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Hb A_{1c} in Pregnancy

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Introduction and Historical Background of Hb A_{1c}

Hb A_{1c}, is a glycated haemoglobin formed by the glycosylation of haemoglobin. The term 'glycosylated' was used initially, but it has been pointed out that this term strictly refers to glycosides. Therefore, the Joint Commission on Biochemical Nomenclature has proposed that the term 'glycation' is appropriate for any reaction that links a sugar to a protein, or in the particular case of a reaction with haemoglobin, the term 'glycated haemoglobin' [1]. Its value represents the glycaemic status of a person over the last two to three months [2].

According to the American Diabetes Association (ADA) Guidelines 2007, the value of Hb A_{1c} should be kept below 7% in all diabetics and according to the same guidelines, Hb A_{1c} is now referred to as A_{1c} [3]. Hemoglobin A_{1c} was first separated from other forms of hemoglobin by Huisman and Meyering in 1958 using a chromatographic column [4].

In 1969 Glycated haemoglobin (Hb A_{1c}) was initially identified as an "unusual" haemoglobin in diabetic patients by Samuel Rahbar, then he noticed a significant increase in the level of HbA_{1c} in diabetes [5]. Another cross sectional study conducted later by Rahbar et al. at Tehran University found a similar abnormality in 57 diabetic patients [6].

After that discovery, numerous small studies were conducted correlating the HbA_{1c} level to the blood glucose level resulting in the idea that HbA_{1c} could be used as a positive objective factor to measure the glycaemic control. In a larger study of diabetic patients, Trivelli et al found a two-fold increase of Hb A_{1c} over values observed in non-diabetic subjects [7].

Thus, by the mid 1970s, it was clear that HbA_{1c} is elevated in humans with diabetes mellitus, although the mechanism of this abnormality was not understood. In 1975, Bunn et al. [8] described the reactions that lead to formation of HbA_{1c} so the nature of the chemical reaction had been explained. Glycation, is a spontaneous non-enzymatic reaction in which glucose binds covalently with haemoglobin at amino terminal of the globin chain. In 1976 Anthony Cerami proposed the idea to use HbA_{1C} level for monitoring the degree of control of glucose metabolism in diabetic patients, then described Hb A_{1C} as a useful mean for monitoring the glycaemic control in diabetic patients [9]. Hb A_{1c} was introduced into clinical use in the 1980s and subsequently has become an important test in Clinical practice [10].

Hb A_{1c} and Gender

Faerch et al. [11] and Gulliford et al. [12] both found somewhat higher levels of HbA_{1c} in men compared to women [11,12], but other studies found no sex-related differences in Hb A_{1c} [13,14]. In women, Hb A_{1c} levels rose particularly at the age of menopause but the use of oral contraceptives or oestrogens made no difference [15].

In Khartoum state at 2016 Ali et al. [16] performed a Cross-sectional study on 20 non-diabetic adult males of ages between 35-45 years and found a mean Hb A_{1c} of 3.8 % 1.17 with a range of (1.2%-5.4 %). Another cross-sectional study also done in Khartoum state at 2016 by Fadul et al. [17] on 20 non-diabetic adult females, their ages was between 35-45 years and found a mean Hb A_{1c} of 3.43 % 1.17 with a range of (1.4-5.3%).

Hb A_{1c} and pregnancy

Diabetes in pregnant women is associated with increased occurrence of both fetal and maternal adverse events, including macrosomia, congenital malformations, spontaneous abortion, perinatal mortality, and preeclampsia [18,19]. The close relationship between the development of such complications and maternal hyperglycemia has been widely documented. Several studies have also shown that strict glycemic control before conception and throughout the gestational period can improve the outcome of pregnancies in women with diabetes, reducing the risk of complications to a rate similar to that found in uncomplicated pregnancies [20-22].

As a consequence, the improvement of glycemic control is considered a major topic in the management of pregnancies complicated by diabetes. Nielsen et al. [23] performed a case control study in Copenhagen, Denmark at 2004 , on 100 healthy pregnant women without previous gestational diabetes (early pregnancy group). A late pregnancy group of 98 healthy pregnant women in week 33 (range 28-37) , the non pregnant control group consisted of 145 healthy women aged 30 years. The result showed that HbA_{1c} was significantly decreased early in pregnancy and

further decreased in late pregnancy compared with age-matched nonpregnant women. The normal range of HbA_{1c} was 4.7-6.3% in nonpregnant women, 4.5-5.7% in early pregnancy, and 4.4-5.6% in late pregnancy.

Mosca et al. [24] conducted a study in Italy and found the HbA_{1C} reference intervals were 4.0%-5.5% for pregnant nondiabetic women and 4.8%-6.2% for nonpregnant controls. The HbA_{1C} results for nondiabetic pregnant women at different gestational periods were 3.8-5.5% at 15-24 weeks, 4.0-5.5% at 25-27 weeks, and a small but significant increase in HbA_{1C} values at 28-36 weeks, 4.4-5.5%.

O'Connor et al. [25] stated that because the pregnant women are younger and the fasting blood glucose increases over age, the relatively older, healthy non-pregnant women may have high Hb A_{1c}. Also, they reported that the lifespan of red blood cells reduces in pregnant women (including those with diabetes mellitus), resulting in reduction in $HbA_{1c.}$

O'Kane et al. [26] proposed that the reference range of HbA_{1C} is 4.1-5.9% in pregnant women without DM, and in the first, second and third trimesters, the level of HbA_{1C} was 5.1%, 4.9% and 5.0%, respectively. Shobha et al. [27] performed a study to measure glycosylated hemoglobin values in nondiabetic pregnant women in the third trimester and found HbA_{1C} values in the third trimester of pregnancy ranged from 4.5% to 6%.

In 2011 Ismail et al. [28] performed A descriptive, cross sectional study in Yastabsheron obstetric hospital at Khartoum state capital of Sudan to estimate the concentration of Hb A_{1c} in apparently healthy 90 pregnant Sudanese women as well as in apparently healthy 30 non pregnant Sudanese women, which showed that, the mean concentration of the Hb A_{1c} in pregnant group was (4.407±1.044) % in the first trimester, (4.797±0.621) % in the second trimester and (4.823±0.616) % in the third trimester, and (5.660 ±0.461%) in control group with a P value of 0.00, indicating the highly significant difference between the two groups.

In 2017 Hussein et al. [29] performed a study aimed to compare the platelets indices in pregnant women with and without Gestational DM and to evaluate the relationship between Mean Platelets Volume MPV and Hb A_{1c}. They found that MPV value was significantly higher in GDM group than normal pregnancies. Moreover, there was a positive correlation between MPV and HbA_{1c} values.

In 2017 Abass et al. [30] performed a cross sectional study aimed to correlate the Glycated hemoglobin and red blood cell indices in non-diabetic pregnant women, they concluded that a significant positive correlation between Hb A_{1c} value with Hb, Hct, and MCHC and there was no significant correlation between Hb A_{1c} and other RBCs parameters.

In 2017 Siddig et al. [31] performed a study in Sudanese healthy pregnant ladies and found The mean value of HbA_{1c} in normal pregnancy was found to be 4.37% with a range of (2.8%-5.5 %). There was no correlation between normal FBG, Hb level, daily caloric intake, age, PH. of DM, PH. of GDM, family history of DM and the level of Hb A_{1c}. According to this study the mean value of Hb A_{1c} in Sudanese healthy pregnant women is 4.37 found within the normal Sudanese values of HbA_{1c}. HbA_{1c} is lower in the third trimester compared to first trimester.

In pregnancy the pregnant mother undergoes significant anatomical and physiological changes in order to nurture and accommodate the developing foetus and prepare the mother for labor and be ready delivery [32]. In a normal pregnancy, between 6 to 10 weeks, there is a decrease in the fasting blood glucose and this continues throughout pregnancy [33]. For the previous 30 years, investigators have attempted to determine whether the glycated hemoglobin A_{1c} (Hb A_{1c}) level during pregnancy may be used as a screening or diagnostic test for gestational diabetes (GDM) [34-35].

One of the studies says the pregnant women had a low Hb A_{1c}, particularly in the first trimester of pregnancy. This might implicate that for prevention of congenital malformations and macrosomia in diabetic pregnant women and HbA1C should be below 5% in the first trimester of pregnancy and below 6% in the third trimester [36-39].

The more recent studies have indicated that the Hb A_{1c} level during pregnancy may predict GDM in women at high risk for diabetes. The New Zealand Ministry of Health recommends that an Hb A_{1c} test be offered to all pregnant women at booking as part of the first antenatal blood screen to detect GDM [40]. The results provided supporting evidence for recent reports that recommended measured the Hb A_{1c} level at early pregnancy as one of blood screening base line tests, and follow the level especially in high risk women.

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