



STUDY OF CORRELATION BETWEEN HbA1c AND BLOOD INDICES IN DIABETIC PATIENTS

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ABSTRACT

Introduction: HbA1c is very good tool for diagnosis and monitoring of diabetic patients. There have been several studies done to find correlation between HbA1c and RBC indices. Finding of correlation between these parameters can be helpful for diagnosis of patients as well as during monitoring of treatment. Correlation study of RBC indices and anemia type with other glycemic control investigation such as oral glucose tolerance test is needed to assess the importance of this observation and provide a more complete understanding of diabetic patients. **Aim and objectives:** To find correlation between HbA1c and RBC indices in adult patients undergoing health package screening at Metropolis healthcare ltd. **Material and Methods:** All the adult (>18 yrs) patients undergoing health packages screening at various subjects of Metropolis laboratory all over India containing HbA1c and CBC hemogram were selected. EDTA sample collected from patients were processed for HbA1c by HPLC method and RBC indices taken from CBC hemogram. These were divided into three groups on the basis of HbA1c values as Normal HbA1c (<5.6), prediabetic (5.6-6.5) and diabetic (>6.5). Statistical analysis done with collected data to find significance of correlation. **Results:** A total of 13193 patients were selected based on above criteria. 8536 were males and 4657 were females. RBC count was abnormal in 24.41% patients. MCH in 22.03%, MCHC 13.51%, MCV 20.69%, RDW 50.12% of patients. Mean RBC count in diabetic patients was (4.69 ± 0.56) , MCH (28.11 ± 2.69) , MCHC (32.82 ± 1.39) , MCV (85.65 ± 6.86) , and RDW (14.63 ± 1.77) . MCV and MCH were negatively correlated found with HbA1c, $r = -0.1146$, $p < 0.0001$ & $r = -0.1140$, $p < 0.0001$ respectively. Whereas there is no statistically significant correlation between HbA1c with RBC count ($r = -0.06397$), MCHC ($r = -0.04177$), RDW ($r = -0.04804$). **Conclusion:** As per the statistical data it is found that there is significant negative correlation between HbA1c values and MCV and MCH values. Therefore, while interpreting the HbA1c reports for diagnosing/follow up of Diabetes MCV and MCH should be taken in consideration for variation in values.

KEYWORDS : HbA1c, RBC indices, Diabetes, India, MCH, MCV

INTRODUCTION:

The burden of diabetes is high and increasing globally, and in developing economies like India, mainly fueled by the increasing prevalence of overweight/obesity and unhealthy lifestyles. The estimates in 2019 showed that 77 million individuals had diabetes in India, which is expected to rise to over 134 million by 2045¹. The rising incidence and chronic nature lead to an increased risk of a complex complication profile of macrovascular and microvascular complications. Hence, following a diagnosis of diabetes, management, regular follow-up with an assessment for complications, and blood sugar monitoring always remain a big challenge for any health care provider, especially in low socioeconomic countries.

The cost-effectiveness of those measures or tools for the assessment of complications status and blood sugar monitoring is highly desirable and encouraged. In this regard, recently, glycated haemoglobin (HbA1c) was used as a tool for glycaemic control but since 2010, it is now accepted for the diagnosis of diabetes too². HbA1c is measured as an index of glycaemic control for a period over eight to 12 weeks. It is a very good tool for diagnosis and monitoring of diabetic patients. However, HbA1c can be affected by changes in RBC lifespan due to blood loss, blood transfusion, anemias, chronic renal or liver disease, erythropoietin treatment and hemoglobinopathies³.

The aim of this retrospective study is to assess the relationship between RBC indices and hba1c. This can be helpful for diagnosis of patients as well as during monitoring of treatment.

MATERIAL AND METHODS:

This study was performed retrospectively for the duration of Jan-22 to July-22 for patients undergoing health package testing at all over lab centers of metropolis healthcare ltd. We

have taken the data of HbA1c, and CBC blood indices of these patients coming to labs or taken home visits. Purpose for taking health packages selection was to ensure all the subjects must have performed CBC and HbA1c. HbA1c was performed by HPLC method and CBC was performed by 5 cell counters.

The patients were selected from below criteria. All patients above 18 years of age irrespective of gender were selected, also they should have performed CBC and HbA1c in the package.

The patients were categorized into 3 groups based upon HbA1c levels as Normal (HbA1c < 5.6), Prediabetic (5.6-6.4), and diabetic (>6.5) as per the ADA 2022 guidelines.

Samples were collected from patient after overnight fasting in EDTA tube. Following data was collected for analysis- HbA1c, MCH, MCV, MCHC, RDW and RBC count taken from complete blood count. All the collected data was statistically analyzed pearsons coefficient correlation. Correlation between HbA1c and blood indices MCH, MCH, MCHC, RDW and RBC count was defined.

RESULTS:

As per the selection criteria total 13193 patients were selected for the study. 8536 (64.70%) were males and 4657 (35.30%) were females. 2872 (21.77%) were having normal HbA1c, 4948 (37.50%) were having prediabetic HbA1c and 5373 (40.73%) were diabetic as per ADA 2022 guidelines. Mean HbA1c in normal patients was 5.34 ± 0.28 %, 6.00 ± 0.22 % in prediabetic and 8.05 ± 1.59 % in diabetic group. Mean RBC count in non-diabetic was 4.65 ± 0.59 , 4.67 ± 0.72 in prediabetic and 4.69 ± 0.56 in diabetic. Mean MCH in diabetics was 29.07 ± 2.79 , 28.46 ± 2.79 in prediabetic and 28.11 ± 2.69 in diabetic. Mean MCHC in normal patients was 33.13 ± 1.45 , 32.88 ± 1.35 in prediabetic and 32.82 ± 1.39 in

diabetic patients. Mean mcv in normal patients was 87.73 ± 7.06 , 86.53 ± 7.11 in prediabetic and 85.65 ± 6.86 in diabetic patients. Mean PCV in normal patients was 40.72 ± 5.23 , 40.30 ± 4.87 in prediabetic and 40.11 ± 4.91 in diabetic patients. Mean RDW in normal patients was 14.14 ± 1.78 , 14.45 ± 1.71 in prediabetic and 14.63 ± 1.77 in diabetic patients (Table-1).

As per pearsons correlation coefficient there is statistically significant negative correlation between HbA1c value and MCV (r^2 value -0.1146) fig 4 and MCH (P value-0.1140) fig 2. MCH value was 28.11 ± 2.69 in diabetics whereas 29.07 ± 2.79 in normal patients. And mean MCV value was 85.65 ± 6.86 in diabetics and 87.73 ± 7.06 in normal patients.

There is statistically insignificant correlation between HbA1c and Hemoglobin (r^2 value -0.01685) fig 7, MCHC (r^2 value -0.04177) fig 3. And there is not any significant correlation between HbA1c and RBC count (r^2 value 0.06391) fig 1, Hematocrit (r^2 value-0.002419) fig 5, RDW (r^2 value-0.04804) fig 6.

Table 1 Summary of correlation between HbA1c and RBC parameters

status	No	Mean Hb A1c	Mean RBC	Mean Hb	Mean HCT	Mean MCV	Mean MCH	Mean MCHC	Mean RDW
Normal	287	5.34	4.65	13.49	40.72	87.73	29.07	33.13	14.14
Prediabetic	494	6.00	4.67	13.24	40.30	86.53	28.46	32.88	14.45
Diabetic	537	8.05	4.69	13.15	40.11	85.65	28.11	32.82	14.63
p value			<0.001	0.0430	0.7811	<0.001	<0.001	<0.001	<0.001
R2 value			0.06391	-0.0168	-0.0024	-0.1146	-0.1140	-0.0417	0.0480

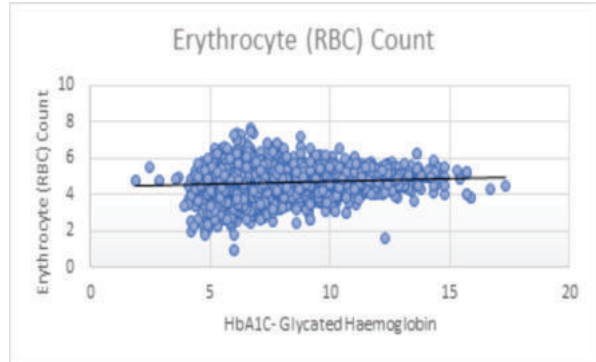


Fig 1 Correlation between HbA1c and RBC count

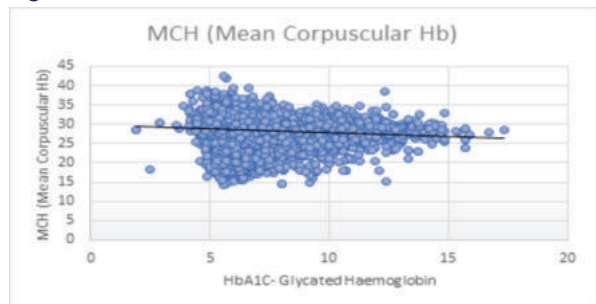


Fig 2 Correlation between HbA1c and MCH

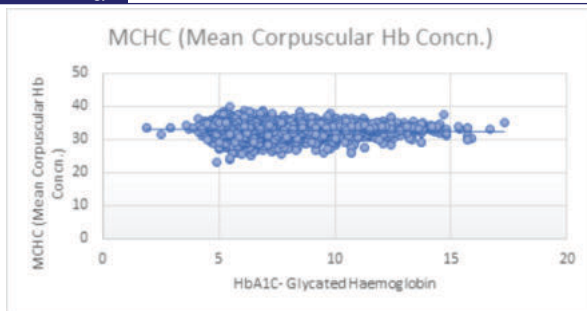


Fig 3 Correlation between HbA1c and MCHC

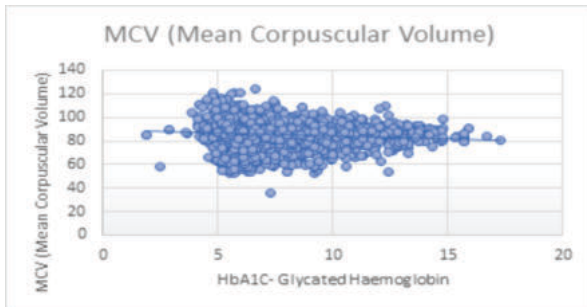


Fig 4 Correlation between HbA1c and MCV

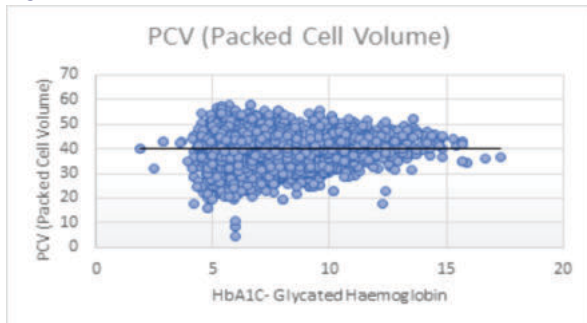


Fig 5 Correlation between HbA1c and PCV

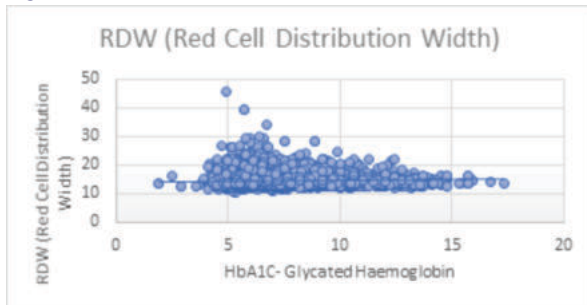


Fig 6 Correlation between HbA1c and RDW

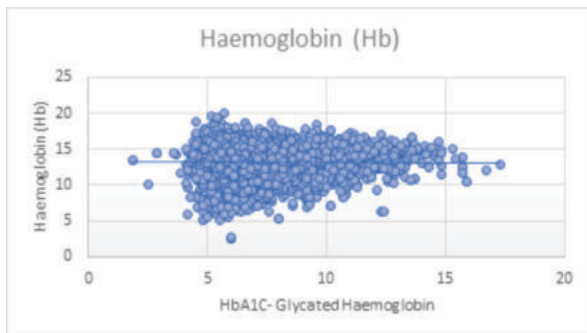


Fig 7 Correlation between HbA1c and Hemoglobin

DISCUSSION:

Nowadays HbA1c is widely used as tool for monitoring treatment of diabetic patients. HbA1c is glycated HbA which is

linked to circulating glucose levels. Also, HbA1c reflect the average lifespan of RBCs which were exposed to high blood glucose.

As this is related to RBC Lifespan hence RBC indices like MCV, MCH, MCHC, HCT, RBC count and RDW may play an important role in determining value of HbA1c.

In our study we have found statistically significant negative correlation of MCH ($P = <0.0001$, $r = -0.1140$) and MCV (P value <0.0001 , $r = -0.1146$) to HbA1c value. Findings of our study are similar to study by Santiago et al. The authors demonstrated that there existed a substantial negative correlation in HbA1c from 6.09- 6.79 (expressed as %) across deciles of MCH & MCV. They showed an increased risk of erroneous HbA1c based identification of glycaemic status in at least 25% of patients, concluding that MCH and MCV should be taken into account while interpreting HbA1c levels in clinical practice⁴. Also Renuka et al in their study found significant negative correlation between HbA1c and MCV, MCH and MCHC³. Koga et al studied the relationship between erythrocyte indices and HbA1c in premenopausal women. They found that MCV and MCHC were negatively associated with HbA1c as found in our study. Every 1 pg decrease in MCH seemed to correlate with 0.03% in increase in HbA1c and the authors suggested that erythrocyte indices influence HbA1c values in pre-menopausal women in the absence of overt anemia⁵. Md sadiqu jaman et al found in their study significant negative correlation of MCV and MCH with HbA1c as some research have been suggested that anaemia occurrence in diabetic mellitus is due to increase enzymatic glycosylation of RBC membrane proteins, which correlated with hyperglycaemia. Oxidation of these glycosylated membrane proteins and hyperglycaemia in diabetes mellitus cause an increase in the production of lipid peroxides causing haemolysis of RBCs or diabetes mellitus may cause anaemia as secondary disorder⁶. Using cell separation techniques (based on the cell density and size), Bosch et al. found a strong inverse correlation ($r = -0.97$) between HbA1c and mean cell volume. This implies that MCV and HbA1c are both highly dependent on a common variable, presumably red cell age⁷. Both MCH and MCV decrease linearly during the lifespan of RBC. MCH is considered as an indirect measure of RBC survival³.

Also in our study we found that there is positive correlation between HbA1c and RDW (p value <0.0001 , $r = 0.0480$) and RBC count (p value <0.0001 , $r = 0.063$) but it is not statistically significant. These findings also comparable with study by Tram et al. The authors said Analysis of the blood glucose level and MCHC and RDW showed a significant correlation between these parameters. Similarly, HbA1c and MCHC also showed a significant correlation⁸. Rashid MR et al in their study mentioned significant negative correlation of HbA1c with MCV and MCH and a significant positive correlation with RBC count⁹. In our study we have not found any significant correlation between HbA1c and Hb, hematocrit and MCHC as compared to study by Jaman MS et al that adult with no history of diabetes, which showed a significantly positive association between MCH, MCHC, RDW with HbA1c³.

As we have not considered factors like iron deficiency, vitamin deficiencies and dietary and other factors, the study may not be completely applicable in these states. More comprehensive study with strict inclusion and exclusion criteria will give robust conclusion. But as study participants are from large geographical area all over India, this data represents fair portion of Indian population with correlation of HbA1c with blood indices.

CONCLUSION:

Our study has emphasized that blood indices particularly MCV and MCH should be considered while interpreting

values of HbA1c in diabetic patients treatment monitoring. Also, other parameters like RBC count and RDW even we haven't found statistically significant correlation, but these parameters also influence the HbA1c value as it denotes RBC Lifespan. As RBC indices are usually done along with other tests it offers additional free parameter to evaluate its effect of HbA1c for treatment of diabetic patients. As our study has not considered factors like iron deficiency and vitamin deficiency, so these factors have to be interpreted separately.

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