International Journal of Research and Review
Vol. 9; Issue: 8; August 2022
Website: www.ijrrjournal.com
Original Research Article *E-ISSN: 2349-9788; P-ISSN: 2454-2237*

Effect of Mild to Moderate Anemia on HbA1c levels in Type 2 Diabetic Patients in Routine Clinical Practice

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DOI: https://doi.org/10.52403/ijrr.20220857

ABSTRACT

Background: Iron deficiency anemia remains a common condition in India and Hemoglobin A1c (HbA1c) is commonly being used in diabetic individuals both as a parameter of glycemic control over previous three months and as a diagnostic tool. HbA1c levels have been reported to be altered by the presence of nutritional anemias, hemolytic anemia and variant hemoglobin (Hb) among others. Interestingly, iron deficiency anemia effect on HbA1c levels were not found in many studies. Hence a study is conducted to observe the effects if any in routine clinical practice scenario of mild to moderate anemia on HbA1c.

Methods: sixty Type 2 Diabetic (T2D) patients HbA1c was analyzed with their Fasting Blood Sugar (FBS), Post Lunch Blood Sugar (PLBS), along with Hemoglobin levels. T2D patients coming for routine follow-up were studied after their consent, with ethical committee clearance. All the parameters were found to have a normal distribution, i.e., they had an acceptable level of skewness - 0.5 to -0.5 -- were then analyzed further with statistical tools viz., Pearson's correlate and linear regression.

Results: The mean HbA1c was found to be 8.9. Further, the mean Hemoglobin (Hb), FBS and PLBS were: 12.29, 157.9 and 229 respectively. The Pearson's correlate and linear regression analysis was done. HbA1c correlated well with FBS and PLBS, one tailed significance *p* value being <0.01 for both FBS and PLBS; but was not found to correlate with Hb: *p* value 0.146 (not significant).

Conclusions : In the present study representing field scenario, the HbA1c was not correlated with mild anemia but was significantly correlated with FBS and PLBS. Hence in a routine clinical practice scenario the presence of mild anemia didn't appear to interfere with the HbA1c levels.

Keywords: Diabetes mellitus, HbA1c, Fasting Blood Sugar, Hemoglobin, Nutritional Anemia, Regression analysis

INTRODUCTION

Anemia is a common health condition in India. In the 2005- 2006 national family health survey (NFHS-3), a high prevalence of anemia in adults was reported. 1 in 2 females in the age group of 15-49 were found to be anemic, as were 1in 4 males anemic. The commonest cause being Iron Deficiency Anemia (1). Additionally, anemia is about two fold more common in diabetes (13, 14). Diabetes, according to the estimates in 2019, affects 77 million individuals in India, which is further expected to increase to 134 million by 2045 (2). Further, more than half of such individuals (57%) remain undiagnosed underlining the importance of the burden of the disease and in turn the need for accurate diagnostic entities. (2) Given that Diabetes and Anemia are both common a possibility of their interferences in the diagnostics armamentarium like HbA1c can cause a sense of alarm and unease in a practitioner.

More so in day to day practice scenario where multiple testing facilities are denied by lack of access and follow up. Anemia's effect on HbA1c is not well understood and various studies have suggested conflicting results with some suggesting anemia resulting in raised HbA1c (A1c) and others suggesting no role. (4-7). Underscoring such a state it becomes imperative to examine the data in individual settings to review if anemia does interfere with A1c values or otherwise. The present study attempts to find out the correlation if any between A1c and Hb in mild to moderate anemia.

MATERIAL AND METHODS

A cross sectional study was conducted in Prathima Institute of Medical Sciences (PIMS), Nagnur, Telangana, from Jan 2022 through May 2022, after approval from the Institutional Ethics Committee (IEC). 60 consecutive Type 2 Diabetes (T2D) patients were enrolled in the study, after due consent, in the Department of Medicine, visiting outpatient (OP) facilities, for routine health checkup. Individuals with a history of hemoglobinopathy, recent trauma or surgery were excluded from the study as were pregnant women. Additionally, there were no cases of severe anemia in the present study as such individuals would need urgent intervention for anemia and would not be fit for such an observational study.

In the selected individuals described above, with prescribed aseptic measures, venous sample were drawn in 5-millilitre (ml) syringe and analyzed for Hemoglobin (Hb), Fasting Blood Sugar (FBS), Post Lunch Blood Sugar (PLBS) and HbA1c (A1c). A1c was estimated by High-performance liquid chromatography (HPLC) method, using Tosoh Fully Automatic analyser-HLC-723GXX. FBS and PLBS were estimated by Glucose oxidase-peroxidase (GOD- POD) method using Vitros-250 Fully automated analyzer. Hb was estimated by Benesphera-H31 automated cell counter. Mean median and standard deviation of the data were calculated, their linearity (normality) established and further statistical analysis as applicable including Pearson correlation, linear regression analysis was conducted using SPSS version-11.

RESULTS

Mean age, Hb, A1c, FBS, PLBS of the cases in the study is illustrated in Table1. There was a significant difference in Hb in male and female as expected which was found to be statistically significant ($p < 0.01$). Additionally, there was a slight significant difference between the FBS in the two genders (p 0.017).

Table--1

			Sum of Squares	df	Mean Square	F	Sig.
HBA1C * Gender	Between Groups	(Combined)	10.318	1	10.318	1.903	.173
	Within Groups		314.531	58	5.423		
	Total		324.849	59			
FBS * Gender	Between Groups	(Combined)	23215.083	1	23215.083	6.151	.017
	Within Groups		169843.896	45	3774.309		
	Total		193058.979	46			
PLBS * Gender	Between Groups	(Combined)	19790.052	1	19790.052	2.945	.092
	Within Groups		376330.844	56	6720.194		
	Total		396120.897	57			
HB * Gender	Between Groups	(Combined)	68.255	1	68.255	37.883	<.001
	Within Groups		88.284	49	1.802		
	Total		156.539	50			

The A1c was found to be less than 7 (Optimal target) in only 25% of individuals reflecting poor control signifying the need of intensified treatment goals and unmet needs. The percentage of individuals having mild to moderate anemic was found to be 60% signifying the commonness of anemia in Diabetic population. FBS on the other hand was found to be normal in 40% of individuals signifying the need to incorporate A1c as a monitoring tool for optimum control. The data was then analysed to evaluate if it is normal/linear by its skewness level and was found to be within limits of linearity. (Figure 1-4).

Figure - 1

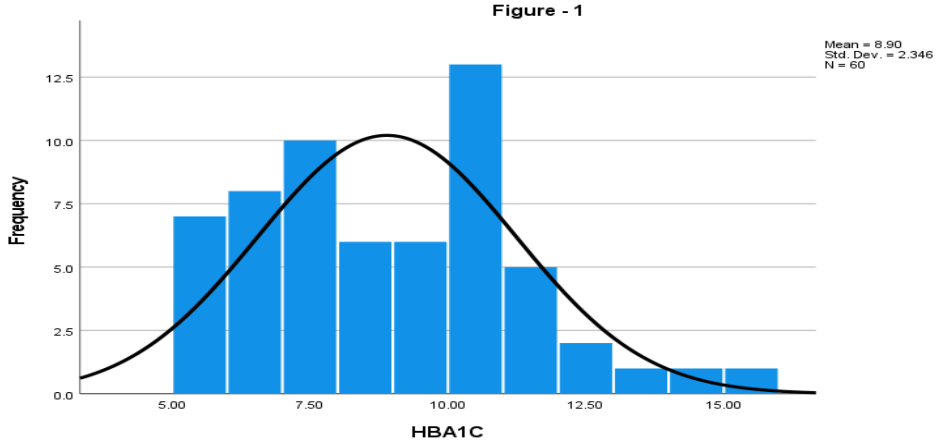


Figure - 2

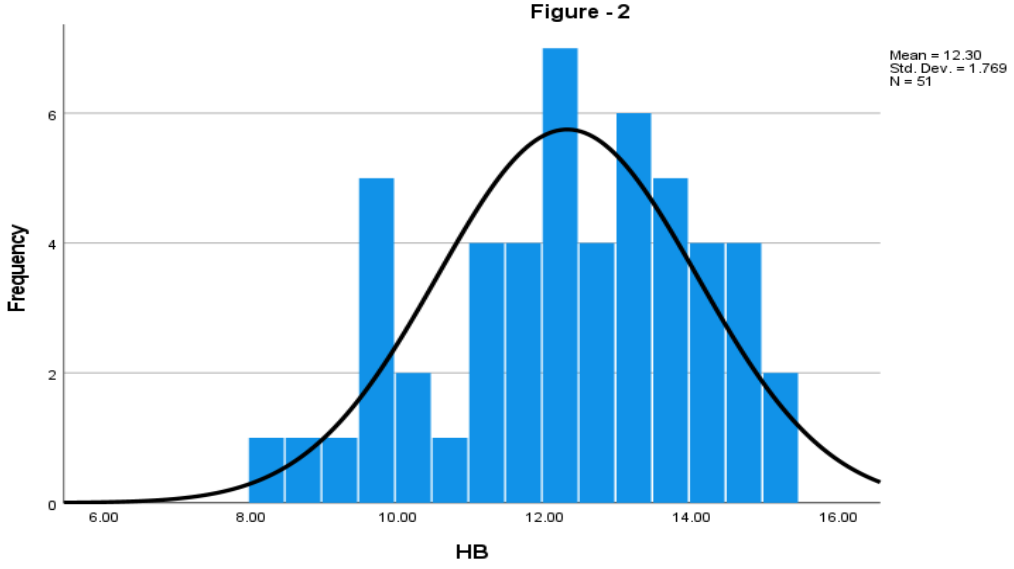


Figure - 3

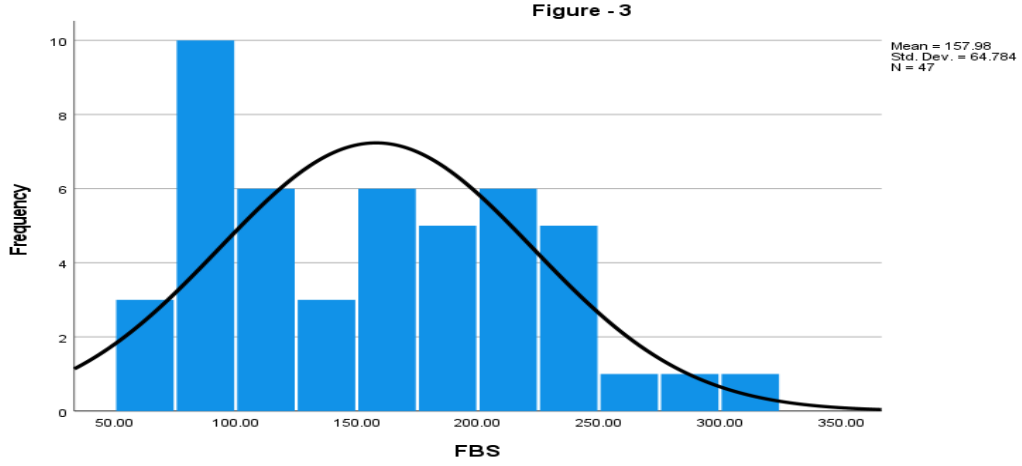
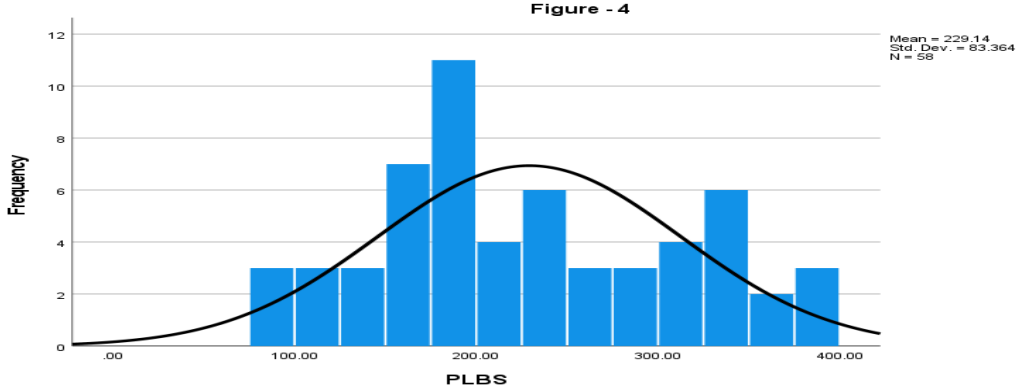


Figure - 4



Pearson's correlation criteria with credible interval percentage of 95 was applied to study the correlation between: HbA1c and Hb, HbA1c and FBS, HbA1c and PLBS. Significant correlation of A1c was found with only FBS and PLBS but not with Hb. Summarised in Table-2 and as shown in Regression Variable plots /scatter plots. (Figure 5-7). Linear Regression analysis was conducted with dependent variable as HbA1c and correlated with the following variables: FBS, PLBS, Hb, Age, Gender. With Regression Coefficient Confidence interval of 95%, the findings are summarized in Table-3. The HbA1c was found to be correlated with only FBS and PLBS *p* value of 0.024 and 0.015 respectively. And was not found to be correlated with age, gender and Hb

Table -2

Correlations					
		HBA1C	HB	FBS	PLBS
Pearson Correlation	HBA1C	1.000	.169	.796	.809
	HB	.169	1.000	.325	.251
	FBS	.796	.325	1.000	.854
	PLBS	.809	.251	.854	1.000
Sig. (1-tailed)	HBA1C	.	.146	<.001	<.001

Figure - 5

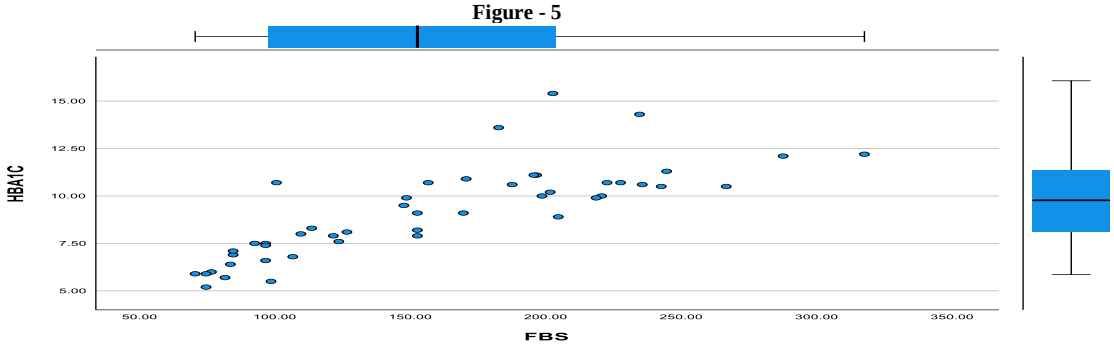


Figure - 6

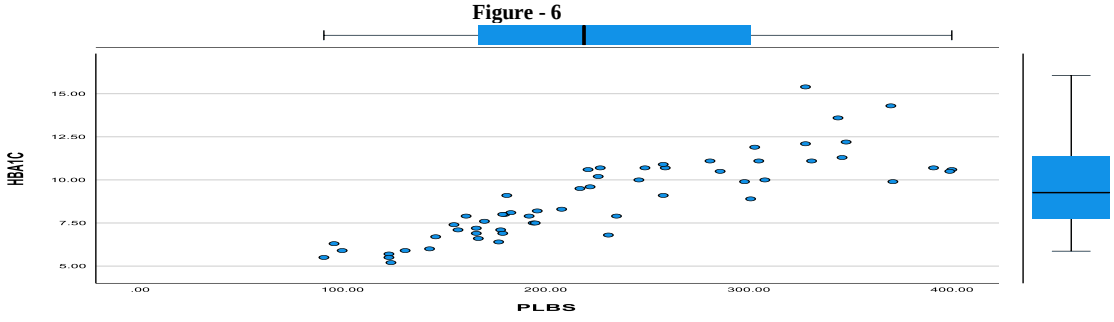


Figure - 7

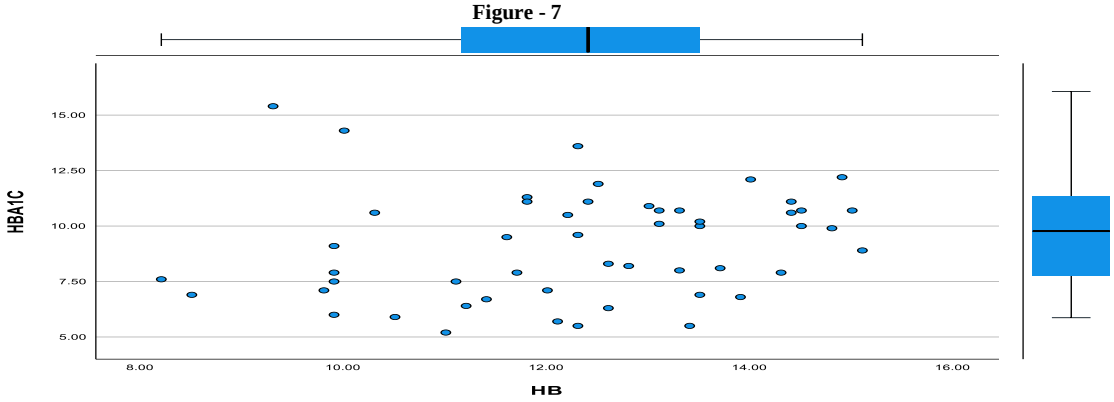


Table -3

Linear Regression Coefficient[a]

Model		Unstandardized Coefficients		Standardized Coefficients			95.0% Confidence Interval for B	
		B	Std. Error	Beta	t	Sig.	Lower Bound	Upper Bound
1	(Constant)	3.856	3.523		1.095	.281	-3.295	11.007
	Age	.007	.019	.037	.354	.725	-.031	.044
	Gender	.115	.712	.022	.161	.873	-1.332	1.561
	FBS	.016	.007	.437	2.358	.024	.002	.031
	PLBS	.013	.005	.463	2.564	.015	.003	.024
	HB	-.076	.190	-.057	-.400	.691	-.461	.309

a. Dependent Variable: HBA1C

DISCUSSION

Poor diabetic control continues to be a challenge in the management of diabetic patients in India (8,9,10). The present study demonstrated the lack of optimal sugar control in 3 out of 4 individuals. 75% of patients in the present study lacked optimal control as desired by an A1c <7. Such findings are similar to the 33% level in western studies. (8). Further using only FBS as a standard of care for optimal diabetic care missed around 15-20% or one in five individuals in comparison to A1c emphasising the role of using both A1c and FBS as diagnostic tools to monitor optimal control in routine clinical practice. (11).

Anemia is reported to be more common in Diabetics (13, 14) than among non-diabetic adults (12), emphasising the need of a diagnostic tool to monitor diabetes which is not altered by the status of anaemia. Certain studies have suggested the possibility of Anemia resulting in increased A1c levels, with the mechanistic association suggested being as follows: One, in iron deficiency the quaternary structure of the hemoglobin molecule is altered, resulting in pronounced glycation of the globin chain in the relative absence of iron (4). Secondly, as red cell age increases in iron deficiency anemia, it can further result in an increased A1c levels (5). Notwithstanding these views, other studies opined normal red cell age in Iron deficiency states (16) and suggested that the observed differences in A1c were possibly due to differences in assessment methods of A1c. (16, 17).

Additionally, Indian studies reflecting more day to day practice scenario didn't find any correlation between A1c and Hb in mild to moderate anemia (7, 18) allying the fears of A1c's possible diagnostics inaccuracy in the setting of mild to moderate Anemia in routine clinical practice. The present study had a substantial proportion of anemic patients (sixty percent), more than double

that of corresponding control general population. Conforming to the finding of increased prevalence of anemia in diabetic individuals (13, 14). Moreover, poor control as assessed by only FBS had a tendency to miss one in five cases of suboptimal control in comparison to the use of both A1c and FBS, emphasising the need of incorporating both A1c and FBS in routine care (11). Pearson's Correlation with A1c, were highly significant for FBS and PLBS only. 1-tailed *p* value being <0.001 in both (highly significant). Similar correlation for Hb was found to be 0.146 (non-significant). Additionally, linear regression analysis done correlating A1c with age, gender, FBS, PLBS and Hb found A1c to be significantly correlated with only FBS and PLBS. But did not correlate with Hb, age or gender.

CONCLUSION

In the present study of 60 adult Type 2 Diabetic (T2D) individuals, documenting correlation of HbA1c with various parameters including FBS, PLBS, Hb, age, gender. Found a positive correlation of A1c with FBS and PLBS only and not with Hb, age gender. Hence proving that in field's settings, mild to moderate anemia in Adult T2D patients didn't interfere with A1c levels. Or in other words, there is no correlation between Hb and A1c in T2D patients with mild to moderate anemia.

Limitations: non inclusion of severe anemia patients and pregnant women among others, limits the generalisation of these findings to those set of patients. Additionally, limited number of patients and short duration of study further binds it, which can only be overcome in a large scale study.

Acknowledgements: the authors acknowledge ample help and support provided by the faculty and staff at PIMS.

Acknowledgement: None

Conflict of Interest: None

Source of Funding: None

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How to cite this article: Ajay Kumar Khandal, Usha Khandal, P. Chakradhar. Effect of mild to moderate anemia on HbA1c levels in type 2 diabetic patients in routine clinical practice. *International Journal of Research and Review*. 2022; 9(8): 690-696. DOI: *https://doi.org/10.52403/ijrr.20220857*

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