Antenatal Screening Using Random Blood Glucose Values

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SUMMARY

For many years it has been established practice to test the urine of pregnant women for the presence of glucose in the belief that this is an efficient way to detect diabetes mellitus. It is now becoming recognized that one of the normal maternal physiologic adaptations during pregnancy is an increase in the renal excretion of glucose; on examination, up to 50% of healthy pregnant women will have detectable glycosuria at some stage. As the definition of diabetes mellitus is based on random blood glucose values or the concentrations achieved at defined times after an oral glucose load, it would seem logical that any antenatal screening procedure should be similarly based. A total of 2403 consecutive antenatal patients had a random venous whole blood glucose concentration determined between 28 and 32 wk gestation. Calculated 99% cutoff values were 110 mg/dl (6.1 mmol/L) within 2 h of a meal or 101 mg/dl (5.6 mmol/L) more than 2 h postprandial. Four patients were found to have previously unsuspected but unequivocal diabetes mellitus and four more had impaired glucose tolerance on the basis of the 1980 WHO criteria. Screening all antenatal patients by this method is efficient, does not inconvenience patients, and is relatively cost efficient in terms of staff and laboratory resources. DIABETES 1985; 34 (Suppl. 2):17–20.

Testing urine for the presence of glucose is a time-honored method for screening for diabetes mellitus. The presumption that a nonpregnant woman who has detectable glycosuria has elevated blood glucose concentrations is not unreasonable. Assuming an average glomerular filtration rate of 100 ml/min and a maximum renal tubular reabsorptive capacity of about 300 mg/min, the presence of glucose in the urine would indicate blood glucose concentrations in excess of 300 mg/dl. However, if the glomerular filtration rate was to increase or the tubular reabsorptive capacity for glucose to decrease, then glycosuria could occur at lower blood glucose concentrations, hence reducing its diagnostic value. Both of these changes occur as part of the normal maternal physiologic adaptation to pregnancy. About 50% of normal healthy pregnant women develop glycosuria expressed either in terms of milligrams excreted per 24 h or as the number of urine samples per day containing detectable glucose. The amount of glucose lost varies not only between patients but within an individual patient from occasion to occasion.[1] Healthy pregnant women with persistent and heavy glycosuria revert to a normal nonglycosuric status within 6 days of delivery (some within 48 h), indicating that this increased excretion is physiologic rather than due to any disorder of carbohydrate metabolism.[2]

The diagnosis of diabetes mellitus is usually based on the concentrations of glucose in blood samples obtained either at random times or at specific intervals after an oral glucose load. While there are differing opinions regarding the levels that are diagnostic of diabetes, the criteria of the World Health Organization (WHO, 1980)[3] are very similar to those of the European Association for the Study of Diabetes (1979)[4] and the National Diabetes Data Group (1979)[5] and are gaining widespread acceptance. It would be logical, therefore, to base a screening technique on glucose concentrations determined in blood rather than urine. However, it would be impractical as well as costly to perform an oral glucose tolerance test (OGTT) on every pregnant woman, and this article reports two studies to determine the usefulness of random blood glucose concentrations obtained during routine antenatal clinic visits as a screening procedure for diabetes mellitus.

PATIENTS AND METHODS

SUBJECTS

Study 1. A venous blood sample was obtained from 186 consecutive women attending the routine antenatal clinic between 28 and 32 wk of gestation. Their ages ranged from 17 to 44 yr (mean, 27.5 ± 4.3 [±SD]); of these, 63% were nulliparous, 27% had one previous pregnancy, 7.5% two previous pregnancies, and 2.5% three or more. Only those

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TABLE 1
Blood glucose concentrations (mean ± SD) at 30-min intervals after a normal meal in 186 healthy, pregnant women at about 28 wk gestation

Time interval (min)	Number of patients	Blood glucose (mmol/L) Mean	SD
Fasting*	19	4.12	0.40
1–30	28	4.71	0.69
31–60	30	5.03	0.83
61–90	21	5.03	0.69
91–120	21	4.52	0.56
121–150	25	4.27	0.58
151–180	23	4.02	0.77
181+	38	4.12	0.73

Note: Average standard deviation within time intervals was 0.71.
*Fasting blood glucose values given for comparison are from a previously published series.[6]

women known to have diabetes mellitus were excluded from the study. The mean length of gestation at delivery was 277 days (± 14.1 SD), and the mean infant birth weight was 3.37 kg (± 0.49 SD). All infants were born alive and healthy.

Study 2. All patients attending the hospital over a 12-mo period had a venous blood sample obtained at their first visit and another between 28 and 32 wk gestation, excluding only those patients with known diabetes mellitus. Because duration of pregnancy at first visit varied between patients and because some aborted spontaneously thereafter or transferred elsewhere for delivery, the data from 2485 patients attending between 28 and 32 wk gestation are presented. Of these, 28 women delivered twins and one patient had triplets; while these 29 mothers did not have blood glucose concentrations outside the normal range, they have been excluded from the final data analysis for the sake of uniformity. In addition, the blood glucose values could not be traced for 53 patients, so data from 2403 patients were available. Of these, 2285 had the time of their last meal accurately recorded, but in 118 instances the clinical record stated that the last meal had been eaten "more than" or "less than" 2 h previously.

BLOOD GLUCOSE DETERMINATIONS

Blood glucose levels were measured on venous whole blood samples taken into tubes containing fluoride-oxalate using a Technicon AA2 system (Technicon Instruments, Tarrytown, New York) utilizing the specific enzyme glucose oxidase. Assays were usually performed the same day, but always within 24 h. At the time the blood sample was taken the patient was asked when she had last eaten and the interval recorded in the notes; any high-carbohydrate "snacks" such as chocolate or sweet biscuits were regarded as meals for this purpose. The concentrations were reported in millimoles per liter (mmol/L) and when converted to milligrams per deciliter the values have been expressed to the nearest milligram.

RESULTS

Study 1. The blood glucose values for the 186 women were grouped by 30-min intervals from the time of the last meal, and their mean values and standard deviations calculated (Table 1). As no patient could be regarded as being in a fasted state, the data from 19 patients studied on a previous occasion[6] are given for comparison. The data were then regrouped by hourly intervals and the mean glucose values recalculated; the range of standard deviations at each time interval was narrow, so the average standard deviation (SD = 0.706) was used to calculate the 95% and 99% upper limits (Table 2). For prospective screening purposes, the 99% values were chosen, i.e., 115 mg/dl (6.4 mmol/L) within 2 h and 104 mg/dl (5.8 mmol/L) more than 2 h after a meal.

Two patients in this index group had blood glucose values of 130 mg/dl (7.2 mmol/L) within 2 h of a meal and were referred for a 75-g OGTT; one patient achieved a concentration of 119 mg/dl (6.6 mmol/L) more than 2 h after eating and was similarly referred. All three had normal responses; the highest postload value in any patient was 158 mg/dl (8.8 mmol/L).

Study 2. As with study 1, the patients were divided into groups by ½-h intervals from the time of their last meal and the mean, standard deviation, and 99% cutoff values determined using the 2285 patients in whom the time intervals were known (Table 3). They were then regrouped according to whether or not they had eaten within 2 h of testing, which allowed all 2403 patients to be included (Table 4). These new 99% levels varied slightly from those of study 1 (110 mg/dl [6.1 mmol/L] versus 115 mg/dl [6.4 mmol/L] within 2 h of eating, and 101 mg/dl [5.6 mmol/L] versus 104 mg/dl [5.8 mmol/L] more than 2 h postprandially).

If the screening criteria had been strictly applied, about 24 women (1%) would have been referred for an OGTT; however, 59 patients (2.6%) had the test performed. Of these, 38 mothers were referred on the basis of their random blood glucose value, 32 of whom (1.4% of the total group) had actually achieved or exceeded the 99% value; the remaining six had lower concentrations and, therefore, were incorrectly referred for an OGTT. Of these 32 patients, two had un-

TABLE 2
The calculated 95% and 99% limits for blood glucose concentrations achieved at hourly intervals after a meal in 186 healthy, pregnant women at 28 wk gestation

Time interval (min)	Number of patients	Mean blood glucose (mmol/L)	Calculated upper limits* 95% (SD × 1.65)	99% (SD × 2.33)
1–60	58	4.876	6.0	6.5
61–120	42	4.776	5.9	6.4
121–180	48	4.131	5.3	5.8
180+	38	4.118	5.3	5.8

*Using the average standard deviation of 0.71 mmol/L.

TABLE 3
Antenatal patients (2285) with accurately timed samples

Time since meal (min)	Number of patients	Blood glucose (mmol/L)		
		Mean	SD	99% Cutoff
1– 30 (21)*	173	4.62	0.71	6.3
31– 60 (47)	144	4.52	0.82	6.4
61– 90 (82)	213	4.39	0.80	6.3
91–120 (110)	428	4.34	0.69	5.9
121–150 (139)	449	4.25	0.67	5.8
151–180 (169)	340	4.15	0.62	5.6
181–210 (196)	247	4.05	0.59	5.4
211–240 (227)	122	4.01	0.56	5.3
241 + (377)	169	3.91	0.56	4.5

*The time in parentheses is the mean for that interval.

equivocal diabetes mellitus and four had impaired glucose tolerance (IGT) as defined by the 1980 WHO criteria. Two further patients had such high random blood glucose levels that an OGTT was not thought necessary; these eight patients will be discussed in more detail below.

Seven women had an OGTT requested on the basis of glycosuria; five had normal responses and two were classified as having IGT. Both of these women reverted to normal responses within 12 wk of delivery.

Six patients were referred because they had previously delivered large babies; all six had normal responses. Two had an OGTT because they had been labeled "diabetic" in a previous pregnancy; one was normal and the other classified IGT, but she reverted to a normal response 6 wk postdelivery. Six others were referred for a variety of reasons and all were normal.

Of the four patients determined as having diabetes mellitus, two were diagnosed on the basis of their random blood glucose concentrations, which were 394 mg/dl (21.9 mmol/L) and 295 mg/dl (16.4 mmol/L), respectively. The other two women were diagnosed on the basis of the results of a 75-g OGTT. None of these women had any of the "stigmata" of diabetes, such as a family history of the condition or a bad past obstetric history, nor did any display symptoms such as thirst or polyuria. Only one patient had had glycosuria previously and this on one occasion only. Three of these mothers required insulin therapy during pregnancy: one has remained insulin dependent; another was changed from insulin to gliclazide after delivery but is now insulin dependent; the third achieved control on diet alone after delivery, although her OGTT remains unequivocally in the diabetes range. The fourth patient responded well to diet during pregnancy and has continued to do so, although her OGTT response is consistently impaired according to the 1980 WHO criteria. All had normal, vaginal deliveries of live, healthy babies, and one of the insulin-dependent mothers has recently had a second successful pregnancy.

TABLE 4
Total patients (2403) screened at 28 wk gestation

Time since meal (min)	Number of patients	Blood glucose (mmol/L)		
		Mean	SD	99% Cutoff
1–120	992	4.43	0.73	6.1
121 +	1411	4.11	0.63	5.6

DISCUSSION

Several practical points have emerged from these studies. First, it seems likely that 99% of a normal healthy antenatal population will have a random venous blood glucose concentration of ≤110 mg/dl even shortly after a meal. If diabetes mellitus is defined[3] on the basis of a random value of 198 mg/dl (11 mmol/L) then from our data this will be about 6 SD above our screening value. Thus, while it is not possible to say that some diabetic patients were not missed, such data suggest it is unlikely. The incidence of four unsuspected diabetic patients in a population of 2403 (approximately 1:600) women of reproductive years is about the expected range. Second, the samples for random blood glucose screening were obtained at the stages of pregnancy during which blood was required for other routine antenatal tests; therefore, the cost of the needle and syringe was shared with several other determinations. It is not possible to give an exact cost for each blood glucose determination, but if the reagent strips used for testing urine, which give much unnecessary data about pH, etc., were replaced by a simple reagent strip to detect proteinuria, the saving would help to compensate for any added cost of blood glucose determinations. Finally, there is no disruption to clinic routine and the patients are not delayed or inconvenienced.

On the basis of random blood glucose screening of a total antenatal clinic population over 1 yr, two patients were found to have diabetes mellitus and 32 were referred for an OGTT. Of these, two more women were found to have diabetes and four had IGT. Of 21 women referred for other reasons, only three mothers had IGT. From another viewpoint, none of the diabetic patients were missed by random blood glucose screening, but only one of the four might have been referred for an OGTT on the basis of one episode of glycosuria.

Is it necessary to screen for diabetes mellitus? The incidence of diabetes appears to be increasing rather than decreasing[7,8] and while the mortality and morbidity rates for women appear to be better than for men they are still high[9] and show wide regional variations. The sooner such women can be detected and returned to a normoglycemic status the better their prognosis should be. The obstetrician must also be concerned for the fetus. In many hospitals the perinatal

mortality for diabetic mothers is not much greater than that for the population at large,[10] which almost certainly reflects increased care in controlling the metabolic status of the mother. If it is accepted that diabetes mellitus should be screened for as part of good antenatal care, then a random blood glucose measurement offers an easy, efficient, and relatively inexpensive method for its detection.

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