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Study of Serum Zinc Levels in Newly Detected type 2 Diabetes Mellitus and it's Correlation with HbA1c

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ABSTRACT

Background: Hyperglycemia is considered as a primary culprit of diabetic complications and is associated with increased metabolic processes and oxidative stress. Both micro vascular and macro vascular complications in diabetes are related to oxidative stress and zinc has antioxidant properties delaying the diabetic complications

Objective: To study the levels of serum zinc and HbA1c in newly detected type 2 diabetes mellitus, To correlate between serum zinc levels and HbA1c in predicting the importance of zinc levels for glycemic control.

Methods: This Cross sectional study was conducted among patients visiting the opd/or admitted in Department of General Medicine, KR Hospital, MMCRI, Mysore, Mysore. Study period was one and a half year from February 2021 to June 2022.

Results: Out of the 105 patients mean age was 49.57yrs with a range of 32 yrs to 70 yrs. Out of 105 patients 59 were females with 46 being males. Approximately 50% of the females were in the age group of 41 to 50 yrs and 18(39.1%) males were in the age range of 51 to 60 yr. Overall mean FBS was 146.99 ± 9.761, mean PPBS was 224.24 ± 15.724, mean RBS was 170.37 ± 14.241, mean HbA1C was 9.34 ± 1.48 and mean Zinc levels was 102.01 ± 75.56. In females, Mean FBS was 146.31 ± 8.518, mean PPBS was 225.12 ± 15.456, mean RBS was 170.59 ± 15.112, mean HbA1C was 9.4 ± 1.5 and mean Zinc levels was 114.6 ± 88. In males, Mean FBS was 147.87 ± 11.192, mean PPBS was 223.11 ± 16.161, mean RBS was 170.09 ± 13.197, mean HbA1C was 9.2 ± 1.5 and mean Zinc levels was 85.8 ± 52.3. Mean Zinc levels were higher for subjects having HbA1c between 8.1 to 10- 109.47 ± 70.90 followed by subjects having HbA1C > 10 - 95.78 ± 103.59.

Conclusion: Very weak, positive and non-significant correlation was seen between PPBS and Zinc (r = 0.076, p=0.440), RBS and Zinc (r=0.089, p=0.367). Hence no significant relation was drawn from the study and in the present study levels of serum zinc didn't correlate with poor control of diabetes mellitus in terms of HbA1c.

Keywords: Diabetes Mellitus, HbA1c, Zinc,Type 2 DM, Mysore

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INTRODUCTION

Diabetes mellitus (DM) refers to a group of metabolic disorders which is characterized by hyperglycemia. For the treatment of this condition, ancient Egyptian physicians were advocating the use of wheat grains, fruit. [1,2] It is one of the diseases described since ancient period in Egypt. At the equivalent time Physicians in Republic of India classified the disease as a separate entity and termed it as Madhumeha or honey urine. [3] During Roman empire DM was considered as rare illness. It was initially seen in upper socioeconomic people due to their life style and food habits. Galen referred the illness as diarrhea urinosa "diarrhea of the urine".

Type 1 and Type 2 diabetes were identified as distinct conditions first time by the Indian physicians Sushruta and Charaka in 400-500 AD .Rhey represented Type 1DM associated with youth and Type 2 DM with being overweight. In 1670, Thomas Willis in Oxford noticed the sweet taste of urine of patients with diabetes. Thomas Cawley, in 1788, was the first to suggest the link between the pancreas and diabetes after he observed that people with pancreatic injury developed diabetes.[4] In end of 1700 AD the term "mellitus" or "from honey" was added to Diabetes to differentiate from Diabetes Insipidus by the Briton John Rolle.

Protamine–Zinc insulin, a long-acting insulin, was introduced in the 1930s; Neutral Protamine Hagedorn insulin(NPH) was introduced in the 1940s; and Lente series of insulin in the 1950s.[5]

The ground work for the production of large quantities of human insulin was laid by Frederick Sanger, who published the structural formula of bovine insulin in 1955.[6] Dorothy Hodgkin (1910–1994) described the three-dimensional structure of porcine insulin in 1969 using X-ray crystallography.[7]

In 1978, Genentech, Inc. and City of Hope National Medical Center, a private research institution in Duarte, California, announced the successful laboratory production of human insulin using recombinant DNA technology. This was achieved by a team of scientists led by Robert Crea, Keichi Itakura, David Goeddel, Dennis Kleid and Arthur Riggs. Insulin thus became the first genetically manufactured drug to be approved by the FDA.

In July 1996, the FDA approved the first recombinant DNA human insulin analog, the insulin lispro. In January 2006, FDA approved inhaled form of insulin marketed under the name of Exubera. This was the first non injectable form of insulin available to patients with diabetes

Ninety percent of those with diabetes have type-2 diabetes, characterized by insulin resistance, hyper insulinemia, B-cell dysfunction and subsequent B–cell failure. Insulin, is stored as a hexamer containing two Zinc ions in B-cells of the pancreas and released into the portal venous system at the time of B-cells de-granulation.

The Zinc ions which are co secreted with insulin suppress inherent amyloidogenic properties of monomeric insulin. Zinc plays a key role in the synthesis and action of insulin, both physiologically and in the pathological state of diabetes.

Hence this study was conducted To study the levels of serum zinc and HbA1c in newly detected type 2 diabetes mellitus, To correlate between serum zinc levels and HbA1c in predicting the importance of zinc levels for glycemic control.

MATERIALS AND METHODS

This Cross sectional study was conducted among patients visiting the opd/or admitted in Department of General Medicine, KR Hospital, MMCRI, Mysore, Mysore. Secondary sources of information including published articles, journals, books and related websites. Study period was one and a half year from February 2021 to June 2022.

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Sample Size: 105

In the present study sample size was calculated using formula- n=Z21-α/2pq /d2

- where Z1-α/2=two failed probability for 95%CI =1.96
- P=10.9%
- Q=[100-P]
- d=6% [absolute allowable error]
- n=[1.96]2[10.9][89.1]/62 =103.5 [approx -105]
- thus the sample size required for study is 105

Inclusion Criteria

1. Age more than 18 years
2. Patients with newly detected type 2 DM

Exclusion Criteria

1. Pregnant and lactating women
2. Patient complaining of chronic diarrhea, on hormonal therapy, on drugs effecting serum zinc levels[proton pump inhibitors,chlroquine,H2 blockers]

Patients with iron deficiency anemia

3. Patients with major systemic illness [chronic liver disease, chronic pancreatitis, IBD] including hemoglobinopathies
4. On zinc supplements
5.Type 1 diabetes mellitus patients

Methodology

Purpose of study will be explained to the patient and attenders. Written informed consent will be taken from the subjects. Relevant history and clinical examination will be done.

Blood samples for FBS, PPBS, RBS, HBA1C, Serum ZINC, shall be sent.

Statistical Analysis

SPSS (Statistical Package for Social Sciences) version 20. (IBM SPASS statistics [IBM corp. released 2011] was used to perform the statistical analysis. Data was entered in the excel spread sheet. Descriptive statistics of the explanatory and outcome variables were calculated by mean, Standard deviation for quantitative variables, frequency and proportions for qualitative variables. Inferential statistics like Chi-square test was applied for qualitative variables. Pearson's correlation test was applied to correlate the glucose levels with Zinc based on gender. The level of significance is set at 5%.

RESULT

Mean age of the subjects is 49.57 ± 8.068 with minimum age of 32 yrs and maximum age of 70 yrs. Out of 105 subjects, majority of the subjects were in the age range of 41 to 50 yrs- 47(44.8%) followed by 34(32.4%) subjects in the age range of 51 to 60 yrs, 14(13.3%) subjects in the age group of 32 to 40 yrs and 10(9.5%) subjects aged > 60 yrs. Percentage of females were slightly higher 59(56.2%) as compared to males- 46(43.8%).

Mean FBS was 146.99 ± 9.761, Mean PPBS was 224.24 ± 15.724, Mean RBS was 170.37 ± 14.241, Mean HbA1C was 9.34 ± 1.48 , Mean Zinc levels was 102.01 ± 75.56.

Table 1: Mean Values

	N	Minimum	Maximum	Mean	SD
	105	130	177	146.99	9.761
PPBS(mg/dl)	105	200	298	224.24	15.724

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RBS(mg/dl)	105	145	213	170.37	14.241
HB1AC(mg/dl)	105	6.80	12.80	9.34	1.48
Zinc level	105	22.00	419.00	102.01	75.56

Approximately 50% of the females were in the age group of 41 to 50 yrs and 18(39.1%) males were in the age range of 51 to 60 yrs.

Pearson's correlation test showed very weak, negative and non-significant correlation between FBS and Zinc (r = -0.072, p=0.466), HbA1C and Zinc (r = -0.048, p=0.624). Very weak, positive and non -significant correlation was seen between PPBS and Zinc (r = 0.076, p=0.440), RBS and Zinc(r=0.089, p=0.367).

Table 2: Pearson's Correlation (Overall) Between Zinc Levels and Glucose Levels

FBS(mg/dl)	r value	-.072
	p value	.466
PPBS(mg/dl)	r value	.076
	p value	.440
RBS(mg/dl)	r value	.089
	p value	.367
HB1AC(mg/dl)	r value	-.048
	p value	.624

In females, Mean FBS was 146.31 ± 8.518, mean PPBS was 225.12 ± 15.456, mean RBS was 170.59 ± 15.112, mean HbA1C was 9.4 ± 1.5 and mean Zinc levels was 114.6 ± 88.

In males, Mean FBS was 147.87 ± 11.192, mean PPBS was 223.11 ± 16.161, mean RBS was 170.09 ± 13.197, mean HbA1C was 9.2 ± 1.5 and mean Zinc levels was 85.8 ± 52.3.

Table 3: Mean Values Based On Gender

Gender		N	Minimum	Maximum	Mean	SD
Females	FBS(mg/dl)	59	130	176	146.31	8.518
	PPBS(mg/dl)	59	200	278	225.12	15.456
	RBS(mg/dl)	59	145	202	170.59	15.112
	HB1AC(mg/dl)	59	7.3	12.7	9.4	1.5
	Zinc level	59	22.0	419.0	114.6	88.0
Males	FBS(mg/dl)	46	130	177	147.87	11.192
	PPBS(mg/dl)	46	201	298	223.11	16.161
	RBS(mg/dl)	46	150	213	170.09	13.197
	HB1AC(mg/dl)	46	6.8	12.8	9.2	1.5
	Zinc level	46	22.0	300.0	85.8	52.3

In females, Pearson's correlation test showed very weak, positive and non-significant correlation between FBS and Zinc (r = 0.031, p=0.814), HbA1C and Zinc (r = 0.055, p=0.681). PPBS and Zinc (r= 0.187, p=0.156); weak, positive and statistically significant correlation was seen between RBS and Zinc (r = 0.27, p=0.039).

Whereas in males, Pearson's correlation test showed weak, negative and non-significant correlation between FBS and Zinc (r = -0.217, p = 0. 147); weak, negative and significant correlation between RBS and Zinc (r = -0.362, p=0.013), HbA1C and Zinc (r= -0.33, p=0.025);

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very weak, negative and non-significant correlation between PPBS and Zinc (r= -0.180, p=0.232).

TABLE 4: Pearson's Correlation Between Zinc Levels And Glucose Levels Based On Gender

Gender			ZINC
Females (59)	FBS [mg/dl]	r value	.031
		p value	.814
	PPBS [mg/dl]	r value	.187
		p value	.156
	RBS [mg/dl]	r value	.270
		p value	.039*
	HBA1C	r value	.055
		p value	.681
Males (46)	FBS [mg/dl]	r value	-.217
		p value	.147
	PPBS [mg/dl]	r value	-.180
		p value	.232
	RBS [mg/dl]	r value	-.362
		p value	.013*
	HBA1C	r value	-.330
		p value	.025*

*significant

Mean Zinc values were higher for age group 51 to 60 yrs-118.40 ± 79.05 followed by zinc levels in age group of 32 to 40 yrs- 107.23 ± 96.42, 41 to 50 yrs- 91.31 ± 62.18 and > 60 yrs- 89.26 ± 89.65.

Table 5: Mean Zinc Levels Based on Age Groups

Age groups	N	Minimum	Maximum	Mean	S.D
32 to 40 yrs	14	22.00	419.00	107.23	96.42
41 to 50 yrs	47	22.00	401.00	91.31	62.18
51 to 60 yrs	34	26.90	374.20	118.40	79.05
> 60 yrs	10	25.00	324.00	89.26	89.65

Mean Zinc levels were higher for subjects having HbA1c between 8.1 to 10- 109.47 ± 70.90 followed by subjects having HbA1C > 10 - 95.78 ± 103.59.

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Table 6: Mean Zinc Levels Based on Hba1c

HbA1C	N	Minimum	Maximum	Mean	S.D
	23	25.00	199.00	90.89	43.71
8.1 to 10	56	25.00	419.00	109.47	70.90
> 10	26	22.00	01.00	95.78	103.59

DISCUSSION

Overall mean FBS was 146.99 ± 9.761, mean PPBS was 224.24 ± 15.724, mean RBS was 170.37 ± 14.241, mean HbA1C was 9.34 ± 1.48 and mean Zinc levels was 102.01 ± 75.56.

In females, Mean FBS was 146.31 ± 8.518, mean PPBS was 225.12 ± 15.456, mean RBS was 170.59 ± 15.112, mean HbA1C was 9.4 ± 1.5 and mean Zinc levels was 114.6 ± 88.

In males, Mean FBS was 147.87 ± 11.192, mean PPBS was 223.11 ± 16.161, mean RBS was 170.09 ± 13.197, mean HbA1C was 9.2 ± 1.5 and mean Zinc levels was 85.8 ± 52.3.

A Positive correlation was found between RBS and zinc in females

Weak negative and significant relation between RBS and Zinc and HbA1c and Zinc in males was found

Mean Zinc levels were higher for subjects having HbA1c between 8.1 to 10- 109.47 ± 70.90 followed by subjects having HbA1C > 10 - 95.78 ± 103.59.

	CURRENT STUDY	**SUNTHARI K et al** .[9]	**NAIK SK et al**.[8]	**DASARATHAN R et al**.[10]
TOTAL	105	100	33	100
MEAN AGE	49.57	54.86	57	

An average age of 53.81 was found, which signifies the common age group to be affected by Diabetes Mellitus to be the middle ages.

	CURRENT STUDY	**SUNTHARI K et al**.[9]	**NAIK SK et al**.[8]	**DASARATHAN R et al**.[10]
TOTAL	105	100	33	100
M/F	46/59	72/28		48/52

The current study and Dasarathan R et al study reflects a higher female population being involved which can be incidental where as Sunthari K et al study reflects a male predominance hence further large scale studies and correlation is required to explain sex distribution among newly diagnosed Diabetics.

	CURRENT STUDY	**SUNTHARI K et al**.[9]	**NAIK SK et al** .[8]	**DASARATHAN R et al**.[10]
FBS	146.99	168.78	164	189.40

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PPBS	224.24	263.90	257	
HbA1c	9.34	8.73	9.3	8.57
ZINC	102.01	77.98	58	58.31

The mean FBS, PPBS, HbA1c, Zinc among the studies was 167.29, 248.38,8.98,74.075 respectively which signifies poor Glycemic control with low Serum Zinc levels.

HbA1c AND SERUM ZINC CORRELATION

	CURRENT STUDY	**SUNTHARI K et al.**[9]	**NAIK SK et al.**[8]	**DASARATHAN R et al.**[10]
r value	-0.048	-0.689	-0.11	-0.543
P value	0.624	<0.001	0.5349	<0.001

In the present study Pearson's correlation test showed very weak , negative and non-significant correlation between HbA1C and Zinc (r = -0.048, p=0.624).
Sunthari K et al study revealed a negative correlation between HbA1c and serum zinc levels
Naik SK et al study revealed insignificant correlation between serum zinc and glycemic parameters. The correlation pattern between zinc and glycemic parameters was varied at different levels of HbA1c . However A positive correlation existed between serum zinc level and HbA1c at higher HbA1c (≥9.5%).
Dasarathan R et al study revealed a strong negative correlation [r -0.543] and statistically significant correlation between serum zinc levels and HbA1c.

CONCLUSION

In the present study many of the subjects were in the age group of 41-50 yrs with mean age of 49 yrs with female predominance ,with mean FBS and PPBS of 146.99 ,224.24 respectively with mean Glycosylated Haemoglobin [HbA1c] at diagnosis of a newly detected diabetes mellitus was 9.34%, which indicates the poor control blood sugar levels. This can lead to complications like neuropathy, nephropathy and retinopathy.
Our study assessed the serum zinc levels in newly diagnosed diabetes mellitus with Glycosylated haemoglobin [HbA1c] where the mean zinc levels were higher in poor glycemic control subjects interms of high HbA1c,which is a negative correlation Persons correlation between serum zinc levels and HbA1c in overall study subjects showed a very weak ,negative and non significant correlation between them. In General Estimating the level of serum zinc becomes important to know the status of insulin in diabetic patients and correlating the levels of HbA1c and Serum zinc in Type 2 DM patients, can monitor the levels of glycemic control and prevent the risk of development of complications. But however the results of our study weren't able to conclude the significant correlation between glycemic control and serum zinc levels. Hence further studies with large sample size is required to extrapolate the findings.

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