Correlation of Red Blood Cell Distribution Width (RDW) and Hemoglobin A1C (HbA1c) Levels, In Patients with Type 2 Diabetes Mellitus

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ABSTRACT

The incidence of Diabetes Mellitus is increasing worldwide, with almost 1/3 of adults being affected. It is the major contributor to the morbidity of a man with its multi-organ system complications. Control of blood glucose levels is vital to decrease organ damage and complications. Routine diagnostic tests conducted are blood glucose, lipid profile, renal function tests, HbA1c, and insulin assays with a baseline CBC (Complete Blood Count). HbA1c values continue to be the gold standard for the assessment of glycemic control. The RDW (Red Cell Distribution Width) is a parameter of Complete Blood Count. Several studies have shown elevated RDW values in patients with poor glycemic control and as an early marker for Diabetic nephropathy and cardiovascular complications. 610 patients with type 2 Diabetes Mellitus attending the Diabetic Clinic in Saveetha Medical College were included in a cross-sectional study to compare HbA1c values with RDW values with age and gender. The ratio of patients with poor HbA1c levels: acceptable HbA1c levels of glycemic control was 1:4 in the age group 25 years and below. The ratio rose to 1:1 in the 36-45 years age group with a reversal of ratio to 4:1 in patients >65 years of age. There was a significant correlation between the values of HbA1c with age - with the number of patients increasing with age and showing elevated HbA1c levels. There was no significant correlation between the values of RDW and age. There was a significant positive correlation between HbA1c and RDW- (p = 0.003, < 0.05 standard). For patients with HbA1c values between 6.2- 6.8 %, there was a particularly strong positive correlation with RDW values. In conclusion, there was a significant positive correlation between values of RDW and HbA1c, which emphasis that RDW is a good predictive factor for glycemic control.

INTRODUCTION

Diabetes mellitus is fast approaching to be perhaps the most significant contributor to global morbidity, with every third person of the adult population impacted by the disease and its multi-organ system complications. The prevalence of diabetes is predicted to double globally from 171 million in 2000 to 366 million in 2030, with a maximum increase in India. It is anticipated that by 2030, diabetes mellitus may afflict up to 79.4 million individuals in India, while China (42.3 million) and the United States (30.3 million) will also see significant
increases in those affected by the disease. (Kaveeshwar, 2014). The current prevalence of Diabetes Mellitus in Chennai, Tamil Nadu, is 11.8%, which is higher than the previous documented prevalence of 10.4 %. (Anusuya and Gopalakrishnan, 2015). Glycemic control forms the primary modality of treatment to ensure protection against organ damage and the multitude of complications that occur in the course of Diabetes Mellitus. (Stolar, 2010). In this setting, it is essential to have reproducible criteria and diagnostic tools to ensure that people with diabetes can keep a check on disease progression, and those at risk are identified as early as possible.

Clinically the routine tests conducted include blood glucose, lipid profile, renal function tests, HbA1c, and insulin assays when required. The RDW (Red Cell Distribution Width) is reported as part of Complete Blood Count, and RDW can be used intermittently and alternately along with HbA1c in monitoring the Glycemic Index in such patients. Increased RDW has also been reported as an early and reliable marker to detect two dreaded complications of Diabetes Mellitus - diabetic nephropathy when associated with an abnormal renal profile and impending cardiovascular complications. RDW values in patients with diabetes mellitus studied alongside healthy subjects were more significant in patients with poor glycemic control. (Nada, 2015). High levels of RDW were associated with increased risk of macrovascular complications in Type 2 Diabetes mellitus. (Sherif et al., 2013)

MATERIALS AND METHODS

Study setting
This study was conducted at Saveetha Medical College Hospital, Thandalam, a multispecialty tertiary care hospital in Chennai. The approval for conducting this study was obtained from the Institutional Ethics Committee prior to the study. The study was conducted during the period from May 2018 to June 2016.

Sample size
Around 610 Patients with Type 2 diabetes mellitus, selected at random from those attending the Diabetic outpatient clinic at Saveetha Medical College and Hospital for their routine checkup, were included in the study.

Study population
Both new and old Patients attending the Diabetic Clinic of Saveetha Medical College Hospital were included in the study. Patients with any anemia or other red cell or hemoglobin disorders, hemolytic disorders including infections like malaria, patients with hypo or hyperthyroidism, congestive cardiac failure, kidney disease, type I Diabetes Mellitus were excluded from the study.

Study data collection
The levels of Glycated Hemoglobin (HbA1c) and RDW (Red Cell Distribution Width) were collected from the patient records. The RDW was noted from the CBC results done using by Automated Hematology Analyzer – Sysmex 6 part hematology analyzer using the flow cytometry method. HbA1c was measured by the Biorad ion-exchange HPLC method. All data were tabulated in a case record form with details of age, gender, RDW, and HbA1c of each patient. The HbA1c was classified into 4 categories (≤ 6.2 %, 6.3-6.8 %, 6.9-7.6 %, > 7.6 %) and the Red cell distribution width into 2 categories (≤ 14.5 and > 14.5) based on the hospital's laboratory reference range.

Statistical Analysis
Analysis of data was performed using SPSS 19 (Statistical Package for Scientific Studies) for Windows. Data were statistically described in terms of mean and standard deviation (SD). Correlation between various variables was done using the Pearson coefficient of correlation equation for linear relation in normally distributed variables. P-value of less than 0.05 was considered statistically significant.

RESULTS AND DISCUSSION

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The mean age of the patients was 50.02 years (SD±13.1). More than one-third of the patients were in the age range of 46-55 years (33.4%, n=204). More than three-fourths of the patients were in the age group 36-65 years (75.2%, n=459). There were fewer patients and at the extremes of ages < 25 years (3.3%, n=20) and > 65 years (10.5%, n=64) as shown in the Figure 2.

The ratio of patients with poor HbA1c levels: acceptable HbA1c levels of glycemic control was 1:4 in the age group 25 years and below. There was a significant correlation between the values of HbA1c with age, with the number of patients increasing as age increased, so did the proportion of individuals with elevated HbA1c levels, as shown in Figure 3.

There was no significant correlation between the values of RDW and age. The mean RDW in this study was 14.24(SD±2.51) and a median value of 13.5%. (Normal RDW <14.5) as shown in Table 1.

The results showed a significant positive correlation between HbA1c and RDW; as HbA1c values increased, there was a concomitant rise in RDW values for the patients. The Chi-Square test showed that there was a significant correlation between the RDW and HbA1c values (p = 0.003, which was less than the 0.05 standard); thus, the null hypothesis can be rejected. The logistic regression analysis with the odd’s ratio of 1.360 showed that for the group of patients with HbA1c values between 6.2-6.8%, there was a particularly strong positive correlation with RDW values, as shown in Table 2.

In Table 3, the left-hand column lists the independent variables and the other columns show the values of (in order): the partial logistic regression coefficients (b), the standard errors of the partial slope coefficients (SE), the z-ratio, the significance level (sig), and the odds ratio/ exponentiated slope coefficient (o.r)

RDW (Red Cell Distribution Width) is an effective predictive index in the evaluation of patients.
Table 1: Frequency table showing the distribution of the study population across all variables

| Characteristic | Frequency (n = 610) | Percentage (%) |
|----------------|---------------------|----------------|
| **Gender**     |                     |                |
| Male           | 323                 | 53             |
| Female         | 287                 | 47             |
| **Age (years)**|                     |                |
| ≤ 25           | 20                  | 3.3            |
| 26-35          | 67                  | 11             |
| 36-45          | 120                 | 19.7           |
| 46-55          | 203                 | 33.3           |
| 56-65          | 135                 | 22.1           |
| > 65           | 65                  | 10.7           |
| **HbA1c (%)**  |                     |                |
| ≤ 6.2          | 235                 | 38.5           |
| 6.3-6.8        | 62                  | 10.2           |
| 6.9-7.6        | 56                  | 9.2            |
| > 7.6          | 257                 | 42.1           |
| **RDW (%)**    |                     |                |
| ≤ 14.5         | 424                 | 69.5           |
| > 14.5         | 186                 | 30.5           |

Table 2: Correlation between the variables & Chi-Square and p values

| Characteristic | Red Cell Distribution Width (%) | Total | \( \chi^2 \) value | p-value |
|----------------|---------------------------------|-------|---------------------|---------|
|                | ≤ 14.5                          | > 14.5|                    |         |
| **Gender**     |                                 |       |                    |         |
| Male           | 247                             | 76    | 323                 | 15.702  | 0.000   |
| Female         | 177                             | 110   | 287                 |          |         |
| **Age (years)**|                                 |       |                    |         |
| ≤ 25           | 15                              | 5     | 20                  | 4.949   | 0.422   |
| 26-35          | 50                              | 17    | 67                  |          |         |
| 36-45          | 80                              | 40    | 120                 |          |         |
| 46-55          | 139                             | 64    | 203                 |          |         |
| 56-65          | 100                             | 35    | 135                 |          |         |
| > 65           | 40                              | 25    | 65                  |          |         |
| **HbA1c (%)**  |                                 |       |                    |         |
| ≤ 6.2          | 163                             | 72    | 235                 | 14.135  | 0.003   |
| 6.3-6.8        | 33                              | 29    | 62                  |          |         |
| 6.9-7.6        | 34                              | 22    | 56                  |          |         |
| > 7.6          | 194                             | 63    | 257                 |          |         |
Table 3: Logistic regression analysis for HbA1c values

| HbA1c (%) | b   | se  | z ratio | sig  | o.r  |
|---------|-----|-----|--------|------|------|
| ≤ 6.2  | 0.308 | 0.203 | 13.742 | 0.003 |
| 6.3-6.8 | -0.382 | 0.308 | 1.536 | 0.215 | 0.683 |
| > 7.6  | -0.688 | 0.291 | 5.579 | 0.018 | 0.503 |
| Model χ² | 13.671 | p value | 0.003 (< 0.05) |
| Pseudo R² | 0.022 | n | 610 |

with diabetic nephropathy or in the presence of other diabetes-associated complications and predicted. The microalbuminuria in patients with type 2 Diabetes Mellitus with a sensitivity of 71.3% and specificity of 66.9 %. (Zhang et al., 2015). These results are similar to our study. Another study done by Yin et al. (2018) revealed a noteworthy association between RDW and the risk of being in poor glycemic control among Type 2 diabetes mellitus subjects, which is on par with the results of our study.

Chowta et al. (2013) studied the hemogram profile of 2 groups of elderly diabetics < 60 years &> 60 years and found that the RDW of patients > 60 years had a higher value than the younger group which was statistically significant (p-value 0.002) which can be correlated with our study.

CONCLUSIONS

In conclusion, this study of 610 patients of Type 2 Diabetes Mellitus attending a specialty clinic in a tertiary care hospital was done to compare the HbA1c values with their RDW values with an aim to discover if there was a positive correlation between the two values. Further, there are several studies done the world over that have concluded that measurement of RDW, which has been established as an inflammatory marker in patients with Type 2 Diabetes Mellitus, is also a predictor of complications such as cardiovascular or renal disease that may be impending or have already affected patients with long-standing diabetes. The results of this study also indicate that measurement of RDW could indicate to the diabetologist, which patient was likely to be manifesting poor glycemic control and therefore require a more thorough evaluation. Hence, RDW, along with HbA1c values when within normal limits, may be considered as markers of glycemic control and, when abnormal, be a prognostic marker for future complications such as cardiovascular disease or diabetic nephropathy in diabetic individuals.

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