Carbohydrate Metabolism in African Women with Twin Pregnancy

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Carbohydrate metabolism was evaluated in 21 twin pregnancies and in 21 women with singleton pregnancies. The groups were matched for age, weight, parity, and period of gestation. A 100-g oral glucose tolerance test was performed on all 42 subjects. No significant differences in venous plasma glucose responses were found between singleton and twin pregnancies. The only significant difference between the insulin responses of the two groups was a lower plasma insulin concentration at 60 min in the twin group ($P < 0.03$). DIABETES CARE 7: 72–74, JANUARY–FEBRUARY 1984.

There have been few reports in the literature examining carbohydrate metabolism in twin pregnancies. MacGillivray et al.[1] and, more recently, Dwyer et al.[2] state that chemical diabetes is more common in women having a twin pregnancy and suggest that a glucose tolerance test be performed in the last trimester in all such patients.

On the other hand, Spellacy et al.,[3] in a study of 24 women with twin pregnancies and 24 matched controls, did not find a higher incidence of glucose intolerance in women with twin pregnancies using a 25-g intravenous glucose tolerance test (IVGTT). A similar study, performed at King Edward VIII Hospital (Durban, South Africa), using a 50-g oral glucose load confirmed the findings of Spellacy et al.[4] Although no significant differences in venous plasma glucose or insulin profiles were found between patients with singleton and twin gestations in our previous study, there was, however, a trend to hypoinsulinemia in the twin pregnancies. Because of this trend to lower insulin levels in twins and the fact that the 50-g glucose load might not have been an adequate stimulus to bring out a difference in the two population groups, the present study of carbohydrate metabolism in twin pregnancy was designed using a 100-g oral glucose load instead.

PATIENTS AND METHODS

Informed consent was obtained from 42 African patients of negroid stock in the last trimester of pregnancy. The women were attending the antenatal clinic of King Edward VIII Hospital (Durban, South Africa) and were quite sure of the date of their last menstrual period. Twenty-one patients had the diagnosis of twin pregnancy confirmed by ultrasound after multiple pregnancy was suspected clinically. The 21 patients with twin pregnancies were individually matched for age, parity, weight, and gestational age with 21 patients with singleton pregnancies. None of the patients in the study was on any form of drug therapy except prophylactic iron and vitamin therapy. No patient had any medical disorders or features that would require that a glucose tolerance test be performed. The patients were encouraged to partake in a high-carbohydrate diet for at least 1 wk before the glucose tolerance test was performed.

After an overnight fast, venous blood samples were withdrawn from a peripheral vein in which a butterfly cannula was inserted. The cannula was flushed and kept open with a solution of heparinized saline. Venous blood samples were taken for glucose, insulin, and human placental lactogen (HPL) estimations initially. A 100-g glucose load dissolved in 300 ml H_2O was then given orally to the patient and blood samples withdrawn for glucose and insulin estimations at half-hourly intervals for a period of 3 h.

The samples for glucose were taken in tubes containing sodium fluoride and potassium oxalate, while the specimens for insulin and HPL were taken in tubes containing no preservative. Plasma glucose was measured by the ferricyanide method on an autoanalyzer.[5] HPL was assayed in duplicate by radioimmunoassay techniques (Amersham, United Kingdom). Serum insulin levels were measured in duplicate by a radioimmunoassay in which the antibody was coupled to a solid phase (Pharmacia, Uppsala, Sweden). A control was incorporated in each assay undertaken. The intra- and interassay coefficients of variation for all three assays were <5% and <10%, respectively.

The areas under the glucose and insulin curves were com-

TABLE 1
Characteristics of the two groups in the study

	Singleton	Twin	
Age (yr)*	28.8 ± 7.2	29.0 ± 7.1	P > 0.20
Parity†	3.0 (0–10)	3.0 (0–9)	P > 0.3
Weight (kg)*	73.1 ± 11.8	73.6 ± 12.9	P > 0.20
Gestational age (wk)*	33.2 ± 3.3	33.7 ± 3.1	P > 0.20
HPL (μg/ml)*	5.1 ± 1.6	8.2 ± 1.8	P < 0.001

*Results expressed as mean ± SD, the two groups compared using Student's *t* test.
†Results expressed as median (minimum-maximum), the two groups compared using the Mann-Whitney U test.

puted according to Chiles and Tzagournis.[6] The data for each set of parameters were subjected to a goodness-of-fit test to determine if the data were normally distributed (parametric) or not; parametric data were analyzed by the unpaired Student's *t* test, while nonparametric data were analyzed by the Mann-Whitney U test. All results are expressed as mean ± 1 SD unless stated otherwise.

RESULTS

One patient in the twin-gestation group was found to be frankly diabetic according to O'Sullivan's criteria (1964). She was not included in any further comparative analyses. Thus, at King Edward VIII Hospital (Durban, South Africa) a total of 47 women with twin pregnancies (including a previous study)[4] have been studied with an OGTT and only one (2.1%) had gestational diabetes. The characteristics of the two population groups are given in Table 1. The groups were of similar age, parity, weight, and gestational age. However, plasma HPL levels were significantly higher in women with twin pregnancies than in women with singleton pregnancies (Table 1).

Analysis of the blood glucose results is shown in Table 2. There was no significant difference between the two groups throughout the period of testing. As well, there was no significant difference in the area under the glucose curve between the two groups. A comparison of the plasma insulin responses is depicted in Table 3. Although at most points the values tended to be lower for the twin-pregnancy group, these differences did not attain significance except at 60 min ($P < 0.03$). In addition, the areas under the insulin curve were not significantly different between the two groups.

DISCUSSION

At King Edward VIII Hospital (KEH, Durban, South Africa), where the incidence of multiple pregnancies is very high (one in 26 pregnancies[7]), the clinical impression is that the frequency of carbohydrate intolerance in twin gestation is not very high. The present study and a previous study[4] at KEH confirm this clinical impression. In the two studies, there

TABLE 2
Analysis of the blood glucose levels during an oral glucose tolerance test (mmol/L)

Time (h)	Singleton		Twin
Fasting	3.7 ± 0.5	NS	3.5 ± 0.7
0.5	6.0 ± 1.1	NS	5.9 ± 1.4
1	6.3 ± 1.5	NS	6.6 ± 1.2
1.5	6.3 ± 1.6	NS	6.4 ± 1.3
2	5.9 ± 1.3	NS	5.9 ± 1.6
2.5	5.3 ± 1.1	NS	5.4 ± 1.2
3	4.7 ± 1.3	NS	4.4 ± 1.3
Area under glucose curve (mol/min)	1.0 ± 0.2	NS	1.0 ± 0.2

Results expressed as means ± SD.
Group compared using Student's *t* test.
NS, not significant ($P > 0.05$).

was only one diabetic patient in 47 women with twin gestation (2.1%). Although the incidence of diabetes in the African patient with a singleton pregnancy attending KEH is not known, the figure of 2.1% is much lower than that quoted for twin gestation by Dwyer et al.[2] They conducted a retrospective study on 288 women with twin gestation and 20,030 women with singleton pregnancies. The incidence of gestational diabetes was 5.6%, which was more than twice that of singleton pregnancies (2.5%). They also found that the fasting plasma glucose value in twins was significantly lower than that in singletons ($P < 0.001$), but that the 1-, 2-, and 3-h levels were not significantly different. This finding of a lower fasting plasma glucose level in women with twin gestation accords with the findings of Spellacy et al.[3] However, the present study, Naicker et al.,[4] and Campbell and MacGillivray[8] have failed to demonstrate significantly lower fasting plasma-glucose levels in the twin gestation group as compared with the singleton pregnancies. In the only other

TABLE 3
Analysis of plasma insulin during oral glucose tolerance test (μU/ml)

Time (h)	Singleton		Twin
Fasting	13.6 ± 9.8	NS	13.0 ± 4.5
0.5	68.1 ± 46.2	NS	72.4 ± 57.5
1	74.8 ± 34.1	*	58.3 ± 33.8
1.5	69.7 ± 32.9	NS	61.7 ± 38.1
2	63.0 ± 31.8	NS	51.2 ± 36.6
2.5	54.1 ± 34.4	NS	43.2 ± 20.7
3	37.6 ± 26.2	NS	36.0 ± 25.8
Area under insulin curve (mU/min)	10.1 ± 4.5	NS	9.2 ± 5.1

Results expressed as mean ± SD.
Groups compared by the Mann-Whitney U test.
NS, not significant ($P > 0.05$).
*$P < 0.03$.

report in which the insulin response to glucose was studied, a trend to lower insulin levels in the women with twin gestation was noted, which only reached significance 15 min after the i.v. glucose bolus.[3] In accordance with these findings, the present study showed a trend to lower insulin levels, and this only reached statistical significance at 60 min ($P < 0.03$) after the oral glucose load. The lowest plasma level of insulin at 60 min corresponded to the highest plasma glucose level. Fowden,[9] in an elegant study on the effect of twin pregnancy on insulin secretion in the ewe, found that an exogenous glucose infusion stimulated insulin secretion in three groups of ewes. Plasma-insulin concentrations rose with increasing glucose levels in the nonpregnant, singleton-pregnant, and twin-pregnant groups of ewes; however, the insulin levels were much lower in ewes with twins than the other two groups, especially at higher glucose levels. Hence, the response of the β-cells of the pancreas to raised glucose levels was smaller in ewes with twin gestation. These observations show that, although insulin secretion is regulated by the level of glucose during pregnancy irrespective of the number of fetuses, pancreatic β-cell sensitivity to glucose is depressed when the ewe is carrying more than one fetus. However, it should be pointed out that the decreased circulating insulin concentrations in twin pregnancies do not necessarily reflect decreased insulin secretion, since these individuals may also have increased insulin clearance. Since C-peptide levels were not measured and insulin clearance studies were not undertaken, it is not possible to discount the relative contribution of either mechanism in the genesis of the hypoinsulinemia.

It has been suggested that the changed hormonal milieu of pregnancy may be "antagonistic" to insulin or that the peripheral tissues become resistant to insulin action. HPL is regarded by many authors as the major pregnancy factor that causes insulin resistance. The present investigation does confirm that HPL levels in women with twin gestation is significantly higher than that of women with singleton pregnancies ($P < 0.001$), but there was no demonstrable relationship between glucose HPL and insulin profiles.[4] Thus, it would be an oversimplification to hold any one hormone, such as HPL, as being diabetogenic.

In the light of the findings of this investigation and at this stage of our knowledge on carbohydrate metabolism in pregnancy, the routine use of a glucose tolerance test in all women with twin gestation, especially in developing countries with a high incidence of multiple pregnancy, will not be cost beneficial.

ACKNOWLEDGMENTS: This work was supported by the Medical Research Council (South Africa). We thank Prof. S. M. Joubert for his useful criticisms.

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