ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Relation between Hemoglobin and HbA1c in Non-GDM Mothers.

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ABSTRACT

Hemoglobin A1c (HbA1c) is the major form of Glycohemoglobin. It correlates with Glycemic control and is elevated abnormally in chronic hyperglycemic diabetic patients. Prior studies state that pregnancy significantly alters the HbA1c levels and the erythrocyte turnover (anemia) also affects HbA1c levels. This study was designed to assess the relationship between the HbA1c concentration and the Hemoglobin levels among non-diabetic pregnant mothers. This is a descriptive cross sectional study. A total of 50 non diabetic pregnant mothers were selected and divided into two groups based on the Hemoglobin levels. Group A with Hemoglobin less than 10gms% and Group B with Hemoglobin more than 10gms%. The Hemoglobin level in both the groups was compared with their HbA1c levels along with the Fasting and Postprandial blood sugar, BMI and Age. This study showed significantly raised HbA1c levels among anemic group (5.6±0.43) when compared to normal group(5.1±0.46) with Pearson's correlation r = -0.5 (P=0.000). Our study shows that in Non-GDM mothers with anemia, have an increased HbA1c levels and that precautions should be taken while interpreting the Glycemic status and control based on HbA1c levels.

Keywords: Glycosylated Hemoglobin, Hyperglycemia, Fasting blood sugar.

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ISSN: 0975-8585

INTRODUCTION

Diabetes mellitus is a syndrome of impaired carbohydrate, protein and fat metabolism caused by either lack of insulin secretion or decreased sensitivity of the tissues to insulin [1].

In the past two decades prevalence of Diabetes Mellitus has increased dramatically worldwide. According to the World Health Organization (WHO) Geneva - by the year 2020 the number of prevalent Diabetes cases will increase to 69.7 million [2].

Diabetic care can be maintained by regular monitoring of the glycemic status. A direct relationship persists between the mean blood glucose and the progression of diabetic complication. This shows the importance of regular monitoring of the glycemic status of the individual. Nowadays, Blood Glucose and Glycated Hemoglobin is the most common test used for this purpose [3]. Glycated Hemoglobin, most commonly known as Hemoglobin A1c (HbA1c) is useful clinically, to measure the glycemic status over the past 3 to 4 months. As the name indicates, it is formed by glycation of Hemoglobin. Glycation of Hemoglobin is a non enzymatic, irreversible reaction where the free aldehyde groups of carbohydrates get attached to the free amino groups of the Hemoglobin protein [4]. Approximately 60% of the bound glucose get glycated at the most predominant site which is the N-terminal amino acid valine of the four polypeptide chains of Hemoglobin protein [4,5].

Half of the HbA1c levels in the blood will be formed in the current month of the test, 25% will be formed during the month prior to that and the rest 25% in the previous 2 to 4 months 6,7]. Glycated Hemoglobin shows the average plasma glucose levels for the last 120 days, which is now a well established method to evaluate the blood glucose level [8].

REVIEW OF LITERATURE

Many factors other than blood sugar is said to influence or alter the HbA1c levels especially the conditions that affect the erythrocyte survival such as hemolytic anemia's, hemoglobinopathies, acute or chronic blood loss, pregnancy and uraemia [9-12]. Recent researches have shown that Hba1c levels are altered in conditions like anemia particularly, Iron deficiency anemia. According to the study done by Koga et al., [13] perimenopausal women with iron deficient state have higher HbA1c levels even in the absence of anemia. Brooks et al., [14] Tarim et al., [15] and Coban et al., [16] have all shown increased HbA1c levels in relation to glycemia in patients with Iron deficiency anemia.

HYPOTHESIS

In India, where Iron deficiency anemia is more prevalent, we hypothesized that HbA1c levels are higher in relation to glycemia among subjects with iron deficiency anemia. Since more studies were done among Diabetic and Non-Diabetic males and females, we want to perform the study among pregnant women who are more prevalently anemic and also undergo HbA1c evaluation to determine their glycemic status before being determined as GDM or Non-GDM

ISSN: 0975-8585

(Gestational Diabetes Mellitus).Since GDM mothers may have fluctuating HbA1c levels due to alterations in plasma glucose beyond the effect of iron metabolism, we choose to perform the study among Non-GDM mothers.

OBJECTIVE

To evaluate the HbA1c levels among Non-GDM mothers with Iron Deficiency Anemia (IDA).

MATERIALS AND METHODS

This is a descriptive cross sectional study. Permission from the Institutional Ethical Committee was obtained. Subjects were pregnant women from the OBG – OPD of Sree Balaji Medical College, Chrompet, Chennai, who attended their regular Antenatal check up. We selected 86 Antenatal singleton mothers who were in their second trimester based on the inclusion and exclusion criteria.

Inclusion criteria:

- Mothers in second trimester.
- Aged between 21 to 30 years.
- No previous h/o pregnancy complications.
- Singleton
- First or second gravida.

Exclusion criteria:

- H/o previous pregnancy complications (GDM).
- Family h/o DM.
- Chronic infertility treated.
- Prolonged h/o iron supplementation.
- Known case of iron deficiency anemia.
- K/c/o liver disease, heart or kidney disease, TB epilepsy etc.
- H/o bleeding disorders, blood transfusions.
- H/o previous abortions.

In this cross sectional study, 86pregnant women were selected based on the inclusion and exclusion criteria. Care was taken to check that the mothers have not yet started their oral iron supplementation that is regularly given for antenatal mothers. After obtaining an informed consent from the subjects in their own language, a structured questionnaire was used for collecting data using personal interview method. We collected all particulars regarding the subject's age, height, weight, month of pregnancy etc. Blood was collected using standard techniques. Fasting blood sugar was done followed by Post Prandial blood sugar along with

Hemoglobin and HbA1c. HbA1c was assessed by terbitometric method. Fasting and post prandial blood samples were assessed by GOD-POD (Glucose oxidase - Peroxidase) method. Hemoglobin was assessed by Drabkin's method.

RESULTS

Out of the 86 women, 36 pregnant women were diagnosed to be GDM mothers. Hence, excluding them only 50 pregnant women were taken into account for the study. The general parameters such as height, weight, BMI, Hemoglobin, HbA1c, Fasting blood sugar and post prandial blood sugar were all collected and analyzed. Since we need to correlate the relationship between the Hemoglobin and HbA1c, the mothers were grouped into two groups based on their hemoglobin levels.

As per WHO, the level of Hemoglobin for Anemia among pregnant women (according to Indian standard) is said to be less than 10 gms% (Park's textbook of Preventive and Social medicine, 20th edition, 2009). To evaluate the prevalence of anemia among the mothers, the subjects were divided into two groups based on the hemoglobin levels above and below 10gms%.

Among the 50 antenatal mothers 32(64%) had Hemoglobin below 10gms% (Group A) and 18(34%) mothers had Hemoglobin more than 10gms% (Group B).

Table: Comparing the general parameters among the groups A and B.

VARIABLES	GROUP A	GROUP B
AGE (years)	25.2 ± 4.3	25 ± 3.9
HEIGHT (cms)	155.8 ± 5.8	156.1 ± 4.5
WEIGHT(kgs)	59.2 ± 5.3	61.1 ± 7.2
BMI (kg/m^2)	24.2 ± 1.8	25.4 ± 1.9
FBS (gm/dl)	75.4 ± 7.7	75.2 ± 9.3
PPBS (gm/dl)	106.8 ± 13.5	102.7 ± 14.7
HbA1c (mmol/L)	5.6 ± 0.4	5.1 ± 0.4**
HEMOGLOBIN (gms%)	8.9 ± 0.8	10.4 ± 0.6

In the above table, the mean values with the standard deviation for the general parameters were statistically analyzed, among which the HbA1c and Hemoglobin showed significant P value of less than 0.05 using "t" test for independent variability.

The following bar chart shows that the HbA1c levels are higher among the group A mothers compared to the group B mothers.

ISSN: 0975-8585

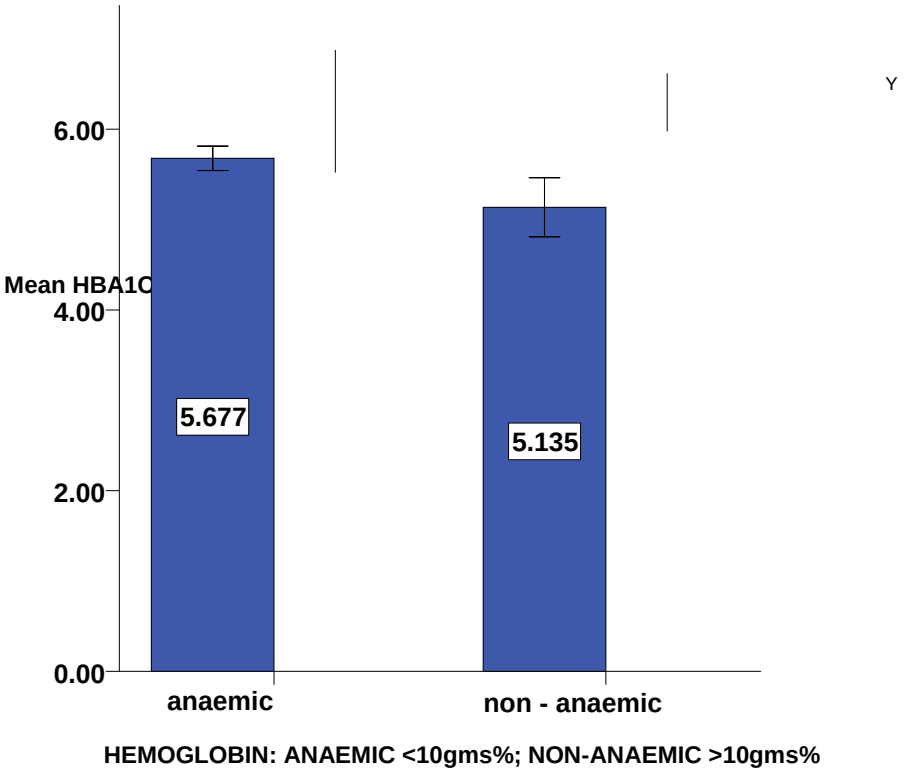
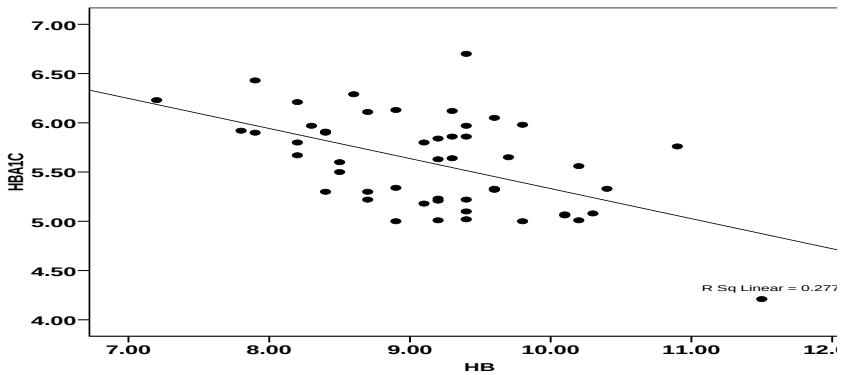


Figure 1: Diagram showing the mean HbA1c levels among the anaemic and non-anaemic groups.

To understand the correlation between Hemoglobin and Hba1c, we compared the parameters using Pearson's co-efficient ratio. The following graph shows the correlation.
r = -0.5 (P=0.000)

Graph 1: Represents correlation between HbA1c and Hb.



In the above graph, the Pearson's co-efficient ratio shows r=-0.5, stating that there was an inverse relation between the Hba1c and Hemoglobin, particularly with Iron deficiency anemia.

DISCUSSION

Nowadays estimation of HbA1c level has become a standard investigation along with the OGTT (oral glucose tolerance test) to determine whether the antenatal mother has Diabetes or not. This HbA1c can particularly be an important tool in identifying the related risks for the mother and fetus. We now know that Hba1c is because of the glycation of the Hemoglobin. The glycated hemoglobin formation is directly proportional to the glucose concentration in the blood. This glycation is irreversible and remains the same till the entire life span of the erythrocytes. Hence, conditions that alter the erythrocyte cycle and its turnover play a major role in altering HbA1c levels.

The parameters that would alter HbA1c levels are commonly a variety of systemic conditions like dyslipidemia, malignancies, liver cirrhosis, various medications and also anemia such as Hemolytic anemia, iron deficiency anemia, presence of carbamylated Hemoglobin in uremia, pregnancy and so on [17,18].

Iron deficiency anemia is one of the most common nutritional deficiencies worldwide, nearly 50% of the world population is affected by Iron deficiency anemia [19]. It is more prevalent among middle and low income groups compared to high income groups. Indian women also come under the same category and particularly pregnant mothers.

During antenatal checkup, HbA1c along with OGTT helps to classify the pregnant mothers as GDM and Non-GDM for the need to start treatment and for the need to avoid maternal and fetal complications. Recent researches have stated that HbA1c levels do alter with condition such as anemia, particularly iron deficiency anemia which is more prevalent among Indian women.

One of the initial study regarding this correlation was done by Brooks etal [14]. He studied 35 non-diabetic but iron deficiency anemic subjects for their Hba1c levels before and after Iron supplementation. They identified that HbA1c was elevated before Iron supplementation and decreased after treatment with the same. The mechanism was unclear but proposed it to be that in Iron deficiency anemia, the quaternary structure of the Hb molecule was altered due to absence of iron and thus the glycation occurred more readily in the globin chain.

Another study done by Sluiter et al, [20] claimed that the hemoglobin that gets glycated is irreversible and hence the concentration of glycation in a single erythrocyte will remain in it and will also increase linearly with the cells age. If the condition extends for long, the erythrocyte production comes down leading to increased life span of the existing erythrocytes and ultimately this leads to elevated HbA1c.

These above said findings matched with Zuberi et al, [21] who stated in their study that HbA1c is not only raised in Iron deficient Diabetic patients but also in non-diabetic anemic patients.

There are also studies that suggested no particular difference in HbA1c among anemic and non-anemic subjects. They include the studies done by Mitchel et al, [22] Heyningen et al, [23] and Hansen et al, [24] who proved from their study that Iron deficient anemia does not have an effect on HbA1c.

In our study again we found an increased HbA1c levels among mothers with Iron deficient anemia compared to the mothers without anemia with their Fasting and post prandial sugar levels commonly normal in both the groups.

Our study parallels the study done by Coban et al [16] and El-Agouza et al [25] both assume that the elevated HbA1c among iron deficiency anemia subjects is due to the fact – if serum glucose remains constant, decrease in the hemoglobin concentration might lead to an increase in the fraction of glycation.

Even though our study closely relates the above findings, the subjects recruited in our study are pregnant women compared to the previous studies. It has been stated that in pregnancyHbA1c levels are substantially reduced compared to non-pregnant women [26-28]. If the above study is taken into consideration, an elevated HbA1c levels among pregnant women with iron deficiency anemia proves that the deficient iron status plays a role in elevating the HbA1c level. Such elevated levels may alter the interpretation of the glycemic status in individual's particularly pregnant women.

In our study we did not do any confirmatory tests for Iron deficiency anemia, as it is the most common type of anemia prevalent particularly in women population. Moreover the iron status can be more precisely evaluated using serum ferritin, Total iron binding capacity, serum iron, Hematocrit and so on. But again the above studies were not executed. The study group was also comparatively smaller.

Further studies should be done to identify the level or the rate at which the erythrocytes alter their life span based on the iron status would help to unravel the correlation between HbA1c and body iron.

CONCLUSION

From this study, we put forth the concept that based on the above mentioned findings, caution should be taken while interpreting the glycemic status of pregnant mothers with iron deficiency anemia by performing HbA1c.

ISSN: 0975-8585

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