

Hemoglobin A_{1c} as an Index of Long-term Blood Glucose Regulation in Diabetic Pregnancy

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SUMMARY

To evaluate hemoglobin A_{1c} (Hb A_{1c}) as an indicator of prolonged glucose control in pregnant diabetics, four groups of subjects were studied—16 pregnant diabetic, 13 pregnant nondiabetic, 12 nonpregnant diabetic, and 18 healthy control subjects.

Hb A_{1c} was significantly lower in the pregnant diabetic than in the nonpregnant diabetic subjects, $7.8\% \pm 1.6$ vs. $9.9\% \pm 1.9$ (mean \pm SD). No difference was present in the nondiabetic groups ($4.0\% \pm 0.7$ vs. $4.3\% \pm 0.8$, respectively). Hb A_{1c} correlated significantly with the average glucose concentrations of the preceding 60 days in both diabetic groups, suggesting that the lower concentration of Hb A_{1c} in pregnant as compared with nonpregnant diabetic patients was because of better control of blood glucose. This was also borne out by the average of fasting glucose levels being 6.1 ± 1.7 mmol/L in the pregnant diabetic and 10.7 ± 2.2 mmol/L in the nonpregnant diabetic subjects. *DIABETES* 28:694–696, July 1979.

In management of diabetic pregnancy, one of the principal aims is to obtain blood glucose concentrations as close to normal pregnant values as possible.

The importance of optimal glucose regulation for the prognosis of the fetus is widely accepted.^{1,2}

This goal often requires hospitalization for a substantial part of pregnancy, and, as with diabetics in general, the problem remains as to whether the glucose control during the outpatient periods was strict enough or better regulation may be obtained.

With hemoglobin A_{1c} (Hb A_{1c}), a tool in monitoring the

degree of glucose control is suggested Hb A_{1c} in the nonpregnant diabetics was shown by several groups of investigators to vary with the integrated blood glucose concentration over time.^{3–6} Schwartz et al.⁷ found lower levels of Hb A_{1c} in pregnant diabetics than in nonpregnant diabetics. In this situation, the lowered values might be because of either better control or an inhibitory effect of pregnancy itself on the formation of Hb A_{1c}. In order to distinguish between these two possibilities, we decided to investigate the usefulness of Hb A_{1c} as an index of prolonged blood glucose control during pregnancy.

MATERIALS AND METHODS

Four groups were studied: (a) 16 insulin-dependent pregnant diabetics (PD), with a known duration of diabetes from a few weeks to 34 yr, were admitted in the third trimester for control and regulation. In two of these patients, diabetes was diagnosed during pregnancy, and both remained insulin dependent postpartum. The diabetics were treated according to the scheme of Pedersen¹ with two insulin injections and five meals a day. One, however, took only one insulin injection a day. (b) 13 pregnant nondiabetics (P-non-D), admitted for various causes in third trimester. (c) 12 nonpregnant, ambulatory, insulin-dependent diabetics (non-PD) with a duration of diabetes from 2 to 25 yr examined at their routine visits to the diabetes clinic. (d) 18 healthy, ambulatory, nonpregnant nondiabetics (non-P, non-D).

Hb A_{1c} was determined once in all subjects by the method of Trivelli et al.⁸ as modified by Schwartz et al.⁷ using Bio-Rex 70 as an ion exchange resin. Capillary blood glucose measurements were performed with the Technicon Auto-Analyzer.⁹ The non-D, non-P had fasting values not exceeding 4.6 mmol/L and the postprandial glucose in the P-non-D was below 5.6 mmol/L.

In the PD, blood glucose was measured fasting and postprandially at an average of 29 occasions during the preceding 120 days. In the non-PD, fasting glucose was determined weekly during the preceding 60 days only.

The statistical methods used were nonparametric: a

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Mann-Whitney's test for nonpaired samples was used to determine the difference between groups, and Spearman's r_s was used for correlation analysis.¹⁰

RESULTS

The Hb A_{1c} and average glucose values of the same day are presented in table 1. Hb A_{1c} levels were higher in both diabetic groups as compared with the corresponding non-diabetics, $7.8\% \pm 1.6$ vs. $4.0\% \pm 0.7$ (mean \pm SD) ($P < 0.01$) for the pregnant group and $9.9\% \pm 1.9$ vs. $4.3\% \pm 0.8$ for the nonpregnant group ($P < 0.01$). However, Hb A_{1c} levels in the pregnant diabetics were lower than those of the nonpregnant diabetics ($P < 0.05$). No significant difference was found in the nondiabetic groups.

As indicated in table 2, the average fasting glucose levels during the 60 days preceding the Hb A_{1c} determination in the PDs were lower than the non-PDs, $6.1 \text{ mmol/L} \pm 1.7$ vs. $10.7 \text{ mmol/L} \pm 2.2$ ($P < 0.01$). In both diabetic groups a significant, positive correlation was found between the fasting blood glucose level and Hb A_{1c} concentrations, and there was no significant difference between the slopes of the regression lines. Figure 1 indicates the regression line that the two diabetic groups had in common.

In the PDs, the correlation between glucose values and Hb A_{1c} was better for postprandial than for fasting glucose levels. Extending the time span of previous glucose monitoring from 60 to 120 days did not increase correlations for either fasting or postprandial values. No correlation was found between Hb A_{1c} and both the average glucose levels of time periods shorter than 60 days and the glucose values on the day of the Hb A_{1c} determination. In the P-non-Ds, however, postprandial blood glucose correlated well to Hb A_{1c} of the same day ($r_s = 0.58$, $P < 0.05$).

DISCUSSION

In this paper, the level of Hb A_{1c} has been shown to vary with the average glucose levels of the preceding two months. There was no significant difference between the degree of correlations of blood glucose to Hb A_{1c} in the two diabetic groups, pregnant and nonpregnant. The decreased levels of Hb A_{1c} during pregnancy thus seems to be due to lowered blood glucose levels and therefore an effect of therapeutic effort, rather than due to an inhibitory effect of pregnancy, itself, on Hb A_{1c} formation. It is known that hemoglobin F(Hb F) coelutes with Hb A_{1c} using Bio-Rex 70 columns.

TABLE 1
Hb A_{1c} and average blood glucose concentrations of the same day

	Pregnant diabetics	Non-pregnant diabetics	Pregnant non-diabetics	Non-pregnant non-diabetics
n	16	12	13	18
Hb A _{1c} (% of total Hb \pm SD)	7.8 ± 1.6	9.9 ± 1.9	4.0 ± 0.7	4.3 ± 0.8
Glucose (mmol/L \pm SD)				
Fasting	5.4 ± 1.8	11.4 ± 3.2	—	4.1 ± 0.3
Postprandial	6.8 ± 3.0	—	4.0 ± 0.6	—

TABLE 2
Mean of blood glucose concentrations measured within 60 days before Hb A_{1c} determination in pregnant and nonpregnant diabetic subjects and correlation to Hb A_{1c}

	Pregnant diabetics (n = 16)			Non-pregnant diabetics (n = 12)
	Fasting (f)	Post-prandial (p)	Total (f + p)	
Average glucose (mmol/L \pm SD)	6.1 ± 1.7	6.9 ± 1.9	6.5 ± 1.8	10.7 ± 2.2
r_s	0.51	0.62	0.63	0.74
P value	<0.05	<0.01	<0.01	<0.01

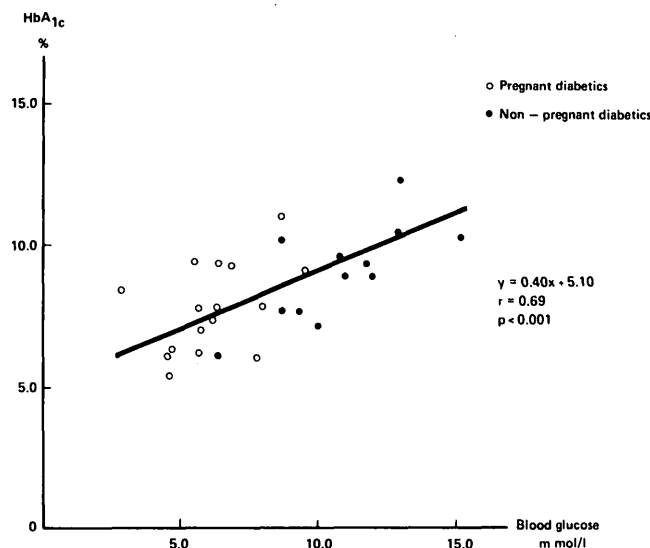
However, in the study of Rucknagel and Chernoff,¹¹ the level of Hb F decreased during pregnancy and in only 2 of 91 pregnancies did Hb F exceed 0.5% in the third trimester. For this reason, no correction for Hb F was made in this study.

No correlation was found between Hb A_{1c} and periods of glucose monitoring shorter than 60 days. This finding is in agreement with a recent study by Leslie et al.¹²

The postprandial blood glucose values correlated better to Hb A_{1c} than did the fasting ones. This might indicate that the postprandial values are a more physiologic expression of average blood glucose levels during the whole day. In the P-non-Ds, the single-determined postprandial blood glucose level showed a significant correlation to the simultaneously determined Hb A_{1c}. This observation is in keeping with the result of Ditzel et al.¹³, showing a correlation between the level of Hb A_{1c} and the area under the glucose tolerance curve in borderline diabetics, again indicating the possibility that postprandial values may be a better expression of the glucose impact in everyday life as expressed by Hb A_{1c}.

The importance of Hb A_{1c} determination in the control of diabetic pregnancy is that, by comparing the Hb A_{1c} values during inpatient and outpatient periods, we can assess

FIGURE 1. The correlation between the mean blood glucose concentration measured within 60 days and the Hb A_{1c} concentration in pregnant and nonpregnant diabetic subjects.



whether glucose regulation during the outpatient periods has been satisfactory, or, whether additional therapeutic efforts are necessary.

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