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Plasma sex hormone-binding globulin (SHBG) level: A comparative study between patients with gestational diabetes mellitus and healthy pregnant women

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ABSTRACT

Gestational diabetes mellitus is a key pregnancy problem worldwide. The aim of this study was to compare the level of globulin binding hormone sex (SHBG) between diabetic pregnant women and healthy pregnant women in Kerman. This descriptive cross-sectional study was performed on diabetic pregnant women where diabetes was confirmed by a 2 h blood glucose tolerance test using 50 g and 100 g glucose. After completion of demographic information and midwifery records blood samples were collected from the patients and the blood glucose levels were measured. Also, SHBG was measured and finally all collected data were analyzed using SPSS software. The serum levels of SHBG were significantly lower in diabetic pregnant women as compared to the control group. However, this level reduction of SHBG in diabetic pregnant women was not significantly associated with other underlying factors and midwifery factors. Therefore, it is suggested that the serum SHBG levels can be used as an early factor in diagnosing the gestational diabetes.

INTRODUCTION

Gestational diabetes mellitus (GDM), as a major pregnancy complication, is defined as intolerance to carbohydrates with different intensities being first diagnosed or arisen during the pregnancy [1].

During pregnancy, the plasma insulin level physiologically increases up to twice of its normal level. Although the exact mechanism is unknown, it could be due to elevated levels of diabetogenic hormones such as cortisol, placental lactogen and progesterone. On the other hand, the lipolysis level increment, particularly in obese pregnant women might cause this phenomenon through increasing the circulating free fatty acids [2]. As evidenced by previous studies, the insulin performance in late pregnancy is lower than 50-70% of its amount in non-pregnant ones, which leads to an increment in the serum insulin level to compensate [3-5].

GDM puts both mother and fetus at risk of some complications. It has been showed that the mother will be at risk of type 2 DM in the future [6]. For the fetus, the most important issue is the high weight, mainly due to the high transfer of glucose from the mother to the fetus, which may cause delivery injuries [7].

Previous epidemiological studies have proposed a relationship between sex hormones, type 2 diabetes, and cardiovascular diseases [8]. Some prior cross-sectional and longitudinal studies have suggested that there is a relationship between serum SHBG

and metabolic syndrome [9]. Different studies have also indicated the relationship between serum SHBG levels and type 2 diabetes mellitus [10-13]. Based on the previous of studies on the role of the SHBG on DM, in this study we evaluate the relationship between the SHBG and GDM.

MATERIALS AND METHODS

This was a cross-sectional descriptive study conducted on diabetic pregnant women whose disease was diagnosed by a 2 h blood glucose tolerance test (GTT) using 50 g or a 3 h 100 g glucose test (fasting level greater than 95, 1 h above 186, 2 h above 153 and 3 h above 140). They were referred to the Gynecology Clinic of Afzal pour Hospital in Kerman, Iraq during 2018.

A total of 80 patients were examined in the study, 40 (50%) participants in each group. Two groups had similar pregnancy age and parity. We matched both case (patients with GDM) and control (healthy pregnant women) groups in terms of the pre-pregnancy body mass index (BMI). Criteria for entry into the study was pregnancy and presence of GDM (for case group); while the participants having pre-pregnancy chronic diabetes, polycystic ovary syndrome (PCOS), and other metabolic disorders were excluded.

Participants were asked to fill out a questionnaire that included demographic information. Blood pressure measurement was performed using the ALPK2 (Japan) sphygmomanometer cuff relationship of pre-pregnancy weight recorded by means of a German SCA scale. Fasting blood glucose, plasma SHBG and cholesterol levels were measured by the enzymatic photometric (GPO-PAP, Pars Azmun company kit), ELISA (ALPCO, Salem, NH), and photometric (CHOD-PAP, Pars Azmun company kit) methods, respectively.

All subjects gave their informed consent for inclusion before they participated in the study. The study was conducted in accordance with the Declaration of Kerman University of Medical Sciences, and the protocol was approved by the ethics Committee (IR.KMU.AH.REC. 1396.1559).

Statistical analysis

Data was analyzed using SPSS analytical software, version 16 (IBM Inc.; Chicago; IL; USA).

RESULTS

There was no significant difference between case group and control in respect of demographic information of study participants (Table 1). We found that the 75-g GTT, white blood cells (WBC) count, and family history of hypertension and DM were higher in people with GDM (Table 2). The rate of cesarean is a bit higher in patients with GDM (Table 2). History of previous GDM is more frequent in case group (Table 2). There was no significant difference between BMI and macrosomia in two groups.

The serum SHBG levels are estimated as 83.5±66.4 and 142.9±65 nmol/l in the case and control groups, respectively and this difference was statistically significant (P value = 0.000) (Table 2). The multivariate analysis between the serum SHBG level in each group and investigated background factors, only the age had a weak direct significant relationship and not statistically one was observed in other cases. Then we divide the

SHBG in 4 groups (quartile). Then, reanalyzed as shown in Table 3. We observed that in the group with the highest SHBG, the number of patients with GDM were the lowest.

Table 1. Demographic information of the study participants.

Variable	Case group	Control group
Age	29.2±7.6	29.6±5.2
Height	159.9±5.6	160.9±6.2
Current weight	65.8±8.7	68.7±15.9
Pre-pregnancy weight	60.3±7.3	65.2±14.3
Pregnancy age	17.7±8.2	14.9±9.3
Parity	2.3±0.8	3.7±11.7
Education		
Academic	19 (39.1%)	28 (60.9%)
Non-academic	21(63.6%)	12 (36.4%)
Contraception		
Normal	27 (51.9%)	25 (48.1%)
Without preventing	1 (33.3%)	3 (66.7%)
Condom	12 (54.5%)	10 (45.5%)
Oral contraceptive pill (OCP)	0(0)	2 (100)

Table 2. Analysis result of other parameters.

Variable	Case group	Control group	P value
75-g GTT	163.4±27.5	113.3±15.1	0.000
White blood cells count	6025.6±849.6	5451.5±128.3	0.022
History of giving birth to newborns weighing more than 4 kg			
Yes	2 (5)	2 (5)	
No	38 (95)	38 (95)	0.692
History of gestational hypertension			
Yes	2 (5)	3 (7.5)	
No	38 (95)	37 (92.5)	0.500
History of gestational diabetes			
Yes	10 (25.6)	2 (5)	
No	28 (71.8)	38 (95)	0.067
Family history of diabetes and hypertension			
Hypertension	3 (7.5)	13 (33.3)	
Diabetes	26 (65)	8 (20.5)	0.000
No history	11 (27.5)	18 (46.2)	
Type of delivery			
Normal	27 (67.5%)	22 (55)	
Cesarean	18 (45)	13 (32.5)	0.055
Regular menstrual cycle			
Yes	32 (80)	27 (69.5)	
No	8 (20)	13 (30.5)	0.200
Weight gain over 15 kg			
Yes	4 (10)	8 (20)	
No	36 (90)	32 (80)	0.161
Increased blood cholesterol above 150 mg/dl			
Yes	0 (0)	2 (5)	
No	40 (100)	38 (95)	0.247
Infertility history			
Yes	0 (0)	2 (5)	
No	40 (100)	38 (95)	0.247
History of drug use			
Yes	1 (2.5)	0 (0)	
No	39 (97.5)	40 (100)	0.506
History of abortion			
Yes	10 (25)	6 (16)	
No	30 (75)	34 (85)	0.201
BMI	25.7 ± 3.2	26.6±5.6	0.356
SHBG	83.5±66	142±65	0.000

Table 3. The level of sex hormone binding globulin

Variable	SHGB quartile				
	1	2	3	4	P value
Case group (gestational DM)	196.8	111.1	37.2	17.4	0.001
Control group (normal pregnancy)	47.7	91.9	193.1	230.4	

DISCUSSION

Eighty patients were included in the study and it was indicated that the 75-g GTT, WBC counts and family history of HTN and DM are higher in those with GDM. However, patients in both groups were replicated in terms of other midwifery factors. The serum SHBG level in the case group is significantly lower than that of the control one. Also, in the conducted multivariate test, there was no statistically significant relationship between the serum SHBG level in each group and examined background factors.

In a review study conducted by Ding et al. in 2006, it was found that SHBG level have a strong inverse relationship with the risk of type 2 DM in both males and females [11]. Similar to this study, the present research also indicated that the serum level of this hormone is lower in people with diabetes. However, the difference between the present and previous studies is that the previous one has been conducted on groups with type 2 DM, including both male and female patients, while the current research has been performed on the pregnant women with GDM.

Another study by Ding et al., conducted in 2009 on 359 newly diagnosed patients with type 2 DM and the same number of healthy individuals, illustrated that increasing serum SHBG levels is associated with a reduced risk of type 2 DM [12-13]. In the present study, as in the previous one, it was shown that the serum level of this hormone in people with DM are lower than those of the control group. Moreover, like the previous one, the current study deals with people with type 2 DM.

In a study by Daniela and colleagues in the Czech Republic, the relationship between SHBG level, type 2 DM, GDM and PCOS were examined. As in the previous studies, a lower serum SHBG level was found to lead to an increased affection of type 2 DM, GDM, and PCOS [14]. The present achievements are consistent with the results of this study, as reflected by the reduced SHBG levels in people with DM. However, the difference between this study and the present research is that the control group selected in the former one contains healthy non-pregnant women being compared to patients with GDM, but this disruptive factor has been eliminated in the present study.

In the study conducted by Bartha et al. in 2000 on 34 pregnant women with GDM and 32 healthy ones, it was concluded that the SHBG concentration decreases in women with GDM [15]. In this study which has been conducted on pregnant women with GDM, as in the current investigation, it has been indicated that the level of the above-mentioned hormone is significantly reduced in diabetic pregnant women compared to the control group. In a study by Hedderson *et al.* 2014, it was indicated that the low serum SHBG concentration is associated with an increased risk of GDM, and this finding can be effective in the early diagnosis of gestational diabetes risk [16]. In the present study, as in the previous one, the serum level of this hormone was significantly lower in people with GDM than in the control group. However, the previous study has reported that this hormone can be used as a factor for the early diagnosis of diabetes, while the current one did not take this issue into consideration.

Another review study published in 2010 by Perry et al., illustrated that SHBG is involved in the etiology of creating type 2 DM [17]. Also, Peter et al. in 2010 found that SHBG hormone prevents type 2 DM through affecting the influential mechanisms in raising the blood glucose level and has no impact on the insulin secretion mechanism [18]. Furthermore, another study by Li et al. conducted in 2010 on 1226 male patients with metabolic syndrome, revealed that a decrease in the serum SHBG level has a strong statistical relationship with an increased prevalence of this syndrome [18].

Another study by Lakshman et al. in 2010 on 1709 male patients with type 2 DM, indicated that SHBG level decreases in people with this disease and this molecule has a preventative effect, although this value is not significant and further investigations are needed [19]. Previous studies have also confirmed the results of this study and it seems that lower levels of this hormone are observable in people with diabetes and it can even be considered as a risk factor.

The main limitation of this study was that we checked only level of SHBG is once during pregnancy, while it is preferred to check it before pregnancy and in each trimester of pregnancy.

CONCLUSION

Our results indicated that the serum SHBG levels significantly decrease in people with GDM, but this decrement is not significantly associated with other background agents and midwifery factors. It is suggested that a study be performed with a larger sample size and hormone level measurement as a self-control group in order to eliminate all possible disruptive factors from the test. A step-by-step measurement of this hormone is also another suggestion to confirm the results of previous limited studies stating that this measure can be used as an early factor in diagnosing the gestational diabetes.

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AUTHOR CONTRIBUTIONS

AM was involved in the conception and design of the experiments. RH contributed to perform the experiments. AM and RH analyzed data. AM contributed to drafting the article. AM and RH made the final approval of the version to be published. All authors have read and agreed to the published version of the manuscript.

CONFLICTS OF INTEREST

There is no conflict of interest among the authors.

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