A STUDY ON FACTORS AFFECTING NEWBORN WEIGHT AND LARGE FOR GESTATIONAL AGE NEWBORNS IN NON-DIABETIC MOTHERS: THE ROLE OF MATERNAL SERUM TRIGLYCERIDES

BY

DR. SITI MARIAM BINTI SH AHMAD

Dissertation Submitted In Partial Fulfilment
Of The Requirements For The Degree of Master of Medicine
(OBSTETRICS AND GYNAECOLOGY)

UNIVERSITI SAINS MALAYSIA
NOVEMBER 2004

BAHAGIAN PENYELIDIKAN & PEMBANGUNAN CANSELORI

UNIVERSITI SAINS MALAYSIA

Laporan Akhir Projek Penyelidikan Jangka Pendek

Nama Penyelidik: Dr Nik Hazlina bt Nik Hussain

Nama Penyelidik-Penyelidik

Lain (Jika berkaitan) :

Prof. Madya Dr. Faridah Abdul Rashid

Dr Che Anuar Che Yaacob

2) Pusat Pengajian/Pusat/Unit: Jabatan Obstetrik & Ginekologi dan Jabatan Patologi Kimia, PPSP, USM, Kelantan

3) Tajuk Projek: " A Study On Factors Affecting Newborn Weight and Large For Gestational Age (LGA) Newborn in Non- Diabetic Mothers: The Role of Maternal Serum Triglycerides".

4) (a) Penemuan Projek/Abstrak

(Perlu disediakan makluman di antara 100 - 200 perkaraan di dalam Bahasa Malaysia dan Bahasa Inggeris ini kemudiannya akan dimuatkan ke dalam Laporan Tahunan Bahagian Peryelidikan & Pembangunan sebagai satu cara untuk menyampaikan dapatan projek fuan/puan kepada pihak Universiti)

A Study on Factors Affecting Newborn Weight and Large for Gestational Age (LGA) Newborns in Non-Diabetic Mothers : The Role of Maternal Serum Triglycerides

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ABSTRACT

Introduction: Triglycerides have been shown to be a biochemical predictor of newborn weight and risk of large for gestational age (LGA) in a few previous small studies. The objective of this study is to ascertain whether mid-pregnancy fasting serum triglycerides can predict the risk of developing LGA and newborn weight in non-diabetic pregnant mothers.

Methodology: Universal sampling of pregnant mothers attending the antenatal clinic at the Hospital Universiti Sains Malaysia (HUSM) and nearby clinics between 24 to 32 weeks gestation was carried out between December 2003 and July 2004. Expectant mothers were screened for exclusion criteria including diabetes, hypertension, pre-

eclampsia, fetal anomaly and multiple gestations. Those who were sure of dates and consented for the study were enrolled. Modified oral glucose tolerance test (MOGTT) was performed and fasting serum triglycerides and total cholesterol were analysed. The subjects were followed up at delivery when the period of gestation, the birth weight and the sex of newborn were noted. The correlations of the variables with newborn weight were tested and multiple linear regressions were used to find the associations. Bivariate logistic regression was used to look at the association of LGA newborn and the variables including triglycerides which were divided into two groups. The associations of the two groups of triglycerides and fasting plasma glucose (FPG) with the incidence of LGA were tested in cross tabulations.

Results: A total of 310 subjects were enrolled and 267 completed data were analyzed, 246 were normal glucose tolerant (NGT) and 21 impaired glucose tolerant (IGT). The incidence of IGT in this study was 7.9%. In NGT, triglycerides correlated poorly ($r=0.14$, $p=0.03$) with newborn weight while maternal body mass index (BMI) ($r=0.30$, $p<0.001$) and FPG ($r=0.28$, $p<0.027$) were the only two variables moderately correlated with newborn weight after adjustment of the gestation and gender of the newborn. FPG (OR 3, $p=0.027$), high triglycerides value (>2.78mmol/L) ($p=0.039$) and 2 hours postprandial plasma glucose (HPPPG) ($p=0.044$) were associated with risk of LGA newborn. With high triglycerides (>2.78mmol/L) and FPG (>4.3mmol/L), risk of getting LGA was 31.8% ($p<0.001$).

Conclusions: In NGT subjects, mid-pregnancy high FPG and high triglycerides value could be used to predict risk of getting LGA newborn.

Keywords: maternal triglycerides, mid-pregnancy, newborn weight, large for gestational

age (LGA)

b) Senaraikan Kata Kunci yang digunakan di dalarn abstrak:

Bahasa Malaysia	Bahasa Inggeris
maternal triglycerides	trigliserida ibu
mid-pregnancy	pertengahan kandungan
newborn weight	berat bayi
large for gestational age (LGA)	anak yang besar bagi tempoh kandungan tertentu

5) Output Dan Faedah Projek

(a) Penerbitan *(Termasuk laporan/kertas seminar)* -
(Sila nyatakan jenis, tajuk, pengarang, tahun terbitan dan di mana telah diterbit/dibentangkan)

1. [1] Siti Mariam Sh Ahmad, [1]N Hazlina NH, [2]Faridah Ab Rashid, [1]Che Anuar C Yaacob, [1]Intan Idiana Hassan, [1]Dept of Obstetrics and Gynaecology and [2]Dept. Of Chemical Pathology, " A Study On Maternal Serum Triglyceride and Newborn Weight In Non Diabetic Mothers" (accepted for publication in The International Medical Journal , Japan)

2. [1] Siti Mariam Sh Ahmad, [1]N Hazlina NH, [2]Faridah Ab Rashid, [1]Che Anuar C Yaacob, [1]Intan Idiana Hassan, [1]Dept of Obstetrics and Gynaecology and [2]Dept. Of Chemical Pathology, " A Study On Maternal Serum Triglyceride and Newborn Weight In Non Diabetic Mothers" MAMANEH, 25th Feb. till 27th Feb. 2005, Crown Princess Hotel, Kuala Lumpur

b) Faedah – Faedah Lain Seperti Perkembangan Produk, Prospek Komersialisasi Dan Pendaftaran Paten.
(jika ada dan jika perlu, sila gunakan kertas berasingan)

-TIADA-

(c) Latihan Gunatenaga Manusia

i) Pelajar Siswazah Dr Siti Mariam bt Sh Ahmad (M.Med O&G) May 2005

ii) Pelajar Prasiswazah:

iii) Lain-Lain :

6. Peralatan Yang Telah Dibeli:

- TIADA-

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BAHAGIAN PENYELIDIKAN DAN PEMBANGUNAN
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UNIVERSITI SAINS MALAYSIA

Laporan Kemajuan Penyelidikan

Nama Penyelidik/Penyelaras: Dr Nik Hazlina bt Nik Hussain

Pusat Pengajian: Jabatan Obstetrik & Ginekologi

Tajuk Projek Penyelidikan:
: A Study On Factors Affecting Newborn Weight and Large For Gestational Age (LGA) Newborn in Non- Diabetic Mothers: The Role of Maternal Serum Triglycerides.

Jumlah Geran Diluluskan : RM 17,998.00

Geran Tambahan yang diluluskan: RM 3,399.00

Baki yang ada: RM 2,334.87

Tarildiprojek bermula dan dijangka siap: 1 April 2004

Lanjutan tempoh yang diluluskan *(sekimnya berkaitan): 31 Mac 2006*

(I)

(ii)

(iii)

Laporan Kemajuan dan segi kerja-kerja yang telah dijalankan:

(Sila beviliipomn Kemajuan yang terperinci setakat mana yang boleh)

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JABATAN BENDAHARI
KUMPULAN WANG PENYELIDIKAN GERAN USM(304)
PENYATA PERBELANJAAN SEHINGGA 31 OGOS 2005

Jumlah Geran:	RM	Tiada Rekod	Ketua Projek:	DR. NIK HAZLINA NIK HUSSAIN
Peruntukan 2004 (Tahun 1)	RM	10,000.00	Tajuk Projek:	Maternal Serum Triglyceride Level and Newborn Weight in Non-diabetic Mothers
Peruntukan 2005 (Tahun 2)	RM	3,399.00		
Peruntukan 2006 (Tahun 3)	RM	0.00	Tempoh:	01 April 04- 31 Mac 06
			No.Akaun:	304/PPSP/6131325

Kwg	Akaun	PTJ	Projek	Donor	Peruntukan Projek	Perbelanjaan Tkumpul Hingga Tahun Lalu	Peruntukan Semasa	Tanggungan Semasa	Bayaran Tahun Semasa	Belanja Tahun Semasa	Baki Projek
304	11000	PPSP	6131325		900.00	1,349.15	(449.15)	-		-	(449.15)
304	14000	PPSP	6131325		-	140.98	(140.98)	-		-	(140.98)
304	15000	PPSP	6131325		-	-	-	-	-	-	-
304	21000	PPSP	6131325		1,800.00	1,029.60	770.40	-	459.00	459.00	311.40
304	22000	PPSP	6131325		-	-	-	-	-	-	-
304	23000	PPSP	6131325		300.00	-	300.00	-	-	-	300.00
304	24000	PPSP	6131325		-	-	-	-	-	-	-
304	25000	PPSP	6131325		-	-	-	-	-	-	-
304	26000	PPSP	6131325		-	-	-	-	-	-	-
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304	28000	PPSP	6131325		-	-	-	-	-	-	-
304	29000	PPSP	6131325		6,100.00	7,093.50	(993.50)	-	523.70	523.70	(1,517.20)
304	32000	PPSP	6131325		-	-	-	-	-	-	-
304	35000	PPSP	6131325		-	-	-	-	-	-	-
					13,399.00	9,990.43	3,408.57	-	1,073.70	1,073.70	2,334.87

Subject: **Fwd: acceptance of paper (IMJ)**
Date: Mon, 22 Aug 2005 06:44:41 +0100 (BST)
From: mariam ahmad <simshahmad@yahoo.com>
To: Nik Hazlina Nik Hussain <hazlina@kb.usm.my>
CC: shukri prof <shukri@eng.usm.my>

Note: forwarded message attached.
Good news, paper accepted. TQ kak nik :)

Subject: **acceptance of paper (IMJ)**
Date: Fri, 19 Aug 2005 13:15:28 +0900
From: "IMJ" <imj-uc@seronjihou.co.jp>
To: <simshahmad@yahoo.com>

Aug 19, 2005

Dr Siti Mariam Sh Ahmad
Department of Obsterics and Gynaecology
Hospital Seberang Jaya

Dear Dr Ahmad :

We are pleased to advise you that your paper, A Study on Factors Affecting Newborn Weight and
Large for Gestational Age (LGA) Newborn in Non-Diabetic Mothers: The Role of Maternal Serum
Triglycerides has been accepted for publication in the IMJ by an editor-in-chief after peer referee's examination. It will be printed in the near future.

Yours faithfully,

IMJ Division

Mr Wataru Uchida
Editorial Office

27th July 2005

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T. Sakuta M.D.
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Dear Sir,

Re: Submission of an original article

I would like to submit an article " A Study On Factors Affecting Newborn Weight and Large for Gestational Age (LGA) Newborn in Non-Diabetic Mothers: The Role of Maternal Serum Triglycerides"

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Methodology: Universal sampling of pregnant mothers attending the antenatal clinic at the Hospital Universiti Sains Malaysia (HUSM) and nearby clinics between 24 to 32 weeks gestation was carried out between December 2003 and July 2004. Expectant mothers were screened for exclusion criteria including diabetes, hypertension, pre-eclampsia, fetal anomaly and multiple gestations.

Those who were sure of dates and consented for the study were enrolled. Modified oral glucose tolerance test (MOGTT) was performed and fasting serum triglycerides and total cholesterol were analysed. The subjects were followed up at delivery when the period of gestation, the birth weight and the sex of newborn were noted. The correlations of the variables with newborn weight were tested and multiple linear regressions were used to find the associations. Bivariate logistic regression was used to look at the association of LGA newborn and the variables including triglycerides which were divided into two groups. The associations of the two groups of triglycerides and fasting plasma glucose (FPG) with the incidence of LGA were tested in cross tabulations.

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Conclusions: In NGT subjects, mid-pregnancy high FPG and high triglycerides value could be used to predict risk of getting LGA newborn.

Keywords: maternal triglycerides, mid-pregnancy, newborn weight, large for gestational age (LGA)

Introduction

Fetal macrosomia is clinically important and increasingly common (Bonellie & Raab, 1997). It is associated with increased rates of induction of labour, operative delivery, prolonged and obstructed labour and subsequently uterine atony and post partum hemorrhage. It may cause perineal tears, anal sphincter rupture and pudendal nerve damage (Sultan & Kamm, 1994; Mocanu & Greene, 2000). The macrosomic baby is at greater risk of fetal asphyxia, shoulder dystocia, birth trauma and neonatal hypoglycemia (Nesbitt *et al.*, 1998). Furthermore, such infants may have an increased susceptibility to obesity and diabetes in later life (Weintrob *et al.*, 1996; Mikulandra *et al.*, 2000).

Fetal macrosomia is most commonly expected and associated with diabetes in pregnancy. Even though it is a well-accepted fact, it is quite surprising to find conflicting data in the literature regarding this. For example, a study by Green et al (1991) showed only a modest association of glucose with increased birth weight when maternal body mass index (BMI) was controlled. While Dang et

al (2000) could not show a relationship between glucose values in oral glucose tolerance test (OGTT) and fetal macrosomia but instead found only maternal BMI correlated significantly with fetal macrosomia.

There were not many studies done on maternal triglycerides as compared to studies on diabetic pregnant mothers. In fact, earlier studies on triglycerides were actually meant to find the metabolic consequences of diabetes in pregnancy or the metabolic changes that occur in pregnancy . One of the earliest studies was by Skryten *et al.* (1976) who found diabetic pregnant mothers have higher serum triglycerides level throughout the pregnancy as compared to non-diabetic mothers and infant birth weight related well with mid-pregnancy maternal triglycerides level. On the contrary, Couch *et al.* (1998) noted that high triglycerides level in diabetic pregnant mothers was not associated with fetal lipid concentration and newborn weight, but in non-diabetics, triglycerides value proved to correlate with both fetal lipid level and newborn weight. These findings were in agreement with the results of the study by Di Cianni *et al.* (2005).

Knopp *et al.* (1992) further strengthened the evidence of association when they found maternal serum triglycerides to be the only screening test significantly associated with birth weight in their study sample, which encompassed both diabetic and non-diabetic mothers. Kitajima *et al.* (2001) followed Knopp's footstep but narrowed his study into positive screened, non-diabetic pregnant

mothers and as postulated, found positive correlation between triglycerides value and newborn weight. He also noted triglycerides were useful in predicting fetal macrosomia.

The objective of this study was to ascertain whether mid-pregnancy fasting serum triglycerides could predict the risk of developing LGA and newborn weight in non diabetic pregnant mothers.

Materiasl and Methods

This controlled prospective study was carried out at four antenatal clinics (ANC): Hospital Universiti Sains Malaysia (HUSM), Kota Bharu Health Cinic, Kubang Kerian Health Clinic and Kedai Lalat Health Clinic.

The study was performed on pregnant women attending the antenatal clinics at gestation between 24 to 32 weeks gestation and they were followed up during delivery. At this gestation, they were required to undergo MOGTT and a fasting lipid profile was taken at the same time. Their age, parity and BMI were recorded. At delivery, weight of the newborn, gestation at delivery, mode of delivery and sex of the baby were noted.

The exclusion criteria are as described below;

1. Diabetic (diagnosed diabetic prior to conception and gestational diabetes requiring insulin). These women were excluded to eliminate therapeutic biases and the association between maternal metabolic variables and fetal growth (Merzouk *et al.*, 2000).
2. Hypertension or preeclampsia (hypertensive disorder), lupus and antiphospholipid syndrome because these conditions are associated with fetal growth restriction due to placental insufficiency rather than metabolic factors (Janbu, 1989; Harvey & Verklan, 1990).
3. Fetal anomaly diagnosed through ultrasound during booking or noted abnormal at birth.
4. Multiple gestation as it is associated with weight discordance result from the inability of the uterine milieu to nurture twins equally. Individually they are smaller in size as an adaptation to the crowding (Blickstein, 2002).
5. Pre-term delivery (delivered before 37 weeks gestation), as fetus has not reached its full potential of growing.

The records of all expectant mothers attending antenatal clinic in the assigned clinics and new cases were scrutinized. Expectant mothers who were eligible for the study were identified and were approached at the clinic. Verbal and written explanation about the study was given and for those who agreed, written consent was taken. The consent was obtained using approved consent

form. Those who agreed to participate in this study were subjected to MOGTT and fasting serum lipids were taken together. All biochemical tests were performed by certified medical laboratory technologists (MLTs) in the Routine Laboratory, Department of Chemical Pathology, School of Medical Sciences, Universiti Sains Malaysia. Both glucose and triglycerides were determined using the Cobas Integra 400 automated chemistry analyzer (Roche Switzerland).

Neonatal birth weight above the 90th percentile of the gender specific birth weight curve of Malaysia (Boo et al. 1994) was defined as LGA. This birth weight curve was taken as it was the only Malaysian data which was available at the time of this study.

In this study, 1000 folders in the four antenatal clinics were scrutinized and out of that, 360 patients were found eligible for this study after considering the inclusion and exclusion criteria. They were approached and consented to participate in this study. They were given appointment for MOGTT within the specified period, i.e., between 24 and 32 weeks gestation. Out of these, 50 (13.9% of 360) patients who were eligible did not turn up on time for MOGTT. Only 310(86.1%) patients recruited managed to complete the blood investigations. Along the way, another 43(13.9%) participants were excluded from the study due to various reasons.

The Statistical Package for Social Sciences (SPSS) statistical software (version 11.0) was used for the analysis of biochemical and personal data in this study. The difference between group means were analyzed using different methods; Student *t*-test for two groups (two independent means) for variable with normal distribution and Mann Whitney test for variable with non-normal distribution. Univariate analysis and multiple logistic regression models were used to calculate the relation between the variables studied. Chi-square (χ^2) test was used to determine the significance of LGA babies in the two different triglycerides and plasma glucose groups. Level of significance (α) was set at 0.05 and $p < 0.05$ was accepted as significant.

Ethical Consideration

The Research and Ethics Committee, Universiti Sains Malaysia and Ministry of Health Malaysia have reviewed and approved this study proposal, with regard to methodology and ethical considerations.

Results

Table 1. Characteristics of mothers in Normal Glucose Tolerant (NGT) group

Parameter (numerical variables)	**NGT** *(n = 246)* **Mean (SD)**
Age (year)	30.87 (6.70)
Gravidity	3.76 (2.69)
BMI (kg/m²)	23.36 (4.04)
POG at blood taking (week)	27.61 (2.64)
POG at delivery (week)	39.00 (1.29)

BMI= body mass index; POG= period of gestation

From 267 expectant mothers who were involved in this study and had MOGTT and fasting lipid profile taken between 24 to 32 weeks gestation, 246(92.1%) patients were NGT and 21(7.9%) were IGT. The incidence of IGT in this study was 7.9%. In the NGT group, the mean age was 30.87±6.70 years, the BMI was 23.36±4.04 kg/m^2 and the mean POG of blood taking was 27.61±2.64 weeks.

The majority of the subjects in this study were Malay. Only 13(4.9% of 267) Chinese participants were involved and 11 of them were in the NGT group making up 4.5% of the group and another two were in the IGT group (9.5%). There were no Indian subjects involved in this study.

The biochemical results at mid-pregnancy were as follows: FPG for the NGT group was 3.99±0.49 mmol/L; 2HPPPG obtained for NGT was 5.47±1.1 mmol/L; Fasting triglycerides for the NGT group was 2.31±0.79 mmol/L. Fasting total cholesterol for the NGT group was 6.47±1.13 mmol/L. Fasting triglycerides above the 75th centile (>2.78 mmol/L) was considered hypertriglyceridaemia and a value less than this was considered normal. Analysis was also done on patients with FPG > 4.3 mmol/L, which was above the 75th centile of FPG measured.

Table 2. Correlation between birth weight ratio and independent variables in NGT (n = 246)

Independent variables	r	p value
Maternal age	0.17	0.007
Gravidity	0.18	0.004
Body mass index (BMI)	0.30	<0.001
Fasting plasma glucose (FPG)	0.248	<0.001
2H postprandial plasma glucose (2HPPPG)	0.198	0.002
Fasting triglycerides	0.122	0.057
Fasting total cholesterol	0.147	0.021

Dependent variable: birth weight ratio
Univariate analysis with SPSS version 11.
P<0.05 was considered significant

After correction of the gestational age at delivery, we found that the BMI of mothers was still the biggest factor contributing to birth weight after eliminating gestation and sex factors ($r = 0.3$ and $p < 0.001$) followed by FPG ($r = 0.25$ and $p < 0.001$) and to lesser extent 2HPPPG ($r = 0.20$ and $p = 0.002$). These relations are highly significant. On the other hand fasting triglycerides was shown not to have any significant correlation with newborn weight ($p = 0.057$).

Table 3. Risk factors for getting Large for gestational age (LGA) newborn in NGT (n = 246)

Risk factor (independent variable)	**Odds ratio (OR)**	**95% confidence interval**	**p value**
BMI	1.098	0.99 – 1.22	0.081
FPG	3.004	1.13 – 7.98	0.027
2HPPPG	1.633	1.03 – 2.53	0.044
High TG	1.476	1.15 – 1.93	0.039

Dependent variable: LGA newborn
BMI= body mass index; FPG= fasting plasma glucose; 2HPPPG= 2 hours postprandial plasma glucose; TG= triglycerides.

When backward Wald mode was used in the binary logistic regression, only four variables were considered in the final model that affected the incidence of LGA newborn. Only FPG (p = 0.027), 2HPPPG (p = 0.044) and high triglycerides (p = 0.039) contributed significantly to LGA newborn. FPG was still the strongest predictor of getting LGA babies. Incidence of LGA was approximately 1.5 times greater for mothers with high triglycerides than those with normal triglycerides.

Table 4. Cross tabulation between triglycerides sub-groups and incidence of LGA in NGT mothers

Triglycerides (mmol/L)	**LGA** No	Yes	**Total**
≤ 2.78 (Normal TG)	172 (92.5% of Normal TG) (78.2% of No LGA)	14 (7.5% of Normal TG) (53.8% of LGA)	186 (75.6%)
> 2.78 (High TG)	48 (80% of High TG) (21.8% of No LGA)	12 (20% of High TG) (46.2% of LGA)	60 (24.4%)
Total	220(89.4%)	26 (10.6%)	246

p = 0.006. Chi square=7.47
TG= triglycerides; LGA= large for gestational age.

In mothers with NGT at POG 24-32 weeks (n = 246), 186 (75.6% of 246) of them had normal triglycerides (< 2.78 mmol/L). In this group, 14 mothers delivered LGA newborns. The percentage of NGT mothers with normal triglycerides who had LGA newborns was 7.5%. On the other hand, 172 of the mothers in this group (92.5%) gave birth to newborns without LGA.

There were 60 pregnant mothers with high triglycerides in the NGT group. They made up 24.4% of the NGT group. As many as 12 of them (20% of 60)

obtained LGA newborns and 48 mothers in this group (80%) did not get LGA newborns.

In the low triglycerides group the incidence of LGA was 7.5% compared to 20% in the high triglycerides group. This association was statistically significant (p = 0.006).

The incidence of LGA newborns in the two FPG groups are as shown in the Table 5.

Table 5. Cross tabulation between FPG groups and incidence of LGA in NGT group

FPG (mmol/L)	**LGA** No	Yes	**Total**
<4.3 (Low FPG)	167 (93.3% of Low FPG) (75.9% of no LGA)	12 (6.7% of Low FPG) (46.2% of LGA)	179 (72.8%)
≥ 4.3 (High FPG)	53 (79.1% of High FPG) (24.1% of no LGA)	14 (20.9% of High FPG) (53.8% of LGA)	67 (27.2%)
Total	220(89.4%)	26(10.6%)	246

p value = 0.001. Chi square=10.39
FPG= fasting plasma glucose; LGA= large for gestational age.

When both high fasting blood glucose and high triglycerides were analysed in NGT mothers, the results are as shown in **Table 6**.

Table 6. Cross tabulation between triglycerides and FPG groups and incidence of LGA in NGT mothers

Number of risk factors	**LGA**		**Total**
	No	Yes	
0 (Low FPG and normal TG)	134 (95%)	7 (5%)	141 (57.3%)
1 (Has high FPG or high TG)	71 (85.5%)	12 (14.5%)	83 (33.7%)
2 (Has both high FPG and TG)	15 (68.2%)	7 (31.8%)	22 (9.0%)
Total	220 (89.4%)	26 (10.6%)	246

p value < 0.001, Chi square = 16.52
FPG= fasting plasma glucose; TG= triglycerides; LGA= large for gestational age.

If a patient had both FPG > 4.3 mmol/L and hypertriglyceridemia, the risk of getting LGA newborn was raised to 31.8%. If a patient did not have any of the factors mentioned above, the risk of getting LGA infant was only 5%. This result was highly significant ($p < 0.001$). In other words, high fasting blood glucose

(≥4.3mmol/L) combined with fasting triglycerides taken between 24 – 32 weeks gestation was an even better predictor of LGA babies in NGT pregnant mothers.

Discussion

Characteristics of study sample

The incidence of IGT obtained in this study was 7.9%. A higher value, 19.7%, was obtained in a previous study conducted in HUSM between July 1999 to October 2000 by Nor Haznita (2002). On the other hand, the results obtained in this study were lower compared to the study in University Hospital, Kuala Lumpur (Premitha, 1994). In the study by Premitha (1994), the prevalence of IGT in Malaysia was 12.7% with 10.2% in Malays. Another explanation for the lower than expected percentage of patients with IGT was the bias in sampling, as many patients with previous history of IGT or other risk factors which indicated a need to check their diabetes status had their MOGTT done earlier in pregnancy and they were reluctant to repeat MOGTT for this study.

Biochemical values and racial bias

The cut-off value for high triglycerides in this study was 2.78 mmol/L which was slightly lower than the value obtained by Kitajima *et al.*(2001) 2.93 mmol/L. This may be explained by the fact that although the subjects in Kitajima's study were non-diabetic, they had positive diabetic screens, while in this study the non-diabetics were grouped without knowing their screening status. The study by Knopp *et al.* (1992) on the other hand, obtained a much lower value which was 2.28 mmol/L. The difference of the findings may be attributed to racial differences and should be looked into further in future studies.

The majority of the subjects in this study were Malay. Only 13 Chinese participants were involved (4.9% of 267 participants) and 11 of them were in the NGT group making up 4.5% of the group and another two were in the IGT group (9.5%). There were no Indian subjects involved in this study. Racial factor, which could affect the biochemical results and the pregnancy outcome, was almost negligible in this study as 95% of the study samples were Malay. This could not be due to bias in sampling because the majority of the local population were Malay and they therefore comprised the majority of mothers who sought antenatal care at the health centers involved.

Outcome measured

When each of the variables was related with birth weight, it was noted that birth weight was seen to be affected by many interactive factors. Four factors which corrrelated significantly with newborn weight were BMI, FPG, 2HPPPG and gestation at delivery. However,after correction of gestational age at delivery, only BMI ($r=0.30$, $p<0.001$) and FPG ($r=0.248$, $p<0.001$) were found to be most significantly associated with birth weight while the rest of the variables showed only very weak correlation with birth weight (check: Table 2 lists 7 variables))

Contrary to previous studies (Knopp *et al.,* 1992; Alvarez *et al.,* 1996; Couch *et al.,* 1998; Kitajima *et al.,* 2001; Di Cianni *et al.,* 2002), this study showed that fasting triglycerides were not significantly associated with newborn weight. This finding supports similar findings by other studies (Roy *et al.,* 1994; Sanchez *et al.,* 2003). May be if gestation at blood taking was narrowed to within one or two weeks rather than eight weeks as in this study, we may get more consistent triglycerides results. The fact that triglycerides increased with duration of gestation was shown by Montelongo *et al.* (1992). The relationship between BMI and dyslipidemia was also confirmed in non pregnant (Wilsgaard & Arnesen, 2004; Zhai *et al.,* 2004) as well as in pregnant patients (Ramsay *et al.,* 2002).

Even though triglycerides did not have significant linear relationship with

newborn weight, high triglycerides was shown to have a significant relationship with risk of having LGA newborn (OR=1.476, p=0.039). After binary logistic stepwise analysis was done on all eight variables (age, gravidity, BMI, diabetes history, FPG, 2HPPPG, fasting triglycerides and fasting cholesterol), both FPG (OR=3, p=0.027) and 2HPPPG (OR=1.633, p=0.044) were also found to have significant relationship with LGA newborn (Table 3).

The associations derived from this binary regression though are still questionable because of inadequate number of samples in LGA group (26) and uneven distribution of number of samples in both groups (LGA = 26 and normal weight = 220) (Table 4). Logistic regression is not the best method to demonstrate relationship when the sample sizes are highly disproportionate. A better way of demonstrating the relationship between the two is through cross tabulation. The effect of other factors could be downplayed here as we have already tested correlation between triglycerides and other variables which were either weak or not significant. From the cross tabulation between triglycerides groups and LGA, high triglyglycerides (n=60) increased the risk of having LGA babies by two fold compared to the general study population (n=246) (20% versus 10.6%).

When non-diabetic sujects were placed in two groups according to their

FPG either above the 75th centile (FPG ≥ 4.3 mmol/L) or below, it was found that subjects with high FPG had triple the risk of getting LGA newborns compared to the other group. This test was highly significant ($p < 0.001$) (Table 5).

When these two factors were considered together, i.e., high FPG and high triglycerides, the incidence of LGA newborn was even better predicted. A patient with both risk factors i.e., a high triglycerides and a high FPG had three times greater the chance of getting a LGA newborn compared to the general study population (n=246) and six times more chance compared to those without these two factors. Indeed this was found to be a significant predictor ($p<0.001$) and could well be applied clinically (Table 6).

Conclusion

From the study we found that in NGT expectant mothers, the level of serum triglycerides in mid pregnancy did not have a significant correlation with newborn weight. Newborn weight after adjustment of sex and gestation at delivery was still best related to maternal FPG and BMI. On the other hand, high triglycerides (> 2.78 mmol/L) was found to be one of the predictors of LGA newborn. The incidence of LGA was also significantly related with MOGTT results. With high triglycerides (≥2.78mmol/l) and FPG (> 4.3 mmol/L) there was an almost 1 in 3 chance (31.8%) that the newborn would be big(oversize > 53 cm

long and overweight > 4.0 kg) . Without both factors, there was 95% likelihood the newborn would be of normal size(approximately 53 cm long and less or equal to 3.0 kg).

Impact of this study

This study has shown that the fasting triglycerides level in mid-pregnancy played a role in predicting the risk of getting large for gestational age newborn. The plasma glucose status in particular, the fasting plasma glucose also played a significant role in predicting large for gestational age incidence. Screening all pregnant mothers for fasting plasma glucose and fasting triglycerides at mid-pregnancy may be adopted as a practice in antenatal clinics to increase the rate of identifying expectant mothers at risk of getting large for gestational age newborn. This screening is simpler and cheaper and is a better option than the universal screening for gestational diabetes mellitus with glucose challenge test, which is more time consuming, costly and less acceptable for most expectant mothers.

Future direction

Based on these data, a larger prospective population-based study seems justified to verify the findings in this study as well as to come up with suggestions which can be used in the screening protocol at antenatal clinics in Malaysia.

Interventional study with diet modification for expectant mothers with high triglycerides at mid-pregnancy could be conducted if justified to investigate the effect of dietary modification on newborn outcome particularly the weight of the newborn.

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