



## Association of Socio Economic Status with Gestational Diabetes Mellitus among Saudi Women

Al-Shaikh G<sup>1,2</sup>, Alshaikh M<sup>1</sup>, Al-Shaikh R<sup>3</sup>, Almanie D<sup>2</sup>, Khan FH<sup>2</sup> and Al-Mandeel H<sup>1\*</sup>

<sup>1</sup>King Saud University, College of Medicine, Riyadh, Saudi Arabia

<sup>2</sup>Princess Nourah Bint Abdulrahman University, College of Medicine, Riyadh, Saudi Arabia

<sup>3</sup>Al Faisal University, College of Medicine, Riyadh, Saudi Arabia

\*Corresponding author: Dr. Hazem Al-Mandeel, Associate Professor, Department of Obstetrics and Gynecology, College of Medicine, King Saud University, Riyadh, Saudi Arabia, Tel: 00966114770895/00966114691175; E-mail: halmandeel@ksu.edu.sa; hmmandeel@yahoo.ca

Rec date: Oct 22, 2015 Acc date: Jan 08, 2016 Pub date: Jan 15, 2016

### Abstract

**Background:** Women with Gestational Diabetes Mellitus (GDM) are at risk of adverse obstetric and perinatal outcome. The association between GDM and socioeconomic status is not well established. The purpose of this study is to find the association between socioeconomic factors and GDM.

**Subjects and Methods:** A prospective case-control study was conducted in December 2013 at King Khalid University Hospital. The sample size was 401 (GDM cases 202 and normoglycemic controls 199). Gestational diabetes mellitus cases were diagnosed using the oral glucose tolerance test (OGTT).

**Results:** Mean age of GDM mothers was more than mothers who were normoglycemic. There was a significant difference ( $p < 0.001$ ) in BMI between the two groups as most of the GDM cases were morbidly obese, and were great grandpara ( $p < 0.001$ ) as well. Low socioeconomic status had a strong significant association ( $p < 0.001$ ) with GDM. There was also a significant difference ( $p < 0.001$ ) in the mode of delivery between the two groups of mothers, as most of the GDM mothers had higher rate of ventouse and cesarean section delivery. More of the newborns of GDM mothers had postnatal complications and needed NICU admission (25%) as compared to just 7% in the control group.

**Conclusion:** Lower socioeconomic status has a strong association with GDM. Advanced maternal age and increased BMI are the risk factors of GDM.

**Keywords:** Gestational diabetes mellitus; Socio economic status; Risk factors

### Introduction

Gestational diabetes mellitus (GDM) is defined as any degree of glucose intolerance with the onset or first recognition during pregnancy with or without remission after the end of pregnancy [1].

The diagnosis of GDM is both a threat to the mother and her baby. For the mother, there is a high risk of pre-eclampsia, preterm deliveries, caesarian section, and development of type-2 diabetes mellitus later in life [2].

The newborn consequently as well is at risk of developing hypoglycemia, hypocalcaemia, hypomagnesaemia, polycythemia, respiratory distress, growth restriction and congenital malformations [3]. Perinatal outcomes, due to poor glycemic control may result in 43% mortality in newborns [4]. The latter side consequences in children could be obesity and early onset of type-2 diabetes mellitus [5,6].

Globally, 2-7% of pregnant women are affected by GDM; however the rates are higher (3-19%) amongst some developed countries [7]. The latest prevalence has been reported up to 30.1% in Mexico and 37.7% in Norway and UAE [8,9].

According to the latest study done in Saudi Arabia the prevalence of GDM was found to be 36.6%, which is three folds higher than the previously reported in the year 2000 [10,11]. This reflects an alarming rapid increase in GDM cases amongst Saudi women.

The International Association of Diabetes and Pregnancy Study Group (IADPSG) have recommended lowering the fasting plasma glucose threshold for GDM diagnosis to  $\geq 92$  mg/dl (5.1 mmol/L). As a result the prevalence of GDM has significantly increased in many countries [12-14]. This recommendation of IADPSG has been adopted by the American Diabetes Association (ADA) in 2011 [15].

Many studies are done internationally to highlight the risk factors for GDM. The most reported risk factors are; obesity, age  $> 25$  years, and family history [16,17]. The association between GDM and socioeconomic status is not well established, however. Previous studies have reported conflicting results due to different definitions used for socioeconomic status.

One of the studies done by Knowler et al. [18] reported a significant relation of socioeconomic status, educational level, parity, maternal age, nutrition status, previous history of GDM, and family history of diabetes. Another study done in 2003 by Cheung et al. [19] reported that lower socioeconomic status is associated with GDM as women with low socioeconomic status are less likely to seek perinatal care and thus having more pregnancy related complications.

A study conducted in New South Wales, Australia 2008, where computerized database of all births ( $n=956,738$ ) between 1995 and 2005 was used in the multivariate logistic regression that demonstrates the association between socioeconomic status and GDM. In this study, it was found that women living in three lowest socioeconomic quartiles had higher adjusted odd's ratio for GDM relative to women in the highest quartile [20].

These studies cannot be compared due to the diverse definition of socioeconomic status which depend upon monthly income, owning a house and car, educational attainment, employment, household characteristics, and type of health care.

The aim of our study is to determine if there is any association between GDM and socioeconomic factors in Saudi pregnant women. Secondary objective is to compare the frequencies of common risk factors for GDM in mothers with and without the condition.

## Methods

### Patients and methods

This was a prospective case-control study of pregnant women with gestational diabetes mellitus. An approval by the Institutional Ethical Review Board was obtained before approaching the patients. Consecutive women were recruited from the GDM Clinic and Prenatal Clinic at King Khalid University Hospital, Riyadh, Saudi Arabia between Jan 2014 and July 2014. The sample size was calculated with Version 6 of Epi Info software. Various inputs were used and the CI was set to 95% and the Power was set to 80. The ratio of case-control was set at 1:1.

We needed a sample size of at least 200 in each group. A total of 401 women agreed to participate and informed consent signed (202 women with GDM as cases and 199 women with normoglycemia as controls). Exclusion criteria for both groups were women with history of diabetes mellitus prior to the onset of pregnancy, women with major chronic diseases like tuberculosis, cardiac disease, renal disease and liver disease.

The International Association of Diabetes and Pregnancy Study Groups (IADPSG) recommended that the findings be identified by at least one abnormal plasma glucose value in a 75-g oral glucose tolerance test (OGTT): fasting PG  $\geq$  92mg/dL (5.1 mmol/L), 1-h PG  $\geq$  180mg/dL (10.0 mmol/L), or 2-h PG  $\geq$  153 mg/dL (8.5 mmol/L) [21]. Based on the above definition, GDM cases were diagnosed in pregnant ladies whose OGTT was positive; while normoglycemic controls were those pregnant ladies who's OGTT in a fasting state was below cut-off values.

The Questionnaire consisted of questions regarding the demographic profile of the patient as her age, educational level,

occupation and number of children. Anthropometric measurements were also taken as height and weight and the BMI was calculated. Socioeconomic variables included monthly income of the household, ownership of a car and house.

Information regarding the obstetric outcomes was: mode of delivery, gestational age at delivery, birth weight, fetal and maternal complications, previous history of GDM and family history of diabetes mellitus were obtained during their delivery admission.

Weights and Heights were measured for all women on the day of recruitment using same electronic scale. Body Mass index (BMI) was calculated for all women defined as weight/height<sup>2</sup>.

### Statistical Analysis

Data was analyzed by using the statistical package SPSS version 11. Descriptive statistics have shown the results in percentages and mean, median and mode. Inferential statistics was done using Chi-square test on proportions and students t-test on means. P-value  $\leq$  0.05 was considered significant to reject the null hypothesis.

### Results

Table 1 shows the comparison of socio-demographic and anthropometric variables between GDM pregnant women and normoglycemic pregnant women.

The table demonstrates that GDM women were older in age as compared to normoglycemic women. There is a highly significant difference ( $p < 0.001$ ) in BMI between the 2 groups.

Characteristics	GDM pregnant (n=202) % or Mean $\pm$ SD	Normoglycemic pregnant (n=199) % or Mean $\pm$ SD	p-value 95% CI
Age in years	31 $\pm$ 6.3	29 $\pm$ 5.5	< 0.001 2.053 – 4.38
Parity	2.79 $\pm$ 2	2.36 $\pm$ 1.8	0.071 -0.0338–0.89
Height in cms.	156.6 $\pm$ 5.1	158.0 $\pm$ 5.6	0.008 2.08 – 8.94
Weight in kg.	83.16 $\pm$ 16.2	77.6 $\pm$ 18.5	0.002 2.08 – 8.94
Body Mass Index (BMI)	44 $\pm$ 8	40 $\pm$ 9	< 0.001 1.81 – 5.28

**Table 1:** Comparison of certain socio-demographic and anthropometric characteristics (quantitative variables) between GDM pregnant women and normoglycemics

In Table 2, further stratification of the 2 groups is done on the basis of BMI classification.

Here it was found that most of the (88/202 or 44%) GDM pregnant women were morbidly obese, i.e. BMI > 35 and this difference is highly significant as  $p = 0.001$  and odd's ratio is 24.

Table 3 shows the comparison of socio-demographic qualitative variables between the 2 groups.

It reveals that there is no difference between the 2 groups with respect to educational attainment, different occupations and family history of diabetes mellitus. However, 30% (59/202) of GDM cases had previous history of gestational diabetes.

BMI classification	GDM pregnant women (n=202)	Normoglycemic pregnant women (n=199)	P-values Odds ratio (95% C.I.)
Normal (BMI <25 ) versus abnormal (BMI >25)	55 (27%)	58 (29%)	p-value = 0.991 OR = 1.016 (0.063 to 16.354)
With obesity (from obese to morbidly obese (BMI > 30)	59 (29%)	76 (38%)	p-value = 0.030 OR = 0.338 (0.013 to 0.88)
Morbidly obese only (BMI > 35)	88 (44%)	65 (33%)	p-value < 0.001 OR = 24.082 (0.165 to 0.473)

**Table 2:** Comparison of different levels of BMI between GDM pregnant women and normoglycemics

Characteristics	GDM pregnant (n=202)	Normoglycemic pregnant (n=199)	p-value
Level of education	2 (1%)	1 (0.5%)	0.362
Uneducated	85 (42%)	70 (35%)	
Up to high school	115 (57%)	128 (64%)	
College and above			
Occupation	129 (64%)	123 (62%)	0.011
Housewife/unemployed	12 (6%)	24 (12%)	
Student	2 (1%)	06 (3%)	
Self employed	9 (5%)	08 (4%)	
Private Company employed	45 (22%)	36 (18%)	
Government employed	05 (2%)	2 (1%)	
Retired			
Previous history of GDM	Yes = 59 (30 %) No = 143 (70 %)	Yes = 0 No = 199(100%)	-
Family History of Diabetes mellitus	Yes = 151 (77 %) No = 39 (20 %) Don't know=12(3%)	Yes = 155(78 %) No = 40 (20 %) Don't know=4(2%)	0.07

**Table 3:** Comparison of certain socio-demographic categorical characteristics (qualitative variables) between GDM pregnant women and normoglycemics

**Table 4** compares the socio-economic factors between the GDM pregnant women and normoglycemic pregnant women. Highlighting all the 3 variables (monthly income, ownership of house and car), which were considered. There is a marked difference between the 2 groups ( $p < 0.001$ ).

The 75% (149/199) of normoglycemic mothers had spontaneous vaginal deliveries whereas just 60% (122/202) of GDM cases had a vaginal delivery. Twenty percent (40/202) and 10% (20/202) of GDM mothers had cesarean section and Ventouse-assisted vaginal delivery respectively; which was statistically significant ( $p < 0.001$ ).

## Discussion

Gestational diabetes mellitus is highly prevalent condition in pregnant women in Saudi Arabia [11,12].

In our study there was a strong and significant association of GDM in relation to socioeconomic status of affected mothers. This is going with what was found in a study done by Knowler et al. [18] Lower socio-economic status is found to be a risk factor for GDM in some other studies conducted in both developed and developing countries [22,23]. For instance, a study done by BoS [24] which found an inverse association of socioeconomic status with incidence of GDM and the study results by Vibeke et al. [20]

Socio economic Variable	GDM pregnant (n=202)	Normoglycemic pregnant (n=199)	p-value
Monthly income/month (in Saudi Riyals)	34(18%)	23(11 %)	0.000
<2999/=	33(16 %)	40(20 %)	
3000-4999/=	84(42 %)	77(39 %)	
5000- 9999/=	35(17 %)	39(20 %)	
10,000- 14,999/=	16(7 %)	20(10 %)	
>15,000/=			
Car – own	48 (24%)	154 (78 %)	0.000
Rent	154 (76%)	45 (22 %)	
House – own	61 (30%)	145 (73 %)	0.000
Rent	141 (70%)	54 (27 %)	

**Table 4:** Comparison of certain socio economic variables between GDM pregnant women and normoglycemics

In comparison to a study done in Saudi Arabia by Al-Rubean et al. [10] the investigators did not find a relationship between incidence of GDM and monthly household income, rather a low percentage of GDM cases were found among those having monthly income less than SR4000/=. We believe that the criteria used to define or describe socioeconomic status in our study were more comprehensive and thus was able to find a difference.

There are many studies which support the association between gestational diabetes and lower socioeconomic status [25]. In Saudi Arabia, women with lower socioeconomic status displayed more risk factors for gestational diabetes: as they more obese and had more pregnancies [25,26] supporting the results of our study. Women of this socioeconomic status had a higher percentage of parental diabetes, confirming the association between type 2 diabetes and socioeconomic status [27,28].

Similarly, in our study, the GDM mothers were morbidly obese (BMI>35). This may be due to a shift in diet style towards a more westernized diet (cheese, burgers, fried food, beverages etc.) among the Saudi population. Western diet has given rise to an increase in body weight and increased the risk of developing gestational diabetes mellitus and ultimately type-2 diabetes in later life [29]. Das et al. [30] and Gomez et al. [31] found that 50% of women with GDM, had obesity. This may be due to increase demands on maternal metabolism during pregnancy from excessive weight gain, resulting in imbalances in hormonal carbohydrate regulation mechanisms, and insulin sensitivity. Nilofer also found obesity as a risk factor in 88.89% of GDM patients [32]. Similar results were found by Garshasbi in Iran and Yang H in China [33,34].

About 30% of GDM cases had previous history of GDM, whereas there is no significant difference in the proportions of GDM and normoglycemic cases with respect to family history of diabetes (77% in GDM cases whereas 78% among normoglycemics p=0.07). This reflects that diabetes mellitus is a prevalent problem among the Saudi population [10,35]. This could be due to diet pattern and sedentary lifestyle of women here which lead to obesity; similarly Al Ghazali L et al. [36] found the same results and correlated it with high consanguinity marriage rates and hence increase in family history of diabetes mellitus among the Saudi population.

This study also showed that the mean age for Saudi GDM pregnant women is higher, as per the results of a recent study [22], contrary to what had been reported in other studies involving the Chinese and Indian populations [34,37]. This could be the result of different cultural factors that encourage women to get pregnant even at an older age, in addition to high parity [35].

With regard to the mode of delivery, 60% of GDM mothers had spontaneous vaginal delivery (as compared to 75% among non-diabetic cases). Whereas, 20% of GDM mothers underwent emergency caesarean section (as compared to 8% among non-diabetic cases). Such findings go along with what shown in other studies where higher cesarean section rates noted in women with GDM. For instance, a study done in 2013 in India, the caesarean delivery rate was 78.8% among GDM patients [38].

Our study has some limitations including possible selection bias as it represents women who live in an urban area with different socioeconomic status than those who lives in remote areas. In addition, the socioeconomic parameters used in the study might not be the best method in assessing the socioeconomic status. On the other hand, the study design and sample size were adequate for the objective.

## Conclusion

The study shows that lower socioeconomic status is associated with gestational diabetes mellitus. Advanced maternal age and obesity are more common in mothers with GDM.

## Significance of the Study

Our study showed that most of the GDM cases belong to a lower socioeconomic status, the status where people are less aware of health issues and their prevention. These women must be targeted for primary and secondary prevention against GDM to reduce morbidity of newborn and themselves and to reduce the prevalence of type -2 diabetes mellitus later in life. Therefore, there is a need to start public health awareness programs for reducing modifiable risk factors for GDM like obesity.

Health care providers and public health workers face numerous challenges in developing and implementing an intervention for this high risk population, and it is likely that meaningful reductions in risk

will require a multilevel approach that includes patient education, development of efficient mechanisms for the transfer of medical information among healthcare providers, establishment of readily available interventions, and environmental changes that support physical activity and healthy eating.

## Acknowledgement

We would like to acknowledge the support we received from the Deanship of Scientific Research at King Saud University for funding this project through Research Group project #RGB-VPP-241 and also an appreciation is given to Ms. Bella Rowena B. Magnaye for all her technical and administrative work done.

## References

1. Seshiah V, Das AK, Balaji V, Joshi SR, Parikh MN, et al. (2006) Gestational diabetes mellitus--guidelines. *J Assoc Physicians India* 54: 622-628.
2. Davey RX, Hamblin PS (2001) Selective versus universal screening for gestational diabetes mellitus: an evaluation of predictive risk factors. *Med J Aust* 174: 118-121.
3. Opara PI, Jaja T, Onubogu UC (2010) Morbidity and mortality amongst infants of diabetic mothers admitted into a special care baby unit in Port Harcourt, Nigeria. *Ital J Pediatr* 36: 77.
4. Otolorin EO, Famuyiwa OO, Bella AF, Dawodu AH, Adelusi B (1985) Reproductive performance following active management of diabetic pregnancies at the university college hospital, Ibadan, Nigeria. *Afr J Med Med Sci* 14: 155-160.
5. Pettitt DJ, Nelson RG, Saad MF, Bennett PH, Knowler WC (1993) Diabetes and obesity in the offspring of Pima Indian women with diabetes during pregnancy. *Diabetes Care* 16: 310-314.
6. Silverman BL, Rizzo TA, Cho NH, Metzger BE (1998) Long-term effects of the intrauterine environment. The Northwestern University Diabetes in Pregnancy Center. *Diabetes Care* 21 Suppl 2: B142-149.
7. Schmidt MI, Duncan BB, Reichelt AJ, Branchtein L, Matos MC, et al. (2001) Gestational diabetes mellitus diagnosed with a 2-h 75-g glucose tolerance test and adverse pregnancy outcomes. *Diabetes care* 24: 1151-1155.
8. Jenum AK, Morkrid K, Sletner L (2012) Impact of ethnicity on gestational diabetes mellitus with the WHO and the modified International Association of Diabetes and Pregnancy Study Groups criteria: a population-based cohort study. *Eur J Endocrinol* 166: 317-324.
9. Agarwal MM, Dhath GS, Shah SM (2010) Gestational Diabetes Mellitus Simplifying the International Association of Diabetes and Pregnancy diagnostic algorithm using fasting plasma glucose. *Diabetes Care* 33: 2018-2020.
10. Al-Rubeaan K (2014) A community-based survey for different abnormal glucose metabolism among pregnant women in a random household survey (SAUDI\_DM). *Open BMJ* 4: 1-6
11. Ardawi MS, Nasrat HA, Jamal HS, Al-Sagaaf HM, Mustafa BE (2000) Screening for gestational diabetes mellitus in pregnant females. *Saudi Med J* 21: 155-160.
12. Wei YM, Yang HX (2011) [Comparison of the diagnostic criteria for gestational diabetes mellitus in China]. *Zhonghua Fu Chan Ke Za Zhi* 46: 578-581.
13. Moses RG, Morris GJ, Petocz P, San Gil F, Garg D (2011) The impact of potential new diagnostic criteria on the prevalence of gestational diabetes mellitus in Australia. *Med J Aust* 194: 338-340.
14. Reyes-Munoz E, Parra A, Castillo-Mora A (2012) Effect of the new diagnostic criteria of the International Association of Diabetes and Pregnancy Study groups on the prevalence of gestational diabetes mellitus in urban Mexican women: a cross sectional study. *Endocr Pract* 18: 146-151.
15. American Diabetes Association (2011) Diagnosis and classification of diabetes mellitus. *Diabetes Care* 34: S62-S69.
16. Bo S, Menato G, Lezo A, Signorile A, Bardelli C, et al. (2001) Dietary fat and gestational hyperglycaemia. *Diabetologia* 44: 972-978.
17. Zargar AH, Sheikh MI, Bashir MI, Masoodi SR, Laway BA, et al. (2004) Prevalence of gestational diabetes mellitus in Kashmiri women from the Indian subcontinent. *Diabetes Res Clin Pract* 66: 139-145.
18. Knowler WC, Barret-Connor E, Fowler SE, Hamman RF, Lachin JM, et al. (2002) Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med* 346: 393-403.
19. Cheung NW, Byth K (2003) Population health significance of gestational diabetes. *Diabetes Care* 26: 2005-2009.
20. Vibeke A, Hidde P, Wah Cheung N, Rachel R, Adrian E (2008) Sociodemographic Correlates of the Increasing Trend in Prevalence of Gestational Diabetes Mellitus in a Large Population of Women Between 1995 and 2005. *Diabetes Care* 31: 2288-2293.
21. International Association of Diabetes and Pregnancy Study Groups Consensus Panel, Metzger BE, Gabbe SG, Persson B, Buchanan TA, et al. (2010) International association of diabetes and pregnancy study groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. *Diabetes Care* 33: 676-682.
22. Tanaka M, Jaamaa G, Kaiser M, Hills E, Soim A, et al. (2007) Racial disparity in hypertensive disorders of pregnancy in New York State: a 10-year longitudinal population-based study. *Am J Public Health* 97: 163-170.
23. Clausen T, Øyen N, Henriksen T (2006) Pregnancy complications by overweight and residential area. A prospective study of an urban Norwegian cohort. *Acta Obstet Gynecol Scand* 85: 526-533.
24. Bo S, Menato G, Bardelli C, Lezo A, Signorile A, et al. (2002) Low socioeconomic status as a risk factor for gestational diabetes. *Diabetes Metab* 28: 139-140.
25. Kühl C (1998) Etiology and pathogenesis of gestational diabetes. *Diabetes Care* 21 Suppl 2: B19-26.
26. Branchtein L, Schmidt MI, Matos MC, Yamashita T, Pousada JM, et al. (2000) Short stature and gestational diabetes in Brazil. Brazilian Gestational Diabetes Study Group. *Diabetologia* 43: 848-851.
27. Brancati FL, Whelton PK, Kuller LH, Klag MJ (1996) Diabetes mellitus, race, and socioeconomic status. A population-based study. *Ann Epidemiol* 6: 67-73.
28. Robbins JM, Vaccarino V, Zhang H, Kasl SV (2001) Socioeconomic status and type 2 diabetes in African American and non-Hispanic white women and men: evidence from the Third National Health and Nutrition Examination Survey. *Am J Public Health* 91: 76-83.

29. Egeland GM, Skjaerven R, Irgens LM (2000) Birth characteristics of women who develop gestational diabetes: population based study. *BMJ* 321: 546-547.
30. Das V, Kamra S, Mishra A (2004) Screening for gestational diabetes and maternal and fetal outcome. *J Obstet Gynaecol India* 54: 449-451.
31. Gómez HL, Martínez ML, Rodríguez ZM (2011) Clinical and epidemiological profile of diabetes mellitus in pregnancy, Isle of Youth, 2008. *Medicc Rev* 13: 29-34.
32. Nilofer AR, Raju VS, Dakshayini BR, Zaki SA (2012) Screening in high-risk group of gestational diabetes mellitus with its maternal and fetal outcomes. *Indian J Endocrinol Metab* 16 Suppl 1: S74-78.
33. Garshasbi A, Faghihzadeh S (2008) The prevalence of gestational diabetes mellitus and its risk factors in Tehran. *J Fam Reprod Health* 2: 75-80.
34. Yang H, Wei Y, Gao X, Xu X, Fan L, et al. (2009) Risk factors for gestational diabetes mellitus in Chinese women: a prospective study of 16,286 pregnant women in China. *Diabet Med* 26: 1099-1104.
35. Al Rowaily MA, Alsalem FA, Abolfotouh MA1 (2014) Cesarean section in a high-parity community in Saudi Arabia: clinical indications and obstetric outcomes. *BMC Pregnancy Childbirth* 14: 92.
36. Al-Gazali L, Hamamy H, Al-Arrayad S (2006) Genetic disorders in the Arab world. *BMJ* 333: 831-834.
37. Soheilykhan S, Mogibian M, Rahimi-saghand S (2010) Incidence of gestational diabetes in pregnant women. *Iran J Reprod Med* 8: 24-28.
38. Kalra P, Kachhwaha CP, Singh HV (2013) Prevalence of gestational diabetes mellitus and its outcome in western Rajasthan. *Indian J Endocrinol Metab* 17: 677-680.