Investigation of Neutrophil Lymphocyte Ratio and Blood Glucose Regulation in Patients with Type 2 Diabetes Mellitus

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ABSTRACT

BACKGROUND
Diabetes Mellitus is a major systemic disease. Neutrophil-Lymphocyte Ratio (NLR) is a marker of systemic inflammation and endothelial dysfunction. Our study was undertaken to assess the role of NLR Ratio and Glycaemic Control among subjects suffering from Type 2 Diabetic Mellitus.

METHODS
A cross sectional observational study was conducted by the Department of General Medicine at Sri Deva Raj Urs Medical College from January 2019 to August 2019. A total 205 study subjects who were diagnosed with diabetes type 2 were enrolled in the study. Patients in group A had HbA1c ≤7% (excellent control), group B HbA1c 7.0-9.0% (poor control) and group C HbA1c ≥9% (worst control). Patients were assessed in terms of complete blood count and NLR ratio.

RESULTS
A total of 205 study subjects were analyzed in our study. The Neutrophil Lymphocyte ratio was found to be increasing among subjects with increase in HbA1c Levels. The ratio was found to be 2.79, 3.74 and 5.95 among subjects with HbA1c value of less than 7%, between 7 to 9% and More than 9% respectively. The NLR was also found to be have a significant statistically significant association with HbA1c levels. But in our study, the duration of Diabetes and The HbA1c Values were found to be statistically non-significant. There was a positive correlation between HbA1c and NLR which was statistically significant.

CONCLUSIONS
In our study, the relation between HbA1c Levels and NLR ratio in determining the glycaemic control is well established with positive correlation and statistically significant association. It can be used as a disease monitoring tool during the follow up of diabetic patients.

KEYWORDS
NLR, Type 2 Diabetes, HbA1c
BACKGROUND

Diabetes Mellitus is a major systemic disease affecting nearly 9% of the adult population between the age group of 20 to 79 years of age. Diabetes Mellitus is a metabolic disorder which affects numerous systems. Diabetes is caused by various interactions involving genetic component, lifestyle component and environmental components. \cite{1,2}

Neutrophil-Lymphocyte ratio (NLR) is a marker of Systemic inflammation and endothelial dysfunction. In recent years, it has been reported that the individual components of differential white cell count, specifically the neutrophil and lymphocyte counts, may have clinical utility in predicting disease. An elevated NLR has been shown to be a prognostic indicator in various malignancies. In the literature, many studies have been shown that NLR have predictive value in determining the prognosis of various diseases.\cite{3}

The presence of increased leukocytes in the circulation is an indirect indication for the presence of acute infection in the body. Studies have shown that increased leukocyte counts are reliable markers of systemic inflammation and have diagnostic as well as prognostic value in patients of angina, myocardial infarction, stroke, peripheral vascular disease and micro and macro vascular complication associated with diabetes. Leukocytosis is also said to be directly involved in the pathogenesis of both atherosclerosis and metabolic syndrome.\cite{4,5}

NLR Ratio is considered to be better marker to determine any kind of inflammation involving systemic infection among both the cardiac and non-cardiac disorders. This NLR Ratio is used to predict the outcome of Myocardial infarction and others life treating diseases. The NLR is comparable to the various other inflammatory mediators like C reactive protein, tumour Necrosis Factor and interleukins in identifying the presence of endothelial dysfunction and subclinical infection.\cite{6}

The advantages of NLR is that the test can be performed in all the laboratories, lesser cost, and good reliability. These features makes NLR to be used even in the screening among population to identify any kind of inflammation or endothelial dysfunction.

HbA1c is considered to be one of the most commonly used investigation to monitor the control of the Diabetes and to check the glycaemic control of the Diabetic patients for the duration to 60 to 90 days.\cite{7} HbA1c is also considered to be predictor of the risk for diabetics among pre diabetic subjects. But it lacks to identify the ongoing inflammatory changes in the body, even the endothelial dysfunction with systemic inflammatory changes will be missed. These things could be easily identified and monitored by the NLR Ratio; hence this study was undertaken to assess the role of NLR Ratio and Glycaemic Control among the subjects suffering from Type 2 Diabetic Mellitus.

We wanted to assess the relationship between NLR and different levels of glycemic control in type 2 diabetic patients.

METHODS

A Cross sectional study was conducted by the Department of General Medicine at Sri Devaraj Urs Medical College from November 2017 to September 2019. A total 205 study subjects who were diagnosed of Diabetes type 2 and are on Hypoglycaemic drugs were enrolled for the study.

All patients who were diagnosed with type 2 diabetes mellitus were included in the study. Patients with complications due to diabetes, patients who are on any kind of medication for any disease other than hypoglycaemic drugs and patients who had received anti-inflammatory or immunosuppressive therapy were also excluded from the study.

After overnight fast, venous samples were collected and total leucocyte count (TLC), neutrophil and lymphocyte count were measured by automated haematology analyser. Neutrophil lymphocyte ratios (NLR) were estimated by dividing the absolute neutrophil ratio to absolute lymphocyte ratio. HbA1c level was measured by high performance liquid chromatography using automated ion exchange method.

The patients were classified into three categories based on the HbA1c levels, the HbA1c levels less than 7, between 7 to 9 and more than 9. The patients with HbA1c less than 7 were classified as good Control, between 7 to 9 Moderate Control and level more than 9 were classified as Poor Control of glycaemic Index.

Data were presented as mean ± SD. SPSS software was used for statistical analysis. T test was used for continuous variables and chi square test for categorical variables. ANOVA test was used to compare three groups.

RESULTS

A total of 205 study subjects were analyzed in our study. Majority of the subjects 44.9% were in 56-70 yrs. age group, followed by 31.7% subjects were in 41-55 yrs. age group, 11.7% subjects were in 71-90 yrs. age group, 9.8% subjects were in 26-40 yrs. age group and 2% subjects were in less than or equal to 25 yrs. group. The mean age of the study patients was 65.78 ± 9.8 years. 64.4% of subjects were male and 35.6% subjects were females. In our study we have 205 subjects. Out of 205 subjects 53(25.86%) of the subjects had (HbA1c <7%) Excellent control, 69(33.66%) of the subjects had (HbA1c 7-9%) Poor control, 83(40.48%) of the subjects had (HbA1c >9%) Worst control. In the study among the subjects who had HbA1c less than 7%, 62.3% were Male and 37.7% were female. Among the subjects with
HbA1c between 7 to 9% 73.9% were male and 26.1% were female. In the subjects with HbA1c value of more than 9%, 57.8% were Male and 42.2% were female. Overall in the study 35.6% of the subjects were female and 64.4% were male. P value 0.110, there was no statistically significant difference found between sex and groups.

Among the study subjects 57.8% were Male and 42.2% were female. Overall in the study 35.6% of the subjects were female and 64.4% were male. The HbA1c Values were found to be statistically not significant. The White Blood cell Count was found to be in the range of 6.69 cells per cubic meter to 6.92 cells per cubic meter. The White Blood Cell count and the HbA1c values was found to be statistically not significant. The Neutrophil Lymphocyte ratio was found to be having a strong positive and significant association with the HbA1c levels. The gender composition in our study showed more predominance among male when compared to female which is in contrast to study findings of Sefil et al and similar to the study finding so Jin Jyu Kim et al.

In our study the age was found to be one of significant factor in regulating the Hba1c Values. The age was found to be having a statistical significant association with HbA1c level. The Neutrophil Lymphocyte ratio was found to be increasing among the subjects with increase in HbA1c Levels. The Ratio was found to be 2.79, 3.74 and 5.95 among subjects with HbA1c value of less than 7%, between 7 to 9% and More than 9% respectively. The NLR was also found to be having a significant statistically association with HbA1c levels. The White Blood cell Count was found to be in the range of count of 6.69 cells per cubic meter to 6.92 cells per cubic meter. The White Blood Cell count and the HbA1c values was found to be statistically not significant. The duration of the Diabetic and the control of diabetic has been found to be closely associated. Among the study subjects with good control the mean duration of diabetic was found to be 6.2 years, among poor control the duration was 8.9 years and among Worst control it was 6.6 years. But in our study the duration of Diabetic and The Hba1c Values were found to be statistically non-significant.

There was positive correlation between Hba1c and NLR which was statistically significant. There was positive correlation between HbA1c and WBC which was not statistically significant. There was Negative correlation between HbA1c and Duration of DM in years which was not statistically significant.

**DISCUSSION**

In the present study the neutrophil lymphocyte ratio was found to be having a strong positive and significant correlation with the HbA1c levels. This investigation of identifying the control of diabetics among subjects by estimating the NLR ratio was found to be significant statistically.

The Estimation of HbA1c Levels is said to costly affair and requires specialized equipment's too. Whereas the NLR is very easy to estimate by routine blood test which can be done even in the remote setup of laboratory. It is easy to calculate the NLR by simply dividing the absolute neutrophil count to absolute lymphocyte count. Another Advantage of estimating the NLR Rati is even identifying the subclinical inflammation in the body which leads to change in the neutrophil count in acute and lymphocyte count in chronic condition. Many Author are of the opinion that the NLR cannot be used as inflammatory marker but it’s nowhere less than any inflammatory marker in detecting the Athero sclerotic changes that occurs due to Diabetic Mellitus.

The men age of the study group in our study was 65.78 years of age which is almost similar to the study findings of Mazhar Hussain et al and higher than Sefil et al study. The gender composition in our study showed more predominance among male when compared to female which is in contrast to study findings of Sefil et al and similar to the study finding so Jin Jyu Kim et al.

The association of gender with the glycaemic control was found to be not significant in our group. Similar results where gender plays no role in diabetic control was seen in the study done by Mazhar Hussain et al, Sefil et al and Chittawar et al.

In our study the Neutrophil Lymphocyte ratio was found to be more among the patients with Poor and Worst Glycaemic control and it was also found to be positively correlated to HbA1c levels. The findings of the present study were found to be similar to the studies done by Sefil et al, De Rooiji S R et al and Tong P C et al. The duration of diabetic also found to significantly involved in determining the glycaemic control of diabetic patients in our study. In the study done by Chittawar ET al also found to significant association with duration of Diabetic and the NLR ratio there by its role in the glycaemic control. Whereas in the study done by Sefil et al and Mazhar Hussain et al the duration of diabetic was found to be statistically non-significant. The role of White Blood cells in estimating the glycaemic control was found to be not significant statistically in our study. But the level of WBC was found to be higher among the patients who had worst control of Diabetics. Such kind of Rise of WBC among the patients with Hba1c level of more than 9 was found in the study done by Sefil et al, Ohshita K et al
Khodabandehlou T et al found no association of WBC count with the Glycaemic Control.

The correlation was found to be positive between the levels of NLR, WBC and Duration of Diabetic in our study. In the study done by Tsai JC and Tong PC et al the WBC and HbA1c was found to having a Positive CO relation similar to our study findings. A significant role of NLR Ratio was found to be associated with the Glycaemic control with positive correlation in our study. Similar results were also seen in the study done by Shiny et al, Lou et al, Sefil et al and Huang et al.

CONCLUSIONS

The role of neutrophils, lymphocytes in acute subclinical and even in chronic inflammatory changes involving all systems among humans is well documented. Among diabetic patients the complication involving micro and macrovascular systems is often directly related to the control of diabetes mellitus. Patients with good control have less and bad control have more complications. NLR ratio is a quick, easy and economical laboratory investigation that can estimate the level of glycomic control among humans in accordance with HbA1c levels. In the present study, the findings of HbA1c levels and NLR ratio in determining the glycomic control is well established with positive correlation and statistically significant association.

REFERENCES


