



Audit of the outcome of pregnancy in diabetic women in Soweto, South Africa, 1992 - 2002

Kenneth R Huddle

Objective. To audit the outcome of pregnancy among diabetic black women in Soweto following the introduction of a specialised service.

Design and methods. An analysis of patients' records was conducted for the period 1992 - 2002. Maternal characteristics, aspects of treatment and its complications, mode of delivery and perinatal outcome are reported. The incidence of postpartum glucose intolerance in women with gestational diabetes was assessed. Major outcomes from this study are compared with those of an earlier study conducted from 1983 to 1992.

Results. A total of 733 diabetic pregnancies was managed over 11 years: 348 women had gestational diabetes, 172 had type 1 diabetes and 213 had type 2 diabetes. Insulin was used in all but 23 women. Mean (\pm standard deviation (SD)) capillary blood glucose levels varied between 5.7 (\pm 0.72) and 6.2 (\pm 0.95) mmol/l in the 3 groups. Severe maternal hypoglycaemia was most common in the type 1 diabetes group (14%). Mean (\pm SD) neonatal weight varied between 2 922.3 g (\pm 753) and 3 073.3 g (\pm 727). Caesarean section rates exceeded 60% in all 3 groups. Overall, 13.1% of women had hypertension, 31.3% of whom had proteinuric hypertension. There were no cases of

progressive pre-eclampsia. The combined perinatal mortality (PMN) rate was 3.7%, compared with 15.6% in the 'control' group. Major congenital malformations occurred in 11 pregnancies (1.5%). There were 2 maternal deaths. Postpartum impaired glucose tolerance/diabetes occurred in 25.9% of women with gestational diabetes. Combining the 2 studies (1983 - 1992 and 1992 - 2002), 1 087 pregnancies were managed over 20 years using a similar protocol. There were no significant differences in major outcomes between the 2 studies. The overall PMN of 4.5% is significantly lower than that of the combined 'control' group (19.9%). Postpartum glucose intolerance was documented in 28.5% of women.

Conclusions. The institution of a specialised service for pregnant diabetic women from Soweto for a sustained period of 20 years proved feasible and was of significant benefit. The interventions, centred around a diabetes nurse educator, were relatively simple and easy to implement. Late presentation/referral of patients remains a problem. Persistence of glucose intolerance postpartum in women with gestational diabetes was common and provides an opportunity for preventive measures to be introduced.

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Great strides were made during the last century in the management of diabetes in pregnancy. Before the discovery of insulin in 1921 the outlook for the diabetic mother and her fetus was abysmal.¹ With the advent of insulin, an emphasis on a team approach to care, improved methods of fetal surveillance, and a focus on metabolic normalisation brought about by intensive insulin regimens and home glucose monitoring, the outlook for both the diabetic mother and her offspring has improved dramatically, approaching that of the non-diabetic pregnancy.^{2,3} However, this success story, which is the experience of many developed countries, is not shared to any great extent in sub-Saharan Africa, where the resources for diabetes management are often lacking, resulting in a situation reminiscent of the pre-insulin era. Reports from this region on the management of diabetes in pregnancy are few, the numbers are small, and the perinatal mortality figures are high.^{4,8}

Against this background, a combined specialist clinic for pregnant diabetic women was established in 1983 at Chris

Hani Baragwanath Hospital (CHBH), a 3 000-bed teaching hospital linked to the University of the Witwatersrand. The initial experience at this clinic has been reported previously.⁹ CHBH performs more than 1 500 deliveries per month, and serves the people of Soweto, a large, sprawling township situated on the outskirts of Johannesburg whose population of several million is almost entirely of African ethnic origin. The majority of the inhabitants are poor and indigent and unemployment is rife. The AIDS epidemic has had devastating effects on this community for over a decade.

The following report covers the period 1992 - 2002.

Design and methods

The combined specialist clinic comprised physician, obstetrician, paediatrician, and diabetes nurse educator. The study population included women almost exclusively of African ethnic origin drawn mainly from Soweto. The diabetes was classified as follows.

Diabetes was considered gestational if the diagnosis was made during pregnancy in women referred because of the presence of risk factors for diabetes, i.e. persistent glycosuria, strong family history, previous unexplained perinatal loss, and

Departments of Medicine and Obstetrics and Gynaecology, Chris Hani Baragwanath Hospital and University of the Witwatersrand, Johannesburg

Kenneth R Huddle, MB BCh, FCP (SA), FRCP

Corresponding author: K R L Huddle (huddlekr@medicine.wits.ac.za)



previous gestational diabetes. Diagnosis was confirmed using the 100 g oral glucose tolerance test (OGTT) (National Diabetes Data Group criteria).¹⁰

Diabetes was considered pregestational if the diabetes was present before conception. This group was further divided into type 1 and type 2 diabetes groups depending on the pregestational use/non-use of insulin.

After some time it became clear that it was necessary to include an additional category of patients, a 'control' group, which refers to those women who, because of late referral or presentation, were unable to receive more than 2 weeks of intensive management before delivery. This group reflects the deficiencies that exist in our referral system, but affords us the opportunity to document the effect of uncontrolled diabetes on pregnancy outcome. It is important to note that in all instances of viable pregnancy in the 'control' group rapid attempts to achieve metabolic control were made and delivery was performed as soon as fetal maturity was confirmed.

All women were hospitalised initially for clinical and biochemical assessment, ultrasonographic examination to assess gestational age and the presence of fetal abnormalities, and determination of treatment. All oral hypoglycaemic agents were withdrawn at presentation. Diabetic retinopathy was assessed using a standard ophthalmoscope after the pupils had been dilated using a short-acting mydriatic agent (tropicamide). Diabetic nephropathy was diagnosed if 'dipstix'-positive proteinuria (protein ≥ 0.3 g/l) was found on repeated testing, in the absence of urinary tract infection or other renal disease. Hypertension was diagnosed if the blood pressure was persistently elevated above 140/90 mmHg (Korotkoff phase V); proteinuric hypertension was diagnosed if persistent 'dipstix'-positive proteinuria developed in association with hypertension in patients who had had no evidence of proteinuria at presentation.

Patients were taught home blood glucose monitoring by the nurse educator – fingerprick capillary blood samples were obtained using lancets and blood glucose levels were read visually using Haemo-glukotest 20-800R strips (Roche Diagnostics GmbH, Mannheim, Germany). Fasting, preprandial and 2-hour postprandial (substituted more recently with 1-hour postprandial) blood glucose levels were recorded in hospital and at home. Glycated haemoglobin (HbA_{1c}) (Tinaquant HbA_{1c}) immunological assay, Roche Diagnostics GmbH, Mannheim, Germany – normal range 4.8 - 6%) was measured at presentation and monthly thereafter from 1995 onwards. All subjects followed an 1 800 - 2 000 kcal complex carbohydrate diabetic diet (comprising 60% carbohydrates, 25% fat, 15% protein) divided into 3 main meals and between-meal and late-night snacks.

Insulin therapy was begun if the fasting blood glucose level exceeded 4 mmol/l and/or the pre-meal and 2-hour (or 1-hour) postprandial levels rose above 7 mmol/l. Multiple doses

of short- and intermediate-acting human insulins were used. The aim of therapy was to maintain the blood glucose levels between 4 and 7 mmol/l and the HbA_{1c} levels < 7% without inducing severe hypoglycaemic reactions.

After initial assessment in hospital, patients returned fortnightly for follow-up until 32 weeks' gestation and then weekly until 37 weeks when they were readmitted. A full clinical assessment was made at each visit, the results of home blood glucose monitoring were recorded and the technique checked, and adjustments in treatment were made accordingly. Ultrasound examinations were repeated at intervals to assess fetal growth, fetal abnormalities, and liquor volume. Predelivery management in hospital consisted of frequent clinical assessments and corrections of deviations from glycaemic control targets. Fetal growth and wellbeing were monitored using serial ultrasound and non-stress tests. The timing and mode of delivery were dictated by obstetric factors and by the duration and degree of glycaemic control. Amniocentesis was performed in cases of preterm delivery to assess fetal lung maturity, and in women at risk for Down's syndrome. During labour or caesarean section diabetes was controlled using dextrose-insulin infusions with frequent monitoring of capillary blood glucose samples. Insulin therapy was terminated in the immediate postpartum period and blood glucose monitoring was recommenced. Usually, insulin was restarted in patients with type 1 diabetes on day 2 - 3 postpartum at the pre-pregnancy doses. The treatment of the remaining groups of patients was dictated by the results of the blood glucose profiles. Gestational diabetic women were recalled at 6 weeks for a 75 g OGTT (WHO World Health Organization criteria for non-pregnant adults).

Neonates were assessed by the paediatric staff for the presence of clinical and/or biochemical complications/abnormalities and managed accordingly. Methods of contraception were discussed with each patient so that informed decisions could be made.

Statistical comparisons were made using analysis of variance (ANOVA), Student's *t*-test and chi-squared tests.

Results

Maternal profiles (Table I)

A total of 733 pregnancies were managed over 11 years. The majority of women had gestational diabetes mellitus (GDM). Most of the women with type 1 (type 1 DM) and type 2 diabetes mellitus (type 2 DM) presented towards the middle and end of the second trimester respectively; women with GDM presented well into the third trimester. Overall, 96 women (13.1%) had hypertension: 30 (31.3%) had proteinuric hypertension, 19 (19.8%) were classified as gestational hypertension, 33 (34.4%) as chronic hypertension, 6 (6.3%) were unclassified, and 8 (8.3%) had hypertension superimposed on



Table I. Summary of maternal characteristics

	Gestational diabetes	Pregestational diabetes	
		Type 1 diabetes	Type 2 diabetes
Pregnancies (N (%))	348 (47.5)	172 (23.5)	213 (29)
Age (yrs) (mean ± SD)	33.9 ± 5.2*	30.5 ± 6.2	34.3 ± 5.0 [†]
Gestational age at presentation (wks) (mean ± SD)	28.3 ± 6.4**	18.5 ± 7.1	21.4 ± 7.2 [†]
Duration of diabetes (yrs) (mean ± SD)	-	6.0 ± 4.2	3.7 ± 3.1
Hypertension (N (%))	50 (14.4)	23 (13.4)	23 (10.9)
Retinopathy (N (%))	5 (1.4)**	30 (17.4)	21 (9.9) [§]
Nephropathy (N (%))	1 (0.3)*	13 (7.6)	4 (1.9) [†]

**p* < 0.01 gestational v. type 1 diabetes.
[†]*p* < 0.01 type 2 diabetes v. type 1 diabetes.
[‡]*p* < 0.01 gestational v. type 2 diabetes.
[§]*p* < 0.03 type 2 diabetes v. type 1 diabetes.

Table II. Aspects of treatment and its complications

	Gestational diabetes	Pregestational diabetes	
		Type 1 diabetes	Type 2 diabetes
Total insulin dose/day (units)* (mean ± SD)	106.9 ± 60.7 [†]	93.3 ± 43.7	114.5 ± 60.6 [§]
Mean capillary blood glucose (mmol/l) (mean ± SD)	6.2 ± 0.95 [‡]	5.7 ± 0.72	5.9 ± 0.84 [†]
HbA _{1c} (%) at first booking (mean ± SD)	7.1 ± 1.7 [‡]	8.2 ± 2.0	7.8 ± 2.0
HbA _{1c} (%) at delivery (mean ± SD)	6.6 ± 1.2	6.8 ± 1.0	6.5 ± 1.0
Maternal hypoglycaemia (% of patients)	0.9 [‡]	14	7 [†]

*At delivery.
[†]*p* < 0.01 gestational v. type 1 diabetes.
[‡]*p* < 0.01 gestational v. type 2 diabetes.
[§]*p* < 0.01 type 2 diabetes v. type 1 diabetes.
[†]*p* < 0.03 type 2 diabetes v. type 1 diabetes.

diabetic nephropathy. There were no instances of progressive pre-eclampsia with coagulatory and/or liver dysfunction, nor were there any cases of eclampsia. Methyldopa was used as monotherapy in 56 (58.3%) of the hypertensive patients, methyldopa plus hydralazine in 17 (17.7%), and 23 hypertensive women (24%) were managed without pharmacological treatment. Diabetic retinopathy and/or nephropathy were most frequent in the patients with type 1 DM. Retinopathy was present in 56 (7.6%) of women overall; with the exception of 1 case of proliferative retinopathy, all were of background type. There was 1 instance of acute deterioration of visual acuity in a woman with type 1 DM and background retinopathy – she developed macular oedema associated with a 5.4% drop in her HbA_{1c} level over a 3-week period. Her condition settled without intervention. Nephropathy was diagnosed in 18 patients (2.5%) overall. Ten had persistent proteinuria without hypertension or elevated serum creatinine level, and 8 had persistent proteinuria with associated hypertension, 2 of whom also had raised serum creatinine levels (117 and 213 µmol/l respectively). The sole perinatal loss among the women diagnosed with diabetic nephropathy was a stillbirth to a woman with persistent proteinuria alone.

There were 2 maternal deaths in this study. The first, a 36-

year-old woman with type 2 DM, died at home at 21 weeks' gestation of unknown cause. She was obese (109 kg) and on high doses of insulin (230 units/day). She had had a severe hypoglycaemic reaction several days beforehand for which she was counselled, and her insulin doses were reduced. No autopsy was performed. The second death involved a 34-year-old woman with type 2 DM. The woman died at home at 19 weeks' gestation. She was on 84 units of insulin per day and weighed 82 kg. There had been no preceding episodes of hypoglycaemia. No autopsy was performed. The cause of death is unknown.

Aspects of treatment and treatment complications (Table II)

Diet was used as monotherapy in 17 patients (4.9%) with GDM and in 5 women (2.3%) with type 2 DM. The remaining patients were treated with diet and insulin. In the majority of women insulin requirements increased progressively with increasing gestational age. The mean capillary glucose levels in all 3 groups of women approximated 6.0 mmol/l. The mean HbA_{1c} (measured from 1995 onwards and within 4 weeks of delivery) was below 7.0% in all 3 groups of patients. The mean ± SD pre-delivery HbA_{1c} levels decreased significantly from the HbA_{1c} levels at first booking in all 3 groups: from 7.1 ± 1.7% to

**Table III. Mode of delivery and perinatal outcome**

	Gestational diabetes	Pregestational diabetes	
		Type 1 diabetes	Type 2 diabetes
Live births (<i>N</i>)	344	172	214
Caesarean section (%)	61.8	63	61.5
Birth weight (g) (mean ± SD)	3 204.9 ± 657 [‡]	2 922.3 ± 753	3 073.3 ± 727 [§]
Gestational age at delivery (wks) (mean ± SD)	37.0 ± 1.6	36.6 ± 2.0	37.0 ± 1.9
Neonatal hypoglycaemia (%)	3.5	5.8	7.5
Perinatal mortality (%)*	4.2	3.9	2.8
Stillbirths (<i>N</i> (%))	10 (2.8)	7 (3.9)	4 (1.8)
Early neonatal deaths (<i>N</i> (%))	5 (1.4)	0	2 (0.9)
Major congenital abnormalities (<i>N</i> (%))	8 (2.3)	1 (0.6)	2 (0.9)

*Overall PNM for 3 groups = 3.7%.
[‡]*p* < 0.01 gestational v. type 1 diabetes.
[§]*p* < 0.04 gestational v. type 2 diabetes.
[§]*p* < 0.04 type 2 diabetes v. type 1 diabetes.

6.6 ± 1.2% (*p* = 0.0001) in the GDM group, from 8.2 ± 2.0% to 6.8 ± 1.0% (*p* < 0.00001) in the type 1 DM group, and from 7.8 ± 2.0% to 6.5 ± 1.0% (*p* < 0.00001) in the type 2 DM group. Maternal hypoglycaemia (1 or more episodes) severe enough to necessitate the administration of intravenous dextrose, occurred significantly more often in women with type 1 DM than in the other 2 groups. No maternal morbidity or mortality was directly attributable to hypoglycaemia.

Mode of delivery and perinatal outcome (Table III)

Caesarean section rates were similar in all 3 groups at just over 60%. The gestational age at delivery was similar in all 3 groups at 37 weeks. The mean birth weights approximated 3 000 g for the 3 groups, with 9.6% of neonates weighing ≥ 4 kg – 12.5% in the GDM group, 5.2% in the type 1 group, and 8.5% in the type 2 group – the percentage being significantly higher (*p* = 0.02) in the GDM group than in the other 2 groups. The overall perinatal mortality for this study was 3.7% (37/1 000) with no significant differences between the 3 groups. The 5 early neonatal deaths in the GDM group comprised the following: 1 instance of birth asphyxia and respiratory distress syndrome following premature rupture of membranes (the baby also had extra digits, undescended testes and choanal atresia); 1 death due to premature delivery at 31 weeks precipitated by the development of pre-eclampsia; 2 deaths due to major congenital malformations; and 1 instance of Down's syndrome associated with congenital leukaemia. The causes of the 2 early neonatal deaths in the type 2 DM group were not defined; both babies had minor congenital abnormalities. Overall, there were 11 (1.5%) major congenital abnormalities including skeletal, neurological, cardiovascular, renal and gastrointestinal defects (Table IV). A total of 8 newborns (1.1%) in the GDM and type 1 DM groups developed hyaline membrane disease requiring ventilation. All were related to premature delivery and were precipitated by pre-eclampsia (2 cases), premature rupture of membranes (2 cases), triplet

pregnancy (2 cases), twin pregnancy (1 case), and antepartum haemorrhage (1 case). One of these 8 newborns died. (It is our policy to use betamethasone in cases of anticipated premature delivery to prevent respiratory distress syndrome.)

'Control group'

The 'control' group comprised a total of 211 pregnancies: 170 women had GDM, 16 had type 1 DM, and 25 had type 2 DM. The overall perinatal mortality rate in the 'control' group was 15.6%, with stillbirths accounting for 90% of deaths. There were 4 major congenital anomalies overall. No maternal deaths occurred.

Table IV. Major congenital malformations

	Type of malformation
Gestational diabetes	
1	Holoprosencephaly; cleft lip and palate; absent radius, tibia, fibula
2	Holoprosencephaly; microcephaly; single nostril; small mouth; rocker-bottom feet
3	Skull defect with encephalocele; midline facial defect
4	Small head; asymmetrical face; closed eye; low-set ears; short neck; patent ductus arteriosus
5	Renal agenesis; hypoplastic lungs; anal atresia; clubbed feet; short limbs
6	Cleft lip and palate
7	Imperforate anus
8	Choanal atresia; undescended testes; extra digits
Type 2 DM	
1	Single cardiac ventricle; dextrocardia; patent ductus arteriosus
2	Anencephaly
Type 1 DM	
1	Ventricular septal defect; patent ductus arteriosus; interrupted aortic arch; aberrant subclavian artery



Persistence of glucose intolerance in the GDM group postpartum

Excluding the 'control' group, 29 women (8.3%) in the GDM group had persistence of diabetes in the immediate postpartum period, and 1 woman developed diabetes 1 year postpartum. Of the remaining 318 women, 148 (46.5%) returned for a 75 g OGTT – 88 (59.5%) were normal, 30 (20.3%) had a diabetic OGTT, and 30 (20.3%) had impaired glucose tolerance (IGT). Therefore, including the 170 women who did not return for an OGTT, 25.9% of GDM women had evidence of IGT (33%) or diabetes (67%) postpartum.

Discussion

The data from this study show the benefits of prolonged exposure to intensified management of diabetes in pregnancy in a Third-World setting. The overall PNM of 3.7% in the 'treated' group of 733 pregnancies is significantly lower than the 15.6% recorded in the 'control' group ($p < 0.001$). The combined PNM for these 2 groups is 6.3% which is considerably lower than the rate reported in studies from other African countries. There are few published studies from sub-Saharan Africa and the numbers of enrolled patients are small. In a review of 5 published African studies,⁴ PNM varied from 12.9% to 25.4% which underscores the need for better care for these vulnerable women. Significant challenges exist in the care of these women – diabetic pregnancies are often unrecognised, antenatal care facilities are often lacking, materials for testing blood glucose are often not available, and even insulin may be in short supply. A more recent report from Tanzania⁸ is more encouraging; here the PNM for 50 diabetic pregnancies was 10% despite the absence of home blood glucose monitoring.

The 2 unexplained maternal deaths in this study are of concern. Maternal mortality among pregnant diabetic women in the UK is reported to vary between 0.1% and 0.5%.¹¹ Between 1988 and 1999 there were 20 maternal deaths among diabetic women in the UK from a total of 1 400 deaths, with hypoglycaemia being a major cause of death.

Caesarean section rates were high, which can be ascribed to our reluctance to allow pregnancies to go beyond 38 weeks, and the fact that 27% of women undergoing operative delivery had had 1 or more prior caesarean sections.

Our patients with pregestational diabetes continue to present late in pregnancy, largely as a result of the poor antenatal services available to women in Soweto. Ideally, all diabetic women should receive preconception counselling and care with the aim of ensuring excellent glycaemic control before and during pregnancy to prevent fetal morbidity and mortality especially with regard to congenital anomalies. A recent meta-analysis¹² of 14 cohort studies has shown that preconception care lowers the rate of major congenital anomalies from 6.5% to

2.1%. This issue remains a challenge for us in Soweto.

The duration of diabetes in the type 1 DM group is relatively short. This can be ascribed to the fact the age of onset for South African black type 1 DM patients is about a decade later than that of their white counterparts (median 22 years versus 10 years respectively).¹³ The GDM group clearly includes women who have had previously undiagnosed pregestational diabetes. This is supported by the fact that 95% of our GDM group required insulin therapy, that 6 of these women had evidence of diabetic retinopathy, that 1 had evidence of diabetic nephropathy, and that 10 of the offspring had major congenital abnormalities.

Including women who did not return for postpartum OGTT, 26% of the GDM group had evidence of IGT (33%) or diabetes (67%) postpartum. Women with GDM have a considerably increased risk of developing diabetes or IGT postpartum. The incidence is variable and is dependent on a number of factors, e.g. the heterogeneity of the patient population studied, the method used for diagnosing GDM in the previous pregnancy, the length of follow-up postpartum, and the selection bias due to incomplete follow-up. In a recent review¹⁴ of the literature the incidence varied from 10% to 64%. Women with IGT postpartum provide an opportunity for intervention. Two studies from different parts of the world have shown that with lifestyle interventions such as diet, exercise and weight loss, the development of type 2 DM in individuals with IGT can be reduced by 58%.^{15,16} This is a challenge for us in the future.

Comparison of 2 studies (Table V)

The methodologies used in the 2 studies (1983 - 1992⁹ and 1992 - 2002) were the same except for the measurement of HbA_{1c} which only became available from 1995 onwards. Therefore, the 2 studies reflect a combined experience of 1 087 diabetic pregnancies extending over 20 years. Comparing the 2 studies, there has been a trend toward a reduction in PNM from 6.1% to 3.7%, although this is not statistically significant ($p = 0.06$). The combined PNM of 4.5% is considerably lower than that of the combined 'control' groups of 19.9% ($p < 0.001$), and is also much lower than PNM figures from studies conducted in other sub-Saharan African countries.^{4,5,7}

Table V. Comparison of two studies

	First study 1983 - 1992 ⁹	Second study 1992 - 2002
Pregnancies (N)	354	733
Perinatal mortality (%)	6.1	3.7
Major congenital abnormalities (N (%))	6 (1.7)	11 (1.5)
Postpartum glucose intolerance (%)	34.6	25.9
Maternal mortality (N)	0	2
'Control' group perinatal mortality (%)	26	15.6



There was no difference in postpartum glucose intolerance (IGT or diabetes) between the 2 studies. Combining the 2 studies, almost one-third (28.5%) of women had evidence of glucose intolerance postpartum. This is probably an underestimate because a significant number of women did not return for OGTT postpartum and long-term follow-up was not possible.

Conclusion

These 2 studies indicate that the introduction of a specialised service for pregnant diabetic women from a Third-World community is both feasible and of benefit. The measures adopted were not particularly sophisticated or costly and allowed for maximum ambulatory care. The patients were highly motivated, which made the education process easy and follow-up reliable. The diabetes nurse educator's role was pivotal in achieving the overall benefits associated with both these studies. Late referral/presentation of our patients remains a vexing problem. The relatively high incidence of postpartum glucose intolerance stresses the importance of postpartum follow-up. The detection of IGT postpartum provides an opportunity to institute preventive measures to reduce the burden of diabetes.

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