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STUDY TO IDENTIFY THE RELATIONSHIP BETWEEN HEMOGLOBIN AND HBA1C LEVELS AMONG DIABETICS WITH ANEMIA.

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ABSTRACT

Background: Diabetes and Anemia are the two common problems in India. HBA1c and HB are the diagnostic markers for the Diabetes and Anemia respectively and are helpful for the assessment of the conditions. Hence there is need to conduct a study on relationship between HB and HBA1c inpatients having coexisting Diabetes and Anemia.
Objective: Estimation of HB and HBA1c levels in Diabetics with Anemia and to assess whether HB has any relation and effect on HBA1c.
Material and Methods: The present study was carried out during February and April 2018 in outpatients attending in a tertiary care Hospital at Guntur. All the patients who fulfilled the criteria were enrolled in the study.
Results: Among the biochemical parameters HBA1c, HB, FBS showed significant difference in statistical analysis.
Conclusion: The HBA1c values in Diabetics with Anemia should be viewed with caution in assessing the Diabetic status .Any condition that increases the erythrocyte survival or decreases the RBC turnover results in erroneously elevated HBA1c. Hence HB has to be corrected and before assessing the HBA1c.

KEYWORDS : Glycogenated Hemoglobin (HBA1c) , Fasting Blood Sugar(FBS) , Hemoglobin (HB).

Introduction:
Diabetes mellitus is a group of common metabolic disorders that share the phenotype of hyperglycemia. Depending on the etiology of diabetes mellitus, factors contributing hyperglycemia include reduced insulin secretion, decreased glucose utilization, and increased glucose production(15).

Measurement of glycated proteins primarily HBA1c is effective in monitoring long term glucose control in people with diabetes mellitus. Chronic hyperglycemia causes increased glycation of protein including hemoglobin resulting in formation of Advanced Glycated End Proteins.(16)

HbA1c is the most predominant fraction of HbA1, and it is formed by glycation of terminal valine at the B-chain of hemoglobin. It reflects the patient's glycemic status over previous 3months. HbA1c used as a screening test for Diabetes mellitus. As per American Diabetes Association HbA1c≥ 6.5% as a diagnostic criterion for Diabetes mellitus.(1) At the present time, the HbA1c is used worldwide as the marker of long term glycemic control and also a therapeutic target in the prevention and delay of development of hyperglycemic complications. HbA1C levels are altered in conditions such as hemolytic anemia, hemoglobinopathies, pregnancy, and vitamin B12 deficiency has been studied in a study conducted by Sinha etal. (2)

Anemia is one of the most prevalent forms of malnutrition. The anemia is classified by severity into mild (110 g/L to normal), moderate (80 g/L to 110 g/L), and severe anemia (less than 80 g/L) in adult males and adult non pregnant females.

Anemia is typically diagnosed on a complete blood count. Apart from reporting the number of red blood cells and the hemoglobin level, the automatic counters measure the size of the red blood cells by flow cytometry. Any condition that increases the erythrocyte survival or decreases the RBC turnover results in erroneously elevated HBA1c.

Hence we performed a study to assess whether HB% has relation on HbA1c levels and HBA1c has to be considered as diagnostic marker for assessing the Diabetes in Anemic individuals.

Materials and Methods
The present observational study was carried out during February and April 2018 in outpatients in a tertiary hospital, Guntur. All the patients who fulfilled the criteria were enrolled in the study. Inclusion Criteria include Type 2 DM patients clinically diagnosed on the basis of WHO criteria, irrespective of duration and treatment were selected for the study in the age group of 30-65 years. Exclusion Criteria include Patients with diabetic complications, any infection, chronic renal failure, other systemic conditions, recent history of iron intake, history of repeated blood transfusion and hypertensive patients and on corticosteroid therapy were excluded from the study. Pregnant women were also excluded from the study.

HBA1c and HB are the diagnostic markers for the Diabetes and Anemia respectively are taken for the assessment of the Diabetes and Anemic status. Three groups of patients are taken for the study. One group having Anemia without Diabetes, second group having Anemia with Diabetes and Third group having Diabetes without Anemia.

Results:
Based on the pilot study conducted in the hospital, the sample size was calculated using the formula

$$n = z^{2\frac{2\sigma^2}{d^2}}$$

Where Z at 95% CI = 1.96
d= (μ2 –μ1) where μ1 = 5.5 and μ2 = 5.6.
Where σ = standard deviation = 0.2

$$n=\frac{1.96^2 x 2 x (0.2)^2}{(0.1)2}$$

=3.84 x 8 = 30.72 = 31 per group

- Hence a sample size of 93 was taken where 31 each in anemia without Diabetes ,Diabetic without anemia, Diabetic with anemia groups
- The age group is 35-65 yrs.
- Gender wise distribution was 39 Males and 54 Females.
- All the results were expressed as mean ± SD

Table 1

AGE	Anemic without diabetes	Diabetic without Anemia	Diabetic With Anemia
Mean ± SD	49.93± 9.00	53.35 ± 8.03	51.90 ± 8.95

There was no significant difference in age between cases and controls.
Figure.1

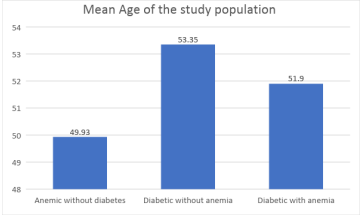


Table 2

SEX	Anemic without diabetes	Diabetic without Anemia	Diabetic With Anemia
Male	8	11	20
Female	23	20	11

Anemia is more common in Males with Diabetics with Anemia, Anemia without Diabetes is more common in Females and Diabetics without Anemia common in Females in study population.

Figure.2

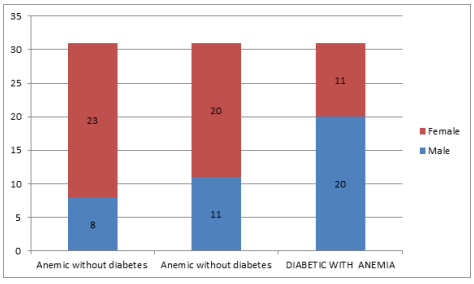


Table 3
Biochemical Parameters HBA1c, FBS, HB :

	Anaemia without diabetes	Diabetic without Anaemia	Diabetic With Anemia	P value
HBA1c Mean ± SD	6.07 ± 0.53	8.63 ± 0.84	7.47 ± 0.97	<0.001
FBS Mean ± SD	96.16 ± 7.92	113.51 ± 15.21	102.41 ± 13.26	<0.05
HB Mean ± SD	8.38 ± 2.24	12.09 ± 0.96	9.50 ± 1.27	<0.0001

Figure.3

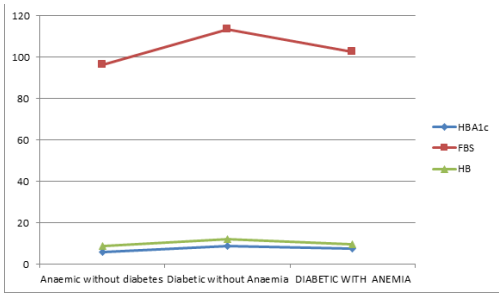


Table 4

HBA1C	Anaemic without diabetes	Diabetic without Anaemia	Diabetic With Anemia	P value
Mean ± SD	6.07 ± 0.53	8.63 ± 0.84	7.47 ± 0.97	<0.001

Statistical test : ANOVA
P value : significant
There is a significant difference observed between the groups with regard to HBA1C

Figure.4

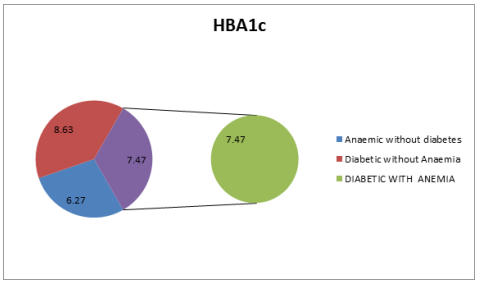


Table 5

Hb in gms	Anaemic without diabetes	Diabetic without Anemia	Diabetic With Anemia	P value
Mean ± SD	8.38 ± 2.24	12.09 ± 0.96	9.50 ± 1.27	<0.0001

Statistical test : ANOVA
P value : significant
There is a highly significant difference observed between the groups with regard to Hb

Figure. 5

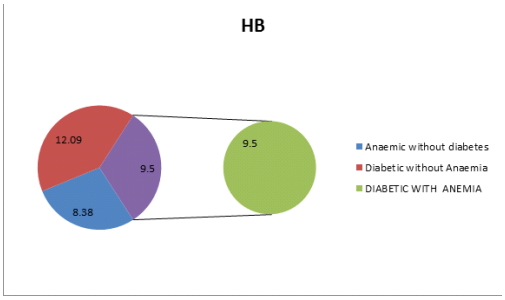
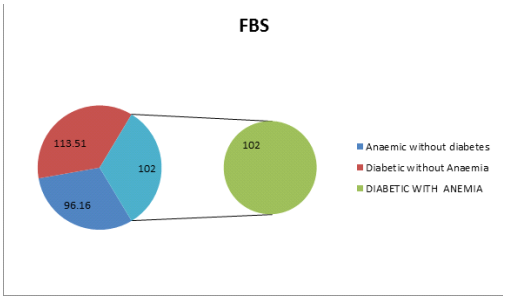


Table 6

FBS	Anemic without diabetes	Diabetic without Anemia	Diabetic With Anemia	P value
Mean ± SD	96.16 ± 7.92	113.51 ± 15.21	102.41 ± 13.26	<0.05

Statistical test : ANOVA
P value : significant
There is a significant difference observed between the groups with regard to FBS

FIGURE.6



There is significant difference observed in biochemical parameters HBA1c, HB, FBS levels.
The p-value was <0.001 for HBA1c (Table 4 ; Figure 4).
The p-value was <0.0001 for HB (Table 5 ; Figure 5).
The p-value was for <0.005 for FBS (Table 6, Figure 6).

Table 7

Hb in gms	Anemic without diabetes	Diabetic without Anemia	
Mean	8.38	12.09	<0.0001
SD	2.24	0.96	

Statistical test : un paired t test
P value : significant
There is a significant difference observed between the groups with regard to Hb

Table 8

Hb in gms	Anemic without diabetes	Diabetic With Anemia	
Mean	8.38	9.50	<0.05
SD	2.24	1.27	

Statistical test : un paired t test
P value : significant
There is a significant difference observed between the groups with regard to Hb

Table 9

Hb in gms	Diabetic without Anemia	Diabetic With Anemia	
Mean	12.09	9.50	<0.0001
SD	0.96	1.27	

Statistical test : un paired t test
P value : significant

There is a significant difference observed between the groups with regard to Hb
HB levels in unpaired t test P value < 0.0001 (table 7,9) and <0.05 (Table 8)

Table 10

HBA1C	Anemic without diabetes	Diabetic without Anemia	
Mean	6.07	8.63	<0.0001
SD	0.53	0.84	

Statistical test : un paired t test
P value : significant
There is a significant difference observed between the groups with regard to HBA1C

Table 11

HBA1C	Anemic without diabetes	Diabetic With Anemia	
Mean	6.07	7.47	<0.0001
SD	0.53	0.97	

Table 12

HBA1C	Anemic without diabetes	Diabetic With Anemia	
Mean	6.07	7.47	<0.0001
SD	0.53	0.97	

Statistical test : un paired t test
P value : significant
There is a significant difference observed between the groups with regard to HBA1C

Table 12

HBA1C	Diabetic without Anemia	Diabetic With Anemia	
Mean	8.63	7.47	<0.0001
SD	0.84	0.97	

Statistical test : un paired t test
P value : not significant
There is a no significant difference observed between the groups with regard to HBA1C
HBA1c levels in unpaired t test p value <0.0001. (Table10,11,12).

DISCUSSION:

Anemia is a common health problem in developing countries. The estimated prevalence of anemia in developing countries is 39% in children <5 years, 48% in children 5–14 years, 42% in women 15–59 years, 30% in men 15–59 years, and 45% in adults >60 years [3].

Anemia is a major health problem in India. In the 2005-2006 National Family Health Survey (NFHS-3), a household survey aimed at having national and state representative data on population health and nutrition; the prevalence of anemia was 70% in children aged 6–59 months, 55% in females aged 15–49 years, and 24% in males aged 15–49 years [4].

Anemia is a commonly observed disorder in patients with diabetes and it contributes to the progression of diabetes related complications.(5).The prevalence of anemia ranges from 13% to 45% in patients with diabetes , depending upon the ethnicity and diagnostic criteria used and it is high when it is associated with renal impairment.(6,7) The risk of anemia increases with severity of renal impairment in patients with diabetes and they are more likely to develop macro vascular complications.(8). The diabetics who have poor glycemic control are at higher risk of anemia than those with good glycemic control.(9)

The pathophysiology linking anemia and diabetes mellitus type2 is multifaceted.

Diabetes Mellitus	• Chronic Hyperglycemia • Chronic inflammation • Decreased Iron intake • VitB12/Folatedeficiency • Autonomic neuropathy • Metphormine use	Anemia

Both erythropoietin deficiency and hypo responsiveness may contribute to early anemia in diabetes mellitus, particularly in those having kidney disease or even in mild decline in kidney function. Hyperglycemia worsens the function of hypoxia–inducible factor 1(HIF-1), a key regulator of erythropoietin production during hypoxia, which is also involved in vasculogenesis and cellular metabolism.

According to the World Health Organization (WHO), there are two billion people with anemia in the world and half of the anemia is due to iron deficiency (3). Anemia is a late indicator of iron deficiency, so it is estimated that the prevalence of iron deficiency is 2.5 times that of anemia.

In a study Ford checked serum insulin, HBA1c, FBS, Ferritin and found a significant correlation between serum ferritin with HBA1c, FBS and serum insulin.(10) In Ashoorapour's study, there was a correlation between serum ferritin and FBS, HBA1c, Serum insulin.(11)

The glycated hemoglobin (HBA1c) is a widely accepted indicator of long –term glycemic levels and it is used for monitoring the glycemic changes in response to diet and medication in addition to diagnosing diabetes mellitus. Certain clinical conditions and any condition that increases the erythrocyte survival or decreases the RBC turnover results in erroneously elevated HBA1c e.g. Iron deficiency anemia, Vitamin B12deficiency..(12, 13)

Use of certain antihyperglycemic agents like metformin and thiazolidinones are associated with risk of developing anemia. Long-term use of metformine is known to cause megaloblastic anemia due to alteration in the small bowel motility, which can stimulate bacterial overgrowth, competitive inhibition or inactivation of B12 absorption, alteration in the intrinsic factor levels.14.

In this study there is significant difference observed in biochemical parameters viz HBA1c, HB, FBS, in Anemia with Diabetes, Diabetes without Anemia and Anemia without Diabetes.

Limitation of the study is that the small sample size, duration of diabetes. Further studies are required with large sample size and optimal cut-off values so that these parameters can be used as glycemic control parameters or prognostic significance.

Conclusion :

HBA1c is wildly accepted indicator of long-term glycemic levels. However, the use is limited in certain clinical conditions that influence the factors involved in HBA1c measurement. In Diabetics with Anemia as there is alteration in HBA1c, HB should also be considered and corrected while altering the treatment regimen for Diabetes and monitoring the Diabetes status.

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