Maternal hemoglobin level and red cell indices as predictors of gestational diabetes in a multi-ethnic Asian population

P.C. Tan[1], J.N. Chai[2], L.P. Ling[3], S.Z. Omar[1]

[1]Department of Obstetrics and Gynecology, University of Malaya, Kuala Lumpur
[2]Faculty of Medicine, University of Malaya, Kuala Lumpur
[3]Hospital Raja Permaisuri Bainun, Jalan Hospital, Perak (Malaysia)

Summary

Objective: To evaluate maternal hemoglobin levels and red cell indices as predictive factors for gestational diabetes (GDM). *Method:* Data from 1,538 women were analyzed. At the first visit for prenatal care, the 50-gram glucose challenge test was followed by the 75-gram glucose tolerance test in those who screened positive. GDM was diagnosed based on the WHO (1999) criteria. Maternal complete blood count was obtained at the first visit, hospitalization for birth, and after birth. Receiver operator characteristic curves were generated to establish thresholds. Multivariable logistic regression analyses were performed to establish independent predictors of GDM. *Results:* GDM was diagnosed in 182/1,538 (11.8%). GDM was associated with hemoglobin level, hematocrit and erythrocyte count at the first visit for prenatal care only. Hemoglobin threshold at the first visit was established at 11.5 g/dl. After adjustment, high hemoglobin [AOR 1.5 (95% CI 1.0-2.1); $p = 0.027$] remained predictive of GDM. *Conclusions:* High maternal hemoglobin level at the first prenatal visit is independently predictive of GDM.

Key words: Hemoglobin; Gestational diabetes; Predictor; Hematocrit; Erythrocyte count.

Introduction

Gestational diabetes mellitus (GDM) is defined as glucose intolerance first recognized during pregnancy. GDM is a common disease. In European and North American populations, low- and high-risk populations typically have a GDM prevalence rate of 1.4-2.8% and 3.3-6.1%, respectively [1]. In recent reports of screened Asian cohorts from Thailand, Malaysia, Bahrain and India, GDM incidence rates in excess of 10% have been reported [2-5].

The importance of identifying and appropriately managing GDM has been supported by recent clinical trials [6, 7]. The Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study has also confirmed that risk of adverse outcome is in continuum with hyperglycemia and there are no obvious threshold levels from which risk increased [8].

There is a still lack of consensus in the best screening method for GDM [9]. There is evidence that risk factor-based screening is effective: the American Diabetes Association and the British Diabetic Association recommend selective risk-related screening [10].

Hemoglobin level at the top quartile (> 13 g/dl) in non-anemic Chinese women is independently associated with GDM diagnosed after 28 weeks gestation [11]. In a study of non-anemic Turkish women, after adjustment, high hemoglobin level (> 50th percentile) is however not associated with GDM [12]. In Indian women with a high background rate of anemia [13], high hemoglobin level (> 10 g/dl) has been associated with GDM based on WHO criteria [14] but no significant association was found when the Carpenter and Coustan diagnostic criteria for GDM [15] was used. A case controlled study of Turkish women also failed to demonstrate an association between high hemoglobin or ferritin levels and development of GDM [16]. The independent association of high hemoglobin level and risk of GDM remains unsettled.

We sought to evaluate maternal red cell indices at the first visit for pregnancy care, at hospitalization for birth, and just after birth to GDM, and to evaluate the pregnancy-stage relationship of these variables to GDM.

Method

This study was conducted in a university hospital located in Kuala Lumpur, Malaysia. Our hospital serves an urban population in a middle income country. Although we are a tertiary referral center, most of our obstetric patients are local residents of average risk. There are over 5,000 births per year at our center.

We have reported on a cohort of 1,600 women with regard to the appropriate threshold of the 50-gram glucose challenge test (GCT) in our population. The women in the cohort were recruited at their first visit for prenatal care and women were excluded if they had established diabetes or a history of GDM [3]. The effect of a false-positive GCT on pregnancy outcome within a subgroup of 1,368 women from this cohort has also been reported [17]. The subjects for the present analysis were derived from the database of the 1,600 women cohort who were universally screened for GDM by a 2-step process.

All subjects filled out a personal characteristics questionnaire. The 1-hour 50 gram GCT was performed for all women in the study population. The diagnostic 75-gram oral glucose tolerance test (GTT) was performed if GCT venous plasma glucose level ≥ 7.2 mmol/l. GDM was diagnosed based on the WHO (1999) criteria (fasted venous plasma glucose ≥ 7.0

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mmol/l or 2-hour venous plasma glucose ≥ 7.8 mmol/l) [14]. We found a GDM incidence rate of 11.4% in our earlier study[3] but we did not evaluate red cell indices as potential predictors of GDM.

Women receiving pregnancy care at our hospital routinely had a complete blood count performed at the first visit for care, hospitalization for birth and within 48 hours after birth. Hepatitis B serology was also performed as standard investigation at the first visit. We retrieved complete blood count components and hepatitis B [18, 19] results from the computerized hospital laboratory reporting system, matched, and added the new data to our original database.

We excluded incompletely screened women, i.e., those who screened positive for GCT but failed to proceed to GTT as well as women with redundant or missing complete blood count data at their first visit for prenatal care from the final analysis. Data on maternal weight, height, gestational age, family history of diabetes, obstetric history and glycosuria were available and these variables were incorporated into the analysis.

Ethical oversight for our previous study[3] was provided by the University of Malaya Medical Centre Medical Ethics committee and participants provided written consent. According to our institutional ethics guideline, specific ethics approval was not needed for this follow-on data analysis study.

Data was entered into SPSS 16 (SPSS Inc., Chicago, IL, USA). We compared the GDM and the screened negative groups on their hemoglobin level, hematocrit, erythrocyte count and mean corpuscular volume, corpuscular hemoglobin and corpuscular hemoglobin concentration using the Student's t-test. These comparisons were made at the first visit, during hospitalization for birth, and after birth. Red cell indices were used to evaluate the effect of different stages of pregnancy. Receiver operator characteristic curves were generated to evaluate the utility and obtain optimal thresholds (if any) of variables with a demonstrated significant association with GDM. Categorized data were analyzed with the Fisher exact test. A model was built for multivariable logistic regression analysis which incorporated all categorical variables with crude $p < 0.2$ on bivariate analysis. Co-variables with significant interactions were dropped and the new model was retested. All statistical tests were 2-sided. $p < 0.05$ was taken as a level of significance.

Table 1. — *Red cell indices of women with and without gestational diabetes at different stages of pregnancy.*

	Gestational diabetes[a]	No gestational diabetes[a]	*p* value
Initial visit	n = 182	n = 1,356	
Hemoglobin (g/dl)	11.6 ± 1.1	11.4 ± 1.1	0.005
Hematocrit	0.35 ± 0.03	0.34 ± 0.03	0.003
Red cell count (million/μl)	4.11 ± 0.41	4.04 ± 0.45	0.057
Mean corpuscular volume (fl)	85.6 ± 6.9	85.3 ± 7.4	0.62
Mean corpuscular hemoglobin (pg)	28.4 ± 2.8	28.3 ± 3.1	0.62
Mean corpuscular hemoglobin concentration (g/dl)	331 ± 13	331 ± 14	0.90
At hospitalization for birth	n = 170[b]	n = 1,150[b]	
Hemoglobin (g/dl)	11.9 ± 1.3	11.8 ± 1.3	0.1
Hematocrit	0.37 ± 0.04	0.37 ± 0.03	0.08
Red cell count (million/μl)	4.32 ± 0.43	4.31 ± 0.44	0.61
Mean corpuscular volume (fl)	86.3 ± 7.4	85.6 ± 7.6	0.28
Mean corpuscular hemoglobin (pg)	27.7 ± 3.0	27.5 ± 3.1	0.26
Mean corpuscular hemoglobin concentration (g/dl)	321 ± 11	320 ± 11	0.43
After birth	n = 167[†]	n = 1,204[†]	
Hemoglobin (g/dl)	11.5 ± 1.6	11.4 ± 1.6	0.47
Hematocrit	0.36 ± 0.05	0.36 ± 0.05	0.50
Red cell count (million/μl)	4.18 ± 0.55	4.17 ± 0.56	0.89
Mean corpuscular volume (fL)	86.1 ± 7.4	85.7 ± 7.7	0.56
Mean corpuscular hemoglobin (pg)	27.7 ± 3.0	27.5 ± 3.1	0.51
Mean corpuscular hemoglobin concentration (g/dl)	321 ± 11	320 ± 12	0.37

Data displayed as mean ± standard deviation, number (%) and median [interquartile range]. Analysis was with the Student's t-test for continuous data, Mann Whitney U test for ordinal data, Fisher's exact test for 2 x 2 categorical datasets and the chi square test for larger than 2 x 2 datasets. Multivariable logistic regression analysis performed incorporating all categorical variables with crude bivariate $p < 0.2$.

[a]Gestational diabetes was diagnosed using a 2 point 75 g oral glucose challenge test (WHO 1999 criteria: fasted venous plasma glucose ≥ 7.0 mmol/l or 2-hour plasma glucose ≥ 7.8 mmol/l). Non-gestational diabetics were all screened negative with the 50 g glucose challenge test (1-hour cut-off set < 7.2 mmol/l) or excluded by 75 g oral glucose challenge test.

[b]Missing data as some women who presented for prenatal care did not deliver at our center. Also a few pre-delivery or post-birth maternal complete blood counts were not obtained.

Results

From the original database of 1,600 women, 62 (3.9%) were excluded due to incomplete 2-step screening, i.e., positive GCT but no follow-on GTT (39 patients), erroneous or duplicated data entry (17 patients), untraceable complete blood count (5 patients) or clotted complete blood count sample (1 patient) leaving 1,538 women for the final analysis.

The GDM rate was 182/1,538 (11.8%). Table 1 shows the association between the red cell indices at different stages of pregnancy against GDM. On analysis with the Student's t-test, mean hemoglobin level and hematocrit at the first visit for prenatal care were higher in the GDM group. Erythrocyte count was not significantly different. At hospitalization for birth and even more so after birth, the mean red cell index values were no longer different between the groups. The association of red cell indices to GDM appeared to be strongest at the earlier stage of pregnancy. We also performed similar analyses for leukocyte count and platelets as a data quality control measure; no association with GDM was demonstrated with these variables at the first visit (data not shown).

Subsequently, we presented analyses based on the data from the complete blood count sample at the first prenatal visit only.

Table 2 shows the result after receiver operator characteristic (ROC) curves were generated to evaluate utility and to obtain optimized thresholds for categorization into high and low levels for the relevant red cell indices at the first prenatal visit against GDM. Hemoglobin level, hematocrit and erythrocyte count showed potential as predictors for GDM with optimized thresholds established at ≥ 11.5 g/dl, ≥ 0.35 and ≥ 4.15 10^{12}/l respectively. Other red cell indices were not useful as a predictor of GDM. We then categorized hemoglobin level, hematocrit and erythrocyte count into high and low groups for analyses by the Fisher exact test. We used these categorized variables in the multivariable logistic regression analysis.

ROC curves (not shown) were also generated to establish optimized thresholds for maternal age, body mass index, weight, gestational age and height at the first pre-

Table 2. — *Receiver operator characteristic curve analyses of red blood indices at first visit for prenatal care versus gestational diabetes.*

	Area under the curve (95% Confidence Interval)	*p* value	Optimized cut-off
Hemoglobin	AUC 0.564 (95% CI 0.520-0.608)	0.005	≥ 11.5 g/dl
Hematocrit	AUC 0.571 (95% CI 0.526-0.615)	0.002	≥ 0.35
Red blood cell count	AUC 0.558 (95% CI 0.515-0.601)	0.011	≥ 4.15 10^{12}/l
Mean corpuscular volume	AUC 0.503 (95% CI 0.459-0.547)	0.900	Not applicable
Mean corpuscular hemoglobin	AUC 0.496 (95% CI 0.453-0.539)	0.862	Not applicable
Mean corpuscular hemoglobin concentration	AUC 0.500 (95% CI 0.455-0.544)	0.987	Not applicable

Table 3. — *Characteristics of women with and without gestational diabetes before and after adjustment.*

	Gestational diabetes[a] n = 182	No gestational diabetes[a] n = 1,356	Relative Risk (95% Confidence Interval)	*p* value	Adjusted Odds Ratio (95% Confidence Interval)[b]	Adjusted p[b]
Age (years)	31.8 ± 4.9	29.3 ± 4.7		$p < 0.001$		
Age > 30 yearsc	105 (57.7)	472 (34.8)	RR 1.7 (95% CI 1.4-1.9)	$p < 0.001$	AOR 2.3 (95% CI 1.7-3.2)	$p < 0.001$
Ethnicity				$p = 0.041$		$p = 0.11$
Malay (referent)	99 (54.4)	871 (64.2)				
Chinese	37 (20.3)	229 (16.9)			AOR 1.5 (95% CI 0.95-2.1)	$p = 0.08$
Indian	37 (20.3)	187 (13.8)			AOR 1.6 (95% CI 1.03-2.5)	$p = 0.04$
Others	9 (4.9)	69 (5.1)			AOR 1.2 (95% CI 0.6-2.6)	$p = 0.56$
Parity	1 [2]	1 [2]		$p = 0.47$		
Parous	105 (57.7)	776 (57.2)	RR 1.0 (95% CI 0.9-1.2)	$p = 0.94$		
Body mass index (initial visit)	28.1 ± 5.5	26.5 ± 4.5		$p = 0.001$		
BMI > 25c	128 (70.3)	814 (60.0)	RR 1.2 (95% CI 1.1-1.3)	$p = 0.008$	AOR 1.3 (95% CI 0.9-1.9)	$p = 0.23$
Weight at initial visit (kg)	67.3 ± 13.3	64.2 ± 11.5		$p = 0.003$		
Weight ≥ 75 kg[c]	47 (25.8)	215 (15.9)	RR 1.6 (95% CI 1.2-2.1)	$p = 0.002$	AOR 1.7 (95% CI 1.1-2.7)	$p = 0.011$
Height (m)	1.55 ± 0.06	1.56 ± 0.06		$p = 0.09$		
Height ≤ 1.55 m[c]	101 (55.5)	642 (47.3)	RR 1.2 (95% CI 1.0-1.4)	$p = 0.04$	AOR 1.6 (95% CI 1.1-2.2)	$p = 0.009$
Gestation at initial visit (wks)	26.3 ± 7.0	28.2 ± 6.8		$p < 0.001$		
Gestation ≤ 26 weeks at initial visit[c]	97 (53.3)	513 (37.8)	RR 1.4 (95% CI 1.2-1.6)	$p < 0.001$	AOR 1.6 (95% CI 1.2-2.3)	$p = 0.005$
Initial visit hemoglobin (g/dl)	11.6 ± 1.1	11.4 ± 1.1		$p = 0.005$		
Hemoglobin ≥ 11.5 g/dl[c]	109 (59.9)	642 (47.3)	RR 1.3 (95% CI 1.1-1.4)	$p = 0.002$	AOR 1.5 (95% CI 1.05-2.1)	$p = 0.027$[d]
Hematocrit	0.35 ± 0.03	0.34 ± 0.03		$p = 0.003$		
Hematocrit ≥ 0.35[c]	108 (59.3)	665 (49.0)	RR 1.2 (95% CI 1.1-1.4)	$p = 0.009$	AOR 1.4 (95% CI 1.0-1.9)	$p = 0.046$[d]
Red cell count (million/µl)	4.11 ± 0.41	4.04 ± 0.45		$p = 0.057$		
Red cell count ≥ 4.15[c]	86 (47.3)	505 (37.2)	RR 1.3 (95% CI 1.1-1.5)	$p = 0.012$	AOR 1.3 (95% CI 0.9-1.8)	$p = 0.18$
Family history of diabetes[e]	51 (28.0)	317 (23.4)	RR 1.2 (95% CI 0.9-1.5)	$p = 0.16$	AOR 1.0 (95% CI 0.7-1.5)	$p = 0.95$
Previous baby ≥ 4 kg	2 (1.1)	10 (0.7)	RR 1.5 (95% CI 0.3-6.8)	$p = 0.64$		
History of unexplained intrauterine death	1 (0.5)	10 (0.7)	RR 0.7 (95% CI 0.1-5.8)	$p = 1.00$		
Glycosuria at initial visit	4 (2.2)	12 (0.9)	RR 2.5 (95% CI 0.8-7.6)	$p = 0.11$	AOR 2.0 (95% CI 0.6-6.6)	$p = 0.25$
Hepatitis B s antigenemia	3 (1.6)	21 (1.5)	RR 1.1 (95% CI 0.3-3.5)	$p = 0.76$		

Data displayed as mean ± standard deviation, number (%) and median [interquartile range]. Analysis: Student's t-test for continuous data, Mann Whitney U test for ordinal data, Fisher's exact test for 2 x 2 categorical datasets and chi square test for larger than 2 x 2 datasets. Multivariable logistic regression analysis performed incorporating all categorical variables with crude bivariate $p < 0.2$.

aGestational diabetes was diagnosed using a 2-point 75 g oral glucose challenge test (WHO 1996 criteria: fasted plasma glucose ≥ 7.0 mmol/l and/or 2-hour plasma glucose ≥ 7.8 mmol/l). Non-gestational diabetics were all screened negative with the 50 g glucose challenge test with 1-hour cut-off set at ≥ 7.2 mmol/l or excluded by 75 g OGTT where GCT was positive.

[b]Adjusted odds ratio and P value shown for variables incorporated in multivariable logistic regression analysis

[c]Cut-offs for these categorizations established using receiver operator characteristic curves versus GDM diagnosis

[d]These results were for either hemoglobin concentration or high hematocrit incorporated into the model for multivariable logistic regression analysis with the all other co-variables. The AOR results shown for the other incorporated covariables were those with hemoglobin concentration in the model. The AOR results for the other covariables with hematocrit in the model were similar.

[e]First degree relative with diabetes mellitus, e.g., at least a parent or sibling with diabetes

natal visit in order to categorize into high or low groups for these variables against GDM.

Table 3 shows the result of bivariate analysis and the follow-on multivariable logistic regression analysis having incorporated all variables with $p < 0.2$ on bivariate analysis into the model. Hemoglobin level and hematocrit demonstrated strong interaction and confounding in the model (correlation -0.71). We therefore performed analyses dropping either hemoglobin or hematocrit from the model: high hemoglobin level had an adjusted odds

ratio AOR 1.5 (95% confidence interval CI 1.05-2.1); p = 0.027 and high hematocrit had AOR 1.4 (95% CI 1.0-1.9); p = 0.046. High hemoglobin level ≥ 11.5 g/dl had a marginally stronger association to GDM compared to high hematocrit ≥ 0.35. High erythrocyte count was not an independent predictor of GDM.

Other independent predictors of GDM were high maternal age and weight, low gestational age at the first prenatal visit, short maternal stature and Indian ethnicity (compared to Malays). Diabetes in first degree maternal relatives and high body mass index (BMI) were not independent predictors of GDM. The AOR values of the independent predictors shown in our study were all very similar, ranging from 1.4 to 2.3. This indicated that high hemoglobin level was of similar weight as an independent predictor of GDM compared to established risk factors like maternal age and weight.

Discussion

High hemoglobin level and high hematocrit at the first visit for prenatal care were independent predictors of GDM in our study population. Our study population was relatively large, ethnically diverse and they were all ideally screened for GDM with the 2-step process.

Our main finding was similar to that reported for non-anemic Chinese women from Hong Kong [11] and for mostly anemic Indian women whose GDM was diagnosed according to the WHO (1999) criteria [13]. We did not exclude women with anemia and we also used the WHO criteria. In contrast to the report from India where 62.5% of their women were anemic (defined as hemoglobin < 10 g/dl) [13], only 11.4% of the women in our study had hemoglobin < 10 g/dl. In the study from Hong Kong, hemoglobin > 13 g/dl demarcated their top quartile whereas only 7% of our study population had hemoglobin > 13 g/dl. Our study population bridged the gap between the non-anemic and high anemia rate populations of previous reports [11, 13]. Our finding confirmed the association of high hemoglobin to GDM regardless of the background rate of maternal anemia.

Our finding was in contrast to other reports that have not shown any association of GDM to high hemoglobin level. Those reports however involved smaller study populations of 253 [12] and 112 women [16] and hence might not have been adequately powered.

High hemoglobin level at the first visit for prenatal care demonstrated the strongest association with GDM compared to hospitalization for birth or after birth. Our subjects' first prenatal visit was at (mean ± standard deviation) 28 ± 7 weeks gestation. The broad range of gestational age in our population at their first visit permitted further evaluation on the effect of gestation on the prediction of GDM. Gestational age ≤ 26 weeks at first visit was independently predictive of GDM. Taken together, our data suggests that high hemoglobin might be a better predictor of GDM earlier in pregnancy. This association was maintained into the third trimester but not to around time of birth. The reason for the loss of association very late into pregnancy might be the confounding effect of oral iron supplementation. Oral iron supplementation at 40 mg elemental iron (as 200 mg ferrous sulphate) orally daily was commonly prescribed during the latter part of pregnancy in our center regardless of hemoglobin status. In our study population, mean hemoglobin rose by 0.4 g/dl ($p < 0.001$) between the first visit and hospitalization for birth.

After adjustment, high BMI was not an independent predictor of GDM but high body weight and short stature were. Our finding in a multi-ethnic Asian population that short maternal stature was independently predictive of GDM was consistent with a recent report that has shown a similar association in Caucasian women [20].

High maternal age is a well established and recognized risk factor for GDM [10, 11]. High maternal age demonstrated the highest odds ratio for GDM in our model. Within our multi-ethnic Asian population generally at high risk for GDM, Indian ethnicity demonstrated the highest risk compared to Malays as referent. A recent report from Chennai in India has reported a very high GDM rate of 16.55% [5] in their unselected but hospital-based population. Ethnic Indians in our study population mostly originated from the Chennai region of India.

About a quarter of our subjects had a history of diabetes in a first degree relative. However, family history was not an independent predictor of GDM in contrast to conventional wisdom [10]. This might mean that in our population, the general genetic predisposition to glucose intolerance might have been expressed in downstream variables like weight, height and hemoglobin level and was no longer independently predictive of GDM after adjustment for these co-variables. Although GDM has been associated with hepatitis B seropositivity [18, 19], we did not find such an association. However, there were only 24 women who were seropositive for hepatitis B in our sample. Our sample size might not be adequate to assess this association.

There were limitations and strengths to our study. We did not perform diagnostic screening on every woman. A 2-step screening process GCT with threshold set at 7.2 mmol/l glucose has a sensitivity of 90% for detecting GDM [21], so only a small proportion of GDM cases would be missed because of false-negative GCT screening. This limitation is present also in previous similar reports [11, 13]. We could not control for serum ferritin as this test was not performed consistently in our study population. GDM cases reportedly had a higher serum ferritin level [22, 23] but in the largest study to date, this association became non-significant after adjustment for prepregnant BMI [24]. A recent randomized trial of iron supplementation from early pregnancy has shown that despite higher hemoglobin and serum ferritin levels in supplemented women, their GDM rate was similar to women on placebo [25]. Hence the basis for the association of high hemoglobin and GDM is not likely to be maternal nutritional status. Compared to previous reports [11-13, 16], our sample size was relatively large and our population was unselected. We also adjusted for other

major risk factors in our analysis. Our finding had therefore provided major support to a high hemoglobin level as an independent predictor for GDM. This is particularly so within the context of Asian populations with a high background risk of GDM.

Conclusion

High maternal hemoglobin level independently predicts gestational diabetes in an unselected multi-ethnic Asian population with a high background risk. This association may be more pronounced earlier in pregnancy. High hemoglobin level had a broadly similar predictive value compared to conventional risk factors like maternal weight and age. As maternal hemoglobin testing is standard in many prenatal care protocols, there should be no incremental cost to incorporating high hemoglobin level into the equation where a risk factor-based screen for GDM is in use. Appropriate threshold values have to be established as thresholds are likely to differ across populations.

References

[1] Brody S.C., Harris R., Lohr K.: "Screening for gestational diabetes: a summary of the evidence for the U.S. Preventive Services Task Force". *Obstet. Gynecol.,* 2003, *101,* 380.

[2] Boriboonhirunsarn D., Sunsaneevithayakul P., Nuchangrid M.: "Incidence of gestational diabetes mellitus diagnosed before 20 weeks of gestation". *J. Med. Assoc. Thai,* 2004, *87,* 1017.

[3] Tan P.C., Ling L.P., Omar S.Z.: "Screening for gestational diabetes at antenatal booking in a Malaysian university hospital: the role of risk factors and threshold value for the 50-g glucose challenge test". *Aust. N.Z.J. Obstet. Gynaecol.,* 2007, *47,* 191.

[4] Al Mahroos S., Nagalla D.S., Yousif W., Sanad H.: "A population-based screening for gestational diabetes mellitus in non-diabetic women in Bahrain". *Ann. Saudi Med.,* 2005, *25,* 129.

[5] Seshiah V., Balaji V., Balaji M.S., Sanjeevi C.B., Green A.: "Gestational diabetes mellitus in India". *J. Assoc. Physicians India,* 2004, *52,* 707.

[6] Crowther C.A., Hiller J.E., Moss J.R., McPhee A.J., Jeffries W.S., Robinson J.S.: "Effect of treatment of gestational diabetes mellitus on pregnancy outcomes". *N. Engl. J. Med.,* 2005, *352,* 2477.

[7] Landon M.B., Spong C.Y., Thom E., Carpenter M.W., Ramin S.M., Casey B. *et al.*: "A multicenter, randomized trial of treatment for mild gestational diabetes". *N. Engl. J. Med.,* 2009, *361,* 1339.

[8] Metzger B.E., Lowe L.P., Dyer A.R., Trimble E.R., Chaovarindr U., Coustan D.R. *et al.*: "Hyperglycemia and adverse pregnancy outcomes". *N. Engl. J. Med.,* 2008, *358,* 1991.

[9] Hillier T.A., Vesco K.K., Pedula K.L., Beil T.L., Whitlock E.P., Pettitt D.J.: "Screening for gestational diabetes mellitus: a systematic review for the U.S. Preventive Services Task Force". *Ann. Intern. Med.,* 2008, *148,* 766.

[10] Reece E.A., Leguizamon G., Wiznitzer A.: "Gestational diabetes: the need for a common ground". *Lancet,* 2009, *373,* 1789.

[11] Lao T.T., Chan L.Y., Tam K.F., Ho L.F.: "Maternal hemoglobin and risk of gestational diabetes mellitus in Chinese women". *Obstet. Gynecol.,* 2002, *99,* 807.

[12] Tarim E., Kilicdag E., Bagis T., Ergin T.: "High maternal hemoglobin and ferritin values as risk factors for gestational diabetes". *Int. J. Gynaecol. Obstet.,* 2004, *84,* 259.

[13] Wani A.I., Bashir M.I., Masoodi S.R., Sheikh M.I., Zargar A.H.: "Relationship of prevalence of gestational diabetes mellitus with maternal hemoglobin". *J. Assoc. Physicians India,* 2005, *53,* 1077.

[14] Report of a WHO Consultation. Definition, diagnosis and classification of diabetes mellitus and its complications. 1999. Accessible on http://whqlibdoc.who.int/hq/1999/WHO_NCD_NCS_99.2.pdf. Last accessed Feb 7, 2010.

[15] Carpenter M.W., Coustan D.R.: "Criteria for screening tests for gestational diabetes". *Am. J. Obstet. Gynecol.,* 1982, *144,* 768.

[16] Gungor E.S., Danisman N., Mollamahmutoglu L.: "Maternal serum ferritin and hemoglobin values in patients with gestational diabetes mellitus". *Saudi Med. J.,* 2007, *28,* 478.

[17] Tan P.C., Ling L.P., Omar S.Z.: "The 50-g glucose challenge test and pregnancy outcome in a multiethnic Asian population at high risk for gestational diabetes". *Int. J. Gynaecol. Obstet.,* 2009, *105,* 50.

[18] Lao T.T., Chan B.C., Leung W.C., Ho L.F., Tse K.Y.: "Maternal hepatitis B infection and gestational diabetes mellitus". *J. Hepatol.,* 2007, *47,* 46.

[19] Lao T.T., Tse K.Y., Chan L.Y., Tam K.F., Ho L.F.: "HBsAg carrier status and the association between gestational diabetes with increased serum ferritin concentration in Chinese women". *Diabetes Care,* 2003, *26,* 3011.

[20] Ogonowski J., Miazgowski T.: "Are short women at risk for gestational diabetes mellitus?". *Eur. J. Endocrinol.,* 2010, *162,* 491.

[21] "Diagnosis and classification of diabetes mellitus". *Diabetes Care* 2006, *29* (suppl. 1), S43.

[22] Lao T.T., Tam K.F.: "Maternal serum ferritin and gestational impaired glucose tolerance". *Diabetes Care,* 1997, *20,* 1368.

[23] Lao T.T., Chan P.L., Tam K.F.: "Gestational diabetes mellitus in the last trimester - a feature of maternal iron excess?". *Diabet. Med.,* 2001, *18,* 218.

[24] Chen X., Scholl T.O., Stein T.P.: "Association of elevated serum ferritin levels and the risk of gestational diabetes mellitus in pregnant women: The Camden study". *Diabetes Care,* 2006, *29,* 1077.

[25] Chan K.K., Chan B.C., Lam K.F., Tam S., Lao T.T.: "Iron supplement in pregnancy and development of gestational diabetes - a randomised placebo-controlled trial". *BJOG,* 2009, *116,* 789.

Address reprint requests to:
P.C. TAN, M.D.
Department of Obstetrics and Gynecology
University of Malaya
Kuala Lumpur, 50603 (Malaysia)
e-mail: pctan@um.edu.my;
tanpengchiong@yahoo.com