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Original Article

UNIVERSAL VERSUS SELECTIVE SCREENING FOR DETECTION OF GESTATIONAL DIABETES MELLITUS IN A MALAYSIAN POPULATION

N Idris[1], **CH Che Hatikah**[2], **MZ Murizah**[2], **MN Rushdan**[2]
[1]Department of Obstetrics & Gynaecology, International Medical University, Malaysia [Nazimah Idris]
[2]Department of Obstetrics & Gynaecology, Hospital Sultanah Bahiyah, Alor Setar, Kedah, Malaysia [Che Hatikah Che Hanafi, Murizah Md Zain, Mohd Rushdan Md Noor]

Address for correspondence: Dr Nazimah Idris, Senior Lecturer, International Medical University, IMU Clinical School, Jalan Rasah, 70300 Seremban, Negeri Sembilan, Malaysia. Email: nazimah_idris@imu.edu.my

ABSTRACT
Objectives: To compare the efficacy of two screenings methods for gestational diabetes mellitus, namely the universal screening using 50g Glucose Challenge Test to that of selective screening based on risk factors.
Methodology: A cross-sectional study involving 366 women between 24 weeks to 28 weeks gestation who attended a community health clinic for their antenatal care between January to May 2003. All women had their risk factors for gestational diabetes identified at the beginning of the study, after which they underwent a 50g Glucose Challenge Test and subsequently the 75g Oral Glucose Tolerance Test.
Results: The prevalence of gestational diabetes mellitus in this population was 18.3%. The universal screening had a sensitivity of 83.5% and specificity of 82.6% compared to that of selective screening, 76.1% and 60.9% respectively. Of all patients diagnosed to have gestational diabetes mellitus, 23.8% were without risk factors.
Conclusion: Universal screening strategy using 50g glucose challenge test is a better predictor of gestational diabetes mellitus compared to risk-based selective screening.
Key words: Gestational diabetes, glucose challenge test, risk-factors, screening, glucose tolerance test.
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INTRODUCTION

Gestational diabetes is carbohydrate intolerance of variable severity, with onset or first recognition of hyperglycaemia during pregnancy.[1] Studies have shown that gestational hyperglycaemia is associated with higher incidence of adverse maternal and foetal outcomes than is seen in normal pregnancy. Untreated gestational diabetes mellitus (GDM) was demonstrated to have increased perinatal mortality rate up to fourfold compared with that of control.[1] Morbidity related to macrosomia includes shoulder dystocia with birth injury and perinatal asphyxia in the foetus. In the mother it causes more genital tract injury, obstructed labour, uterine atony and increased risk of caesarean section. The importance of diagnosis of GDM relates not only to potential immediate morbidities at the time of birth but long term sequelae for the child. Obesity, development of type 2 diabetes mellitus, intellectual and neurological development and mental problems are known long term sequelae.[2] For the mother, GDM is a very strong risk factor for the development of type 2 diabetes later in life. Published studies show that after GDM, 35-60% of women develop type 2 diabetes within 10 years.[3] Therefore it is prudent that gestational diabetes is diagnosed and appropriate treatment and monitoring instituted.

The concept of screening for the disease is the basis of good antenatal care. Rationale of GDM screening include it allows identification GDM and hence treatment disposition thereby reducing the associated maternal and neonatal risk. It also allows identification of a group of women who have an increased risk of developing diabetes mellitus later in life.

The issue of what is the best screening method for gestational diabetes mellitus remains unsolved. Should universal screening be used, or selective screening based on risk factors? The Fourth International Workshop-Conference on Gestational Diabetes recommended selective screening where women <25 years old are only screened if risk factors are present.[1] The American Diabetes Association (ADA) made a similar recommendation.[4] However this will results in at least 90% of pregnant women screened and a high false positive rate. It appears that risk factor assessment approach to screening for GDM may leave room for error without markedly changing the proportion of women requiring laboratory testing.

On the other hand, The Canadian Task Force on Preventive Health Care found in 1992 that the evidence is insufficient

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to make recommendations against or for universal screening.[5] Similar conclusion was derived from the U.S. Preventive Services Task Force which conducted a systematic review on screening for diabetes mellitus.[6] Moreover, Coustan *et al* in a population based study from 1989 demonstrated that even women younger than 25 years and without risk factors can have gestational diabetes.[7] They may represent 10-22% of all gestational diabetes cases.[8]

In the public health service in Malaysia, screening for gestational diabetes is done selectively where only patients with risk factors are screened and diagnosed using a 1-step 75g OGTT. This is done at least once at or around 24 weeks gestation, unless there are indications for it to be done earlier.[9]

However, as Asian ethnicity is considered a risk factor, selectively screening our women without regard to their Asian background may results in gross under-detection of gestational diabetes. On the other hand, to have all pregnant women undergo the 75g OGTT may be cumbersome and have some economic implications, particularly in low resource areas. We intend to study whether a universal screening using 50g Oral Glucose Challenge Test followed by 75g OGTT in screen-positive patients will be a better screening strategy for our population compared to the present method.

METHODOLOGY

This is a cross-sectional study conducted between 1st January to 31st May 2003, at a Maternal and Child Health Clinic in Alor Star, Kedah, Malaysia involving pregnant women between 24 to 28 weeks gestation. Women who are known to have diabetes prior to index pregnancy were excluded from the study.

All women who consented to be in the study were evaluated for presence of risk factors for gestational diabetes mellitus. They then undergo the 50g oral Glucose Challenge Test (GCT) irrespective of their fed state and subsequently had the 75g Modified Glucose Tolerance Test (MGTT) done after at least another 3 days of normal diet and activity.

Patients were considered to be risk-factor positive if any of the following is present:

- age 35 years and above
- previous macrosomic baby with birth weight 4.0kg or more
- previous unexplained still birth
- previous baby with congenital abnormally
- recurrent miscarriages (3 or more)
- previous pregnancy with gestational diabetes mellitus
- history of Diabetes Mellitus in first degree relatives
- obese or pre-pregnancy weight more than 80kg

The 50g oral glucose challenge test was considered positive if the glucose level one hour after the glucose challenge at least 7.8 mmol/L. Gestational diabetes mellitus was diagnosed if the 75 g oral glucose tolerance test showed venous plasma level of <7.0 mmol/L after an overnight fast and at least 7.8mmol per litre at two hours, based on the WHO(1999) criteria.[10]

Data were analysed using SPSS version 11.5. P-value of < 0.05 was used as significant values in any statistical test measurement.

RESULTS

366 women completed the study. The mean age was 30.3 years, 18% were <25 years of age while 24.0% were 35 years and above. 30% of patients were nulliparous. The majority of patients were ethnic Malays (85.8%), while the ethnic Chinese, Indian and others made up the rest, reflecting the demographical distribution of the population of the Kedah state. The prevalence of gestational diabetes mellitus in the study population was 18.3%, and was significantly higher in the older women ($p<0.05$). There was no significant difference in the prevalence of GDM in relation to ethnicity. The demographic data was shown in Table 1.

Table 1. Demographic data and parity of patients with and without gestational diabetes

Characteristics	GDM (n=67) Number (%)	No GDM (n=299) Number (%)
Ethnicity		
Malay	57 (85.1)	257 (86.0)
Chinese	7 (10.4)	28 (9.4)
Indian	2 (3.0)	8 (2.7)
Others	1 (1.5)	6 (2.0)
Age (years)		
Less than 25	2 (3.0)	64 (21.4)
25-34	31 (46.3)	181 (60.5)
35 and above	34 (50.7)	54 (18.1)
Parity		
Nulliparous	13 (19.4)	97 (32.4)
Parity 1-4	51 (76.1)	186 (62.2)
Parity 5 and above	3 (4.5)	16 (5.4)

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We found 45.6% patients had at least 1 risk factor for gestational diabetes mellitus, the commonest being age factor and a positive family history of diabetes mellitus. The type of risks and its relation to the diagnosis of GDM is shown in Table 2. Using this screening strategy, we were able to detect 51 out of 67 GDM patients, giving a test sensitivity of 76.1% and a specificity of 61.2%. 16 or 23.9% of patients with gestational diabetes mellitus were not found to have any risk factors. The positive and negative predictive values of the test were 30.5% and 92.4% respectively.

Table 2. Result of selective screening using risk assessment and the diagnosis of GDM

Risk factor (n)	GDM (n)	NO GDM (n)
Previous GDM (2)	2	0
Positive family history (58)	13	45
Weight > 80 kg (26)	7	19
Age > 35 year old (88)	34	54
History of macrosomia (8)	3	5
Recurrent abortion (7)	3	4
History of unexplained IUD/NND (2)	1	1
History of congenital anomaly (1)	0	1
At least one risk factor : n = 167	51	116
No risk factor : n = 198	16	183
Total n = 366	67	299

* A patient may have more than one risk factor.

We compare the above results with that of the universal screening strategy, as shown in Table 3. We found a better detection rate of 83.5% and an improved specificity of the test at 82.6%, the difference which is statistically significant. The positive and negative predictive values were 51.9% and 95.7% respectively. Using this strategy, five additional patients with GDM were detected with 59 less OGTT done.

Table 3. Result of screening using universal screening by GCT and the diagnosis of GDM

Glucose challenge test – n = 366	Gestational Diabetes – n = 67	Non-gestational diabetes – n = 299
Positive GCT: n = 108	56	52
Negative GCT: n = 258	11	247

Table 4 shows the comparison of results between the two screening strategies which clearly shows that the universal screening results in better detection rate at a lower false positive rate compared to the risk-based screening. (z value 2.494, $p < 0.05$ for sensitivity and z value 10.284, $p < 0.05$ for specificity).

Table 4: Comparison between the universal screening using GCT and selective screening of risk assessment

Screening method	Sensitivity	Specificity
Universal	83.5	76.1
Selective	82.6	60.9

DISCUSSION

Our study aimed to evaluate the value of performing the universal screening using the 50g glucose challenge test to detect gestational diabetes mellitus when compared with the current method of screening which is via the risk screening.

When previously there were doubts whether it was necessary to screen for and treat gestational diabetes mellitus, the case for screening was strengthened following the publication by the ACHOIS trial group. The ACHOIS (Australian Carbohydrate Intolerance Study in Pregnant Women) trial has shown that treating mild gestational diabetes mellitus significantly reduces the serious perinatal complications and may also improve the women's health-related quality of life.[11] The finding from this study indirectly answers the question of whether screening is indicated for gestational diabetes mellitus.

Our study recorded a prevalence of 18.3% for gestational diabetes mellitus in our population-based subjects. In most western population the low- and high-risk populations have a prevalence rate of 1.4%-2.8% and 3.3%-6.1% respectively.[12] That the prevalence is higher than in the western population came as no surprise since Asian population in itself is considered a risk factor. This prevalence is also higher than what was reported in other Asian countries, which range from 8.6% in a Filipino population to in-excess of 16% in an Indian population.[13-16] A local study done also reported high prevalence for gestational diabetes of 11.4%.[17] This finding further emphasized the need for screening and detection of gestational diabetes mellitus in our population to ensure better outcome of the pregnancy.

We used maternal age of 35 years and above, history of diabetes in first degree relative, history of gestational diabetes, weight of at least 80kg at booking, history of a macrosomic baby, unexplained intra-uterine death, history of congenital anomaly in previous pregnancy and recurrent miscarriages in our risk-based screening criteria. 45.6% of our study population has at least one risk factor and be

screened positive. However, if we had used the most recent Malaysian Diabetes Guideline (2009) and the ADA-based screening criteria where the age threshold was 25 years, 82% of our patients would have been screened positive, with an additional 2 cases diagnosed. This has not taken into consideration our universal Asian ethnicity, which in itself is considered a risk factor in the United States population, which if implemented here, will result in all patients having to undergo the 75g glucose tolerance test, which will further increase the false positive rate of the test with minimal improvement in the detection rate. On the other hand, with such a high prevalence recorded, coupled with a strong evidence of the benefit of intervention for GDM by the ACHOIS Trial Group, one step screening may be a worthwhile option for our pregnant population if the economic resources are abundant.

Our study shows the universal screening strategy using 50g GCT was able to detect an additional five out of 16 cases of GDM which risk-based screening missed, and at a significantly lower false positive rate (48.1% vs 69.5%). We also showed the increased specificity of screening with GCT of 82.6%, when compared to 60.9% when using the risk-screening strategy. 59 less OGTT would have been done for non-GDM patients using this strategy. All these can possibly be translated into a substantial cost saving and convenience for patients.

Actual cost impact between the two screening strategies is however, difficult to quantify as it does not only involves cost of tests and procedures, but also unnecessary interventions due to false positive results as well as the cost of therapy and its potential harms. Carr in his review in 1998 found that universal screening for GDM maximizes screening sensitivity, but it is less cost-effective than selective screening. However, he also concluded that 50g 1-hour glucose screen at 24 weeks to 28 weeks gestation offers the best combination of ease and economy of use and reproducibility in screening for GDM.[18] Based on his review and the result of our study, it seems feasible to adopt this strategy for the screening of GDM in our pregnant population.

We have shown that clinical risk-based screening is a poorer predictor of GDM compared to a two-step screening process with oral glucose tests. Our two-step screening process using 50g GCT followed by 75g MGTT using WHO (1999)[10] criteria is similar to the screening process used in a large multicentre trial which uses a similar GCT threshold of 7.8mmol/l (The ACHOIS Trial). It is possible that the sensitivity of GCT can be further improved if the threshold of the glucose level be reduced to 7.6mmol/l, as suggested by Tan *et al* who studied 1600 patients at the antenatal clinic in a local university hospital setting.[17]

The strength of our study is that all our patients underwent both tests, thus we did not discriminate patients who had a negative screening test by excluding them from undergoing the diagnostic OGTT. They were able to act as their own control and the result is a truer reflection of the actual status, without the sampling bias. Our study is also population-based, and representative of the actual situation in the community. One limitation is our small sample size. However, we opined that even with a larger sample, the results would not be very much different as our sample population is quite representative of the general pregnant population.

From the results of this study, due to its convenience and probable cost saving, we would like to recommend that universal screening using 50g GCT be adopted as a screening strategy for the detection of gestational diabetes mellitus in the Malaysian population.

CONCLUSION

Universal screening using 50g glucose challenge test is superior to risk-based screening in detecting gestational diabetes mellitus and is a feasible strategy for use in a Malaysian population.

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Research Digest

Dispensed medications poorly labelled in pharmacies and GP clinics in Penang

Neoh CF, Hassali MA, Shafie AA, Awaisu A, Tambyappa J. Compliance towards dispensed medication labelling standards: a cross-sectional study in the state of Penang, Malaysia. *Curr Drug Saf.* 2009;4:199-203.

Affiliation of first author: Faculty of Pharmacy, Universiti Teknologi Mara (UiTM), Penang, Malaysia

128 pharmacies and 26 GP clinics were visited by simulated patients with the presentation of hypothetical common cold symptoms. Results found were as follow:

Labelling on dispensed medication	Pharmacy	GP clinic
Name of patient	0%	97.9%
Name of medications	19.4%	18.8%
Date of supply	5.4%	85.4%
Expiry date	3.9%	2.1%
Label of "Controlled Medicine"	74.4%	12.5%

This is what the law states…

Poison Regulation 1952

12. (1) Where any poison is sold or supplied as a dispensed medicine, or as an ingredient in a dispensed medicine, the container of such medicine shall be labelled, in a conspicuous and distinct manner, with

(a) the name and address of the supplier or seller ;and
(b) the name of the patient or purchaser; and
(ba) the name of the medicine; and
(c) adequate directions for the use of such medicine; and
(d) the date of delivery of such medicine; and
(e) where such medicine is sold or supplied and entered in a prescription book, with a reference to the serial number of the entry in such book relating to such sale or supply.