Glucose tolerance in rural women with pre-eclampsia

M Mammen, G A B Buga, J E Iputo

Objective. To determine the relationship between pre-eclampsia and glucose intolerance among rural women from the Transkei region of South Africa.

Methods. Women with confirmed pre-eclampsia underwent a 75 g, 3-hour oral glucose tolerance test. A control group of normotensive pregnant women were subjected to a similar glucose tolerance test. Pre-eclampsia was defined as blood pressure (BP) of at least 140/90 mmHg occurring for the first time after mid-pregnancy, in association with proteinuria. The control group comprised women with singleton pregnancy and normal BP, with age, parity and gestational age comparable to those of the pre-eclampsia group.

Results. There were 117 subjects in the pre-eclampsia group and 94 in the normotensive pregnancy group. Mean fasting plasma glucose levels in the pre-eclampsia group (3.88 ± 0.05 mmol/l) were similar to levels in the normotensive group (3.97± 0.05 mmol/l, $p = 0.214$). Peak post-load plasma glucose levels in the pre-eclampsia group (5.96 ± 0.12 mmol/l) were similar to levels in the normotensive group (5.71 ± 0.13 mmol/l, $p = 0.180$), and post-load incremental glucose area under the curve in the pre-eclampsia group (4.16 ± 0.21) was similar to that in the normotensive group (3.95 ± 0.21, $p = 0.495$).

Conclusion. Rural women with pre-eclampsia from the Transkei region of South Africa have normal glucose tolerance.

S Afr Med J 2005; **95:** 955-958.

Pre-eclampsia is defined as the development of hypertension with proteinuria in the second half of pregnancy in a previously normotensive woman. It is a disorder peculiar to human pregnancy and is one of the leading causes of maternal and perinatal death in the Transkei region of South Africa. Although extensively investigated, the pathogenesis of pre-eclampsia is still unclear.[1-6] Studies from Pakistan,[7] China,[8] Scandinavia[9] and the USA[10] have suggested that pre-eclampsia behaves like essential hypertension, where there is glucose intolerance associated with insulin resistance.[11-13] But other studies in the Western world and in Africa have shown normal glucose tolerance and absence of insulin resistance in pre-eclampsia.[14-20] This study investigated the glucose tolerance status of pre-eclamptic women in rural Transkei, an area with a high prevalence of the condition.

Methods and materials

Subjects

Subjects were selected from pregnant women with mild to moderate pre-eclampsia admitted to the antenatal ward of Umtata General Hospital, the regional hospital for the Transkei region. Selection was on the basis of blood pressure (BP) ≥ 140/90 mmHg and proteinuria ≥ 1+ (using the urinary dipstick method) at 25 or more weeks' gestation. The following categories of patients were excluded from the study: those with severe pre-eclampsia or impending eclampsia; those with chronic hypertension, i.e. hypertension before pregnancy; those with diabetes mellitus; and those on any medication known to affect carbohydrate or fat metabolism.

Subjects for the control group were selected from pregnant women attending routine antenatal clinics at Umtata General Hospital and the surrounding primary health care centres. Criteria for selection were pregnancy with normal BP (< 120/80 mmHg), no proteinuria, no diabetes mellitus, and not on any medication known to affect carbohydrate or fat metabolism.

Informed consent was obtained from subjects before recruitment into the study. The subjects were counselled and were free to withdraw from the study at any time if they so wished. The study was approved by the Research Ethics Committee of the University of Transkei (now Walter Sisulu University).

Anthropometric measurements

Single measurements of height were done, to the nearest centimetre (e.g. 0.4 was rounded off to 0, whereas 0.5 was rounded off to 1), with subjects wearing underclothes only, barefooted, feet together, back and heels firmly against the upright of the height scale. Weight was measured on a balance scale to the nearest kilogram. The subjects were weighed in their underclothes with no shoes on.

Blood pressure measurement

BP measurements were performed by a single observer throughout the study. Measurements were taken after a 30-minute rest period, and were done on the mid-arm, with the

Department of Medical Biology, Walter Sisulu University, Mthatha, E Cape
M Mammen, PhD

Department of Obstetrics and Gynaecology, Walter Sisulu University, Mthatha, E Cape
G A B Buga, MB ChB, MMed, PhD

Department of Physiology, Walter Sisulu University, Mathatha, E Cape
J E Iputo, MB ChB, PhD

Corresponding author: *M Mammen (mammenm@getafix.utr.ac.za)*

subject seated upright. A mercury sphygmomanometer was used and the Korotkoff phase IV was taken as the diastolic point. BP measurements were performed before the oral glucose tolerance test (OGTT), 24 hours after delivery, and 6 weeks after delivery.

Proteinuria

Random urine samples were analysed for protein using both the urinary dipstick method and laboratory analysis. A dipstick reading of 1+ or more was indicative of proteinuria. A laboratory reading of urinary protein 100 mg/l or more was confirmatory of proteinuria.

Oral glucose tolerance test

All the glucose tolerance tests were performed in the antenatal wards of Umtata General Hospital. All subjects received a standard diet (8 694 kJ/day) the day before the glucose tolerance test. The test was performed at 07h00 after an overnight (10-hour) fast. The subject remained seated throughout the test.

Each subject was given glucose solution (75 g glucose/300 ml water) orally. Venous blood samples were obtained at the following times: 0, 60, 120 and 180 minutes after the ingestion of glucose. Blood samples were drawn into vaccutainer tubes containing potassium oxalate and immediately centrifuged at 3 000 rpm for 5 minutes. The plasma was transported to the laboratory on dry ice and was stored at –70°C until the time of batch analysis. The plasma glucose was measured using the colorimetric, hexokinase glucose-6-phosphate dehydrogenase method using the Beckman glucose reagent kit (Beckman Synchron CX system, Brea, Calif., USA).

Glucose tolerance was evaluated by means of the fasting plasma glucose level, the peak plasma glucose level following ingestion of a 75 g glucose load, and the incremental glucose area under the curve (GAUC), calculated using the trapezoid formula, following ingestion of a 75 g glucose load.

Statistical analysis

Data were expressed as means ± standard deviation (SD). All the anthropometric, biochemical and BP measurements had normal distribution patterns. Intergroup comparison was done using the Mann-Whitney test. All data were processed and analysed using a commercially available statistics software package (STATISTICA).

Results

Anthropometric measurements

One hundred and seventeen subjects with pre-eclampsia and 94 subjects with normal pregnancy were recruited into the study. Table I shows the characteristics of the pre-eclampsia and the normal pregnancy study groups. The study groups were similar in age, parity and gestational age. The pre-eclampsia group had a significantly higher body weight and body mass index (BMI).

There were subtle differences in the lipid profile between the pre-eclampsia and normal pregnancy groups. The fasting serum total free fatty acid concentration in the pre-eclampsia group (0.44 ± 0.02 mmol/l) was similar to that in the normal pregnancy group (0.40 ± 0.03 mmol/l, $p = 0.7$). The fasting serum triglyceride concentration in the pre-eclampsia group (2.32 ± 0.12 mmol/l) was significantly higher than that in the normal pregnancy group (1.86 ± 0.07 mmol/l, $p = 0.042$). The fasting serum high-density lipoprotein concentration in the pre-eclampsia group (0.92 ± 0.03 mmol/l) was significantly lower than that in the normal pregnancy group (1.10 ± 0.04 mmol/l, $p = 0.037$), and the fasting serum low-density lipoprotein concentration in the pre-eclampsia group (3.03 ± 0.13 mmol/l)

Table I. Anthropometric and biochemical profiles of the study groups

	Pre-eclampsia			Normal pregnancy		
Parameter	*N* (%)	Mean	SD	*N* (%)	Mean	SD
Age (years)	117	26.9	8.5	94	25.7	5.9
< 20	27 (23)			15 (16)		
20 - 29	46 (39)			55 (59)		
30+	44 (38)			24 (25)		
Parity	117	2.8	2.4	94	2.5	1.8
Primigravida	56 (48)			38 (40)		
Gravida 2 - 5	42 (36)			48 (51)		
Gravida 6+	19 (16)			8 (9)		
Gestational age (weeks)	117	33.0	3.5	94	33.6	3.9
Weight (kg)	117	74	18.2	94	69	11.8
Height (m)	117	1.57	0.09	94	1.58	0.08
BMI (kg/m²)	117	30.9	7.6	94	28.3	4.8
< 27.3 kg/m² (lean)	37 (32)			47 (50)		
27.3 - 32.3 kg/m² (overweight)	47 (40)			26 (28)		
≥ 32.3 kg/m² (obese)	33 (28)			20 (22)		

BMI = body mass index.

Table II. Anthropometric and biochemical variables by age and study group (mean (SD))

Age group (yrs)	Pre-eclampsia N	BMI (kg/m²)	Fasting glucose (mmol/l)	Peak glucose (mmol/l)	GAUC	Normal pregnancy N	BMI (kg/m²)	Fasting glucose (mmol/l)	Peak glucose (mmol/l)	GAUC
< 20	27	28.7 (8.4)	3.7 (0.4)	5.66 (1.43)	3.8 (2.2)	15	25.7 (3.1)	3.7 (0.4)	5.10 (0.8)	3.1 (1.5)
20 - 29	46	29.8 (4.4)	4.1 (0.7)	6.15 (1.32)	3.6 (1.8)	55	29.0 (5.2)	3.9 (0.5)	6.00 (1.32)	4.0 (2.0)
30 - 39	44	33.9 (9.8)	3.9 (0.5)	6.57 (1.12)	4.4 (1.9)	24	27.4 (3.8)	3.8 (0.4)	5.86 (0.94)	4.2 (2.1)
All	117	30.5 (7.0)	3.9 (0.6)	6.19 (1.31)	4.2 (2.2)	94	28.3 (4.8)	3.9 (0.5)	5.83 (1.19)	3.9 (1.9)

GAUC = glucose area under the curve.

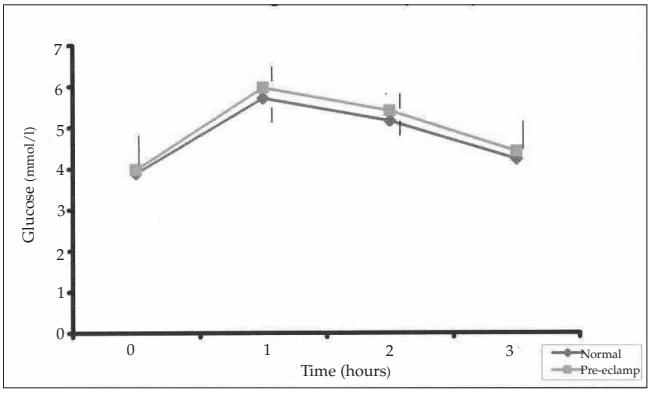

Fig. 1. Glucose levels during the oral glucose tolerance test in the controls v. pre-eclamptics.

was similar to that in the normal pregnancy group (3.06 ± 0.15 mmol/l, $p = 0.85$).

The results of the OGTT are given in Table II and in Fig. 1. The fasting plasma glucose level was similar in both study groups. There was no significant correlation between fasting plasma glucose level and age, parity, or BMI in both study groups.

The OGTT was normal in both study groups. There was no significant difference in the plasma glucose levels at 60, 90 and 180 minutes of the OGTT. The post-loading peak plasma glucose level was similar in both groups. In the pre-eclampsia group, but not in the normal pregnancy group, there was a significant correlation between age and peak plasma glucose level ($r = 0.33$, $p < 0.01$). This correlation was independent of the BMI.

The incremental GAUC, depicted in Fig. 1, was similar in the two groups. In both groups, the GAUC was significantly higher in the fourth decade than in the second decade. In the normal pregnancy group there was a significant positive correlation between GAUC and BMI ($r = 0.21$, $p < 0.05$). This relationship was not evident in the pre-eclampsia group.

Discussion

The present study demonstrated that glucose tolerance was normal in our pre-eclampsia subjects despite the presence of dyslipidaemia. Fasting blood sugar level, the post-load peak glucose level, and the post-load incremental GAUC are markers of insulin sensitivity. All these parameters were shown to be normal in this study, reflecting the relative normalcy of insulin sensitivity in our subjects. Insulin resistance is therefore unlikely to be the main explanation for the relative dyslipidaemia observed in our pre-eclampsia subjects.

The normal glucose tolerance observed in this study is in conformity with findings of other recent studies[14-17] which have shown that pre-eclampsia *per se* is not associated with abnormal glucose tolerance. Abnormal glucose tolerance is observed in the gestational hypertension variant of pregnancy-induced hypertension. In the past, there was lack of uniformity in classifying hypertensive disorders of pregnancy. Often pre-eclampsia and gestational hypertension have been lumped together as different manifestations of the same disease, and studies carried out on the basis of such classification indicated the presence of glucose intolerance in pre-eclampsia.[21,22] But studies that clearly define and separate pre-eclampsia from gestational hypertension demonstrate the difference in glucose tolerance between these variants of pregnancy-induced hypertension, probably pointing to distinctive pathophysiology.[15]

Conclusion

There is normal glucose tolerance in pre-eclamptic rural black women from the Transkei region of South Africa.

Funding for the study was received from the Medical Research Council of South Africa.

References

1. Roberts JM, Taylor RN, Musci JT, *et al*. Preeclampsia: An endothelial cell disorder. *Am J Obstet Gynecol* 1989; **161:** 1200-1204.

2. Buchanan TA, Metzger BE, Freinkel N, Bergman RN. Insulin sensitivity and B-cell responsiveness to glucose during late pregnancy in lean and moderately obese women with normal glucose tolerance or mild gestational diabetes. *Am J Obstet Gynecol* 1990; **162:** 1008-1014.
3. Roberts JM, Redman CWG. Preeclampsia: more than pregnancy induced hypertension. *Lancet* 1993; **341:** 1447-1451.
4. Jaffe EA. Endothelial cells. In: Gallin JL, Goldstein IM, Snyderman R, eds. *Inflammation: Basic Principles and Clinical Correlates*. New York: Raven, 1988: 559.
5. Chesley LC, ed. *Hypertensive Disorders in Pregnancy*. New York: Appleton-Century-Crofts, 1978.
6. Dekker GA, Sibai BM. Etiology and pathogenesis of pre-eclampsia: current topics. *Am J Obstet Gynecol* 1998; **179:** 1359-1375.
7. Khan KS, Daya S. Plasma glucose and preeclampsia. *Int J Gynaecol Obstet* 1996; **53:** 111-116.
8. Fuh MM-T, Yin C, Pei D, *et al*. Resistance to insulin-mediated glucose uptake and hyperinsulinemia in women who had preeclampsia during pregnancy. *Am J Hypertens* 1995; **8:** 768-771.
9. Lorentzen B, Birkeland KI, Endresen MJ, Henriksen T. Glucose intolerance in women with pre-eclampsia. *Acta Obstet Gynecol Scand* 1998; **77:** 22-27.
10. Sowers JR, Saleh AA, Sokol RJ. Hyperinsulinemia and insulin resistance are associated with preeclampsia in African-Americans. *Am J Hypertens* 1995; **8:** 1-4.
11. Ferrannini E, Buzzigoli G, Bonadonna R, et al. Insulin resistance in essential hypertension. *N Engl J Med* 1987; **317:** 350-357.
12. Solomon CG, Graves SW, Greene MF, Seely EW. Glucose intolerance as a predictor of hypertension in pregnancy. *Hypertension* 1994; **23:** 717-721.
13. Pollare T, Lithell H, Berne C. Insulin resistance is a characteristic of primary hypertension independent of obesity. *Metabolism* 1990; **39:** 167-174.
14. Rath W. Treatment of hypertensive diseases in pregnancy – general recommendations and long-term oral therapy. *Z Geburtshilfe Neonatol* 1997; **201:** 240-246.
15. Caruso A, Ferrazzani S, Carolis S, *et al*. Gestational hypertension but not preeclampsia is associated with insulin resistance syndrome characteristics. *Hum Reprod* 1999; **14:** 219-223.
16. Roberts RN, Henriksen JE, Hadden DR. Insulin sensitivity in preeclampsia. *Br J Obstet Gynaecol* 1998; **105:** 1095-1100.
17. Abundis EM, Ortiz GM, Galvan QA, Ferrannini E. Hyperinsulinemia in glucose-tolerant women with preeclampsia, A controlled study. *Am J Hypertens* 1996; **9:** 610-614.
18. Makuyana D, Mahomed K, Ndlovu S, Mawji KGD, Siziya S. Insulin secretion, clearance and sensitivity in black pregnant and non-pregnant women in Harare, Zimbabwe. *Cent Afr J Med* 1999; **45**(1): 11-14.
19. Lutale JK, Justesen A, Swai AB, Alberti KG, McLarty DF. Glucose tolerance during and after pregnancy in nondiabetic women in an urban population in Tanzania. *Diabetes Care* 1993; **16:** 575-577.
20. Okonofau FE, Amole FA, Ayangade SO, Nimalaraj T. Criteria for the oral glucose tolerance test in pregnant and non-pregnant Nigerian women. *Int J Gynaecol Obstet* 1988; **27:** 85-89.
21. Tallarigo L, Giampietro O, Penno G, Micolli R, Gregori G, Navalesi R. Relation of glucose tolerance to complications of pregnancy in non-diabetic women. *N Engl J Med* 1986; **315:** 989-992.
22. Lindsay MK, Graves W, Klein L. The relationship of one abnormal glucose tolerance test value and pregnancy complications. *Obstet Gynecol* 1989; **73:** 103-106.