.W., 2005. Increased mortality risks of pre-diabetes (impaired fasting glucose) in Taiwan. *Diabetes Care*, **28**: 2756-61.
- Castell C., 2010. Epidemiology and classification for diabetes mellitus. *Rev. Enferm.*, **33**(2): 9-15.
- "Diabetes: 'Prediabetes'". Mayo Clinic. Retrieved January 27, 2009.

- Diagnosis and classification of diabetes mellitus. *Diabetes Care*. 2013 Jan; 36 Suppl 1:S67-74.
- Delva P., 2003. Magnesium and coronary heart disease. *Mol Aspects Med.*, **24**(1-3): 63–78.
- Elmarakby A.A. and Sullivan J.C., 2012. Relationship between oxidative stress and inflammatory cytokines in diabetic nephropathy. *Cardiovascular Ther.*, **30**(1): 49-59.
- Hua H., Gonzales J. and Rude R.K., 1995. Magnesium transport induced ex vivo by a pharmacological dose of insulin is impaired in non-insulin-dependent diabetes mellitus. *Magnes Res.*, **8**(4): 359-66.
- He K., Liu K., Daviglius M.L., Morris S.J., Loria C.M. and Van Horn L., 2006. Magnesium intake and incidence of metabolic syndrome among young adults. *Circulation*, **113**(13): 1675-82.
- Kobrin S.M. and Goldfarb S., 1990. Magnesium Deficiency. *Semin Nephrol*, **10**: 525-35.
- Knowler W.C., Barrett-Conner E. and Fowler S.E., 2002. Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N. Engl J. Med.*, **346**: 393-403.
- Maier J.A., 2003. Low magnesium and atherosclerosis: an evidence-based link. *Mol Aspects Med.*, **24**(1-3): 137-46.
- Mima A., 2013. Inflammation and oxidative stress in diabetic nephropathy: new insights on its inhibition as new therapeutic targets. *J. Diabetes Res.*, **2013**: 248563.
- Mitra J.K., Mitra R. and Marandi S., 2017. Study of lipid profile in prediabetes in Jharkhand. *International Journal of Current Research*, **9**(5): 51420-51422.
- Mishra S., Padmanaban P., Deepti G.N., Sarkar G., Sumathi S. and Toora B.D., 2012. Serum magnesium and dyslipidemia in type-2 diabetes mellitus. *Biomedical Research*, **23**(2): 295-300.
- Nichols G.A., Hillier T.A. and Brown J.B., 2007. "Progression from newly acquired impaired fasting glucose to type 2 diabetes". *Diabetes Care*, **30**(2): 228-33.
- Neeland I.J., Turer A.T., Ayers C.R., Powell-Wiley T.M., Vega G.L. and Farzaneh-Far R., 2012. Dysfunctional adiposity and the risk of prediabetes and type 2 diabetes in obese adults. *J.A.M.A.*, **308**(11): 1150-9.
- Nwafor A., Mmom F.C., Obia1 O., Obiandu C., Hart V.O. and Chinko B.C., 2015. Relationship between Blood Pressure, Blood Glucose and Body Mass Index and Coexisting Prehypertension and Prediabetes among Rural Adults in Niger Delta Region, Nigeria. *B.J.M.M.R.*, **9**(7): 1-12.
- Paolisso G., Sgambato S., Gambardella A., Pizza G., Tesaro P. and Varricchio M., 1992. Daily magnesium supplements improve glucose handling in elderly subjects. *Am. J. Clin. Nutr.*, **55**(6): 1161-1167.
- "Prediabetes". *Health cure plus*.
- Rotella F. and Mannucci E., 2013. Diabetes mellitus as a risk factor for depression. A meta-analysis of longitudinal studies. *Diabetes Res. Clin. Pract.*, **99**(2): 98-104.
- Schulze M.B., Schulz M., Heidemann C., Schienkiewitz A., Hoffmann K. and Boeing H., 2007. Fiber and magnesium intake and incidence of type 2 diabetes: a prospective study and meta-analysis. *Arch Intern Med.*, **167**(9): 956-65.
- Touyz R.M., 2003. Role of magnesium in the pathogenesis of hypertension. *Mol Aspects Med.*, **24**(1-3): 107-36.
- Taif K. Hamdan, Abbas M.R. Al-Mussawi, Ghassan AA Al-Shamma, 2011. Hypomagnesemia and Obesity in Relation to Insulin Resistance and Glycemic Control in Type 2 Diabetic Patients. *Iraqi J. Med. Sci.*, **9**(2): 108-113.
- Van Dam R.M., Rimm E.B., Willett W.C., Stampfer M.J. and Hu F.B., 2002. Dietary patterns and risk for type 2 diabetes mellitus in U.S. men. *Ann Intern Med.*, **136**(3): 201-9.
- Wild S., Roglic G., Green A., Sicree R. and King H., 2004. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. *Diabetes Care*, **27**(5): 1047.