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Risk of developing overt diabetes among pregnant women with gestational diabetes

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ABSTRACT

Background: Gestational diabetes mellitus (GDM)is one of the commonest metabolic disorders complicating pregnancy. It is associated with several adverse outcomes for both mother and baby. Numerous studies have reported an association between GDM and increased risk of overt diabetes mellitus.

Objectives: To estimate the incidence rate and define associated factors of overt diabetes in women diagnosed with gestational diabetes mellitus.

Patients and methods: A retrospective cohort study was carried out at the Diabetic center, Hera general hospital in Makkah city, Saudi Arabia through reviewing of medical records of pregnant women with GDM who attended the center throughout the period of (April-June, 2022) and performed oral glucose tolerance test (OGTT) in the first 6 months after delivery.

Results: The study included 178 women with GDM. Their age ranged between 23 and 44 years. The incidence of overt diabetes among them was 27%. Multivariate logistic regression analysis revealed that with every increase in women`BMI by one kg/m^2, the risk of overt diabetes increased by 12% (Adjusted odds ratio "AOR"=1.12; 95% confidence interval "CI": 1.05-1.20, p=0.001). Compared to women with no previous attacks of GDM, those with two or three/more were at significant increased risk of GDM (AOR=3.74; 95% CI: 1.05-13.37, p=0.042 and AOR=7.31; 95% CI: 1.22-43.75, p=0.029), respectively. Women treated with insulin and diet were at almost four-folds risk of developing oveert diabetes compared to those treated with lifestyle modifications and diet (AOR=3.72; 95% CI: 1.63-8.50, p=0.002).

Conclusion: Gestational diabetes in many cases progressed to overt diabetes. Therefore, identifying those at higher risk for both GDM and overt diabetes is very important, to reduce risks of morbidity and mortality associated with these two health problems.

Keywords: Gestational diabetes, Overt diabetes, Incidence, Oral glucose tolerance test

INTRODUCTION

Background/literature review

Gestational Diabetes Mellitus (GDM) is defined according to the World Health Organization (WHO) as "hyperglycemia with onset or first diagnosed during pregnancy", [1]. Also, it has been defined in the Third International Workshop-Conference on as "any form of carbohydrate intolerance that is diagnosed during pregnancy" [2].

Worldwide, the prevalence of GDM is approximately 7%; however in some of the western countries; the prevalence rates were higher reaching up to 19% [3]. Even, higher figures were reported in Norway and United Arab of Emirates (UAE) (37.7%) and Mexico (30.1%)[4, 5]. The prevalence increases with women`s age as being 1% in women aged between 15 and 19 years and reached to 13% in those aged between 44 and 49 years [6]. In addition to aging, other risk factors for GDM include irregular menstrual history, overweight/obesity, multiparity, having a family

history of type 2 diabetes or a personal or family history of gestational diabetes or glucose intolerance, and belonging to certain ethnic groups including Middle Eastern [7].

Since most women do not perform diabetes mellitus screening test before pregnancy, it would be difficult to differentiate GDM from pre-existing diabetes [8]. It has been reported that 7% of pregnancies in United States of America (USA) were complicated by diabetes mellitus and about 86% of the affected women were GDM cases [9].

According to a recently published systematic review, the prevalence of gestational diabetes in kingdom of Saudi Arabia ranges from 10.5% to as high as 51% [10].

Gestational diabetes is one of the commonest metabolic disorders complicating pregnancy [11]. It is associated with several adverse outcomes for both mother and baby, including macrosomia, preeclampsia, maternal and infant birth trauma, large for gestational age infant, as well as increased risk of cesarean delivery [12].

Numerous studies have reported an association between GDM and increased risk of overt diabetes mellitus [13]. However, Kim, et al documented a great variability in the cumulative incidence of overt diabetes mellitus, 6 weeks to 28 years postpartum, ranging from 2.6 to 70% among women with GDM [14].

It had been reported that both lifestyle modifications and metformin therapy were effective in postponing the progression from impaired glucose tolerance to overt diabetes mellitus in previous GDM women [15]. Thus, estimating the incidence rate of overt diabetes mellitus in women with GDM and identifying associated risk factors could be of great importance for effective screening and evidence-based disease management.

Rationale

Gestational diabetes is not uncommon health problem during pregnancy. Furthermore, women with gestational diabetes are more likely to be at risk for developing overt diabetes. Therefore, early discovery and prompt management are highly needed for those women.

Objectives:

-To estimate the incidence rate of overt diabetes in women diagnosed with gestational diabetes mellitus, Diabetic Center, Hera General hospital, Makkah, 2022

-To explore some risk factors associated with development of overt diabetes among women with gestational diabetes, Diabetic Center, Hera General hospital, Makkah, 2022

PATIENTS AND METHODS

Study design:

A retrospective cohort study was carried out through reviewing of medical records of pregnant women with GDM.

Study area

The study was carried out at the Diabetic center, Hera general hospital in Makkah city, Saudi Arabia.

Study population:

All women attending the gestational diabetic clinic at Hera general hospital throughout the period of (April-June, 2022) were eligible for inclusion. Their medical records were reviewed, provided that they had the inclusion criteria

Inclusion criteria

-Pregnant women with confirmed gestational diabetes mellitus

-They have followed up oral glucose tolerance test (OGTT) in the first 6 months after delivery

Exclusion criteria

-Pregnant women with overt diabetes, pre-gestational diabetes or secondary diabetes.
N.B: Pregnant women with incomplete data in their electronic medical records were contacted throygh phone calls to complete their records.

Sample size and sampling technique

The minimum required sample size was calculated using online Roasoft sample size calculator with the assumption that the total number of women registered with GDM at Hera General hospital throughout a period of one year as 1658, and the incidence of overt diabetes among women with GDM as 70% [14]. At confidence level of 90% and 5% margins of error, 200 women were needed. Consecutive sampling technique was adapted to select files of women with inclusion criteria till the required sample size was achieved.

Data collection tool/technique:

The data were collected from electronic medical records of eligible women using a checklist included information regarding file number, age of patient, Body mass index (BMI), family history of diabetes mellitus and/or GDM, previous personal history of gestational diabetes, number of previous attacks, type of treatment (diet or insulin) and results of oral glucose tolerance test (OGTT).

Ethical considerations:

- Ethical approval was obtained from the Local Research and Ethics committee at Hera General hospital in Makkah, Saudi Arabia.
- Permission from director of diabetic center of the Hera General hospital in Makkah, Saudi Arabia was obtained.
- All collected data were kept confidential.

Data entry and statistical analysis

Data entry and analysis were done using statistical software package (SPSS) version 28.0. Data were presented using descriptive statistics in the form of frequencies and percentages for qualitative variables, and mean and standard deviation (SD) for continuous variables. Statistical analysis was done using Chi square (χ^2) and Mann-Whitney test. Multivariate logistic regression analysis was done to define predictors of overt diabetes after controlling for the confounders and its results wre expressed as adjusted odds ratio (AOR) and 95% confidence interval (CI). P-values< 0.05 were considered as statistically significant.

Budget:

This study was completely funded by the researcher herself.

Work plan and time table

Months Tasks	Oct 2022	Nov 2022	Dec 2022	Jan 2023	Feb 2023	Mar 2023	Apr 2023	May 2023	June 2023	July 2023	Aug 2023	Sep 2023
Research Proposal submission and approval												
Data collection												
Data entry												
Data analysis												
Thesis writing												
Finalize thesis and submission												
Publication												

RESULTS

The study included 178 women after exclusion of 22 women according to the exclusion criteria with a response rate of 89%. Their age ranged between 23 and 44 years. It was abnormally distributed as evidenced by significant Shapiro-Wilk test, $p<0.001$. The median age was 37 years with interquartile range of 32.75-40 years. Figure 1

Their body mass index ranged between 18 and 41.8 Kg/m^2. It was abnormally distributed as evidenced by significant Shapiro-Wilk test, $p<0.001$. The median BMI was 26 K/m^2 with interquartile range of 24-32 Kg/m2. Figure 2

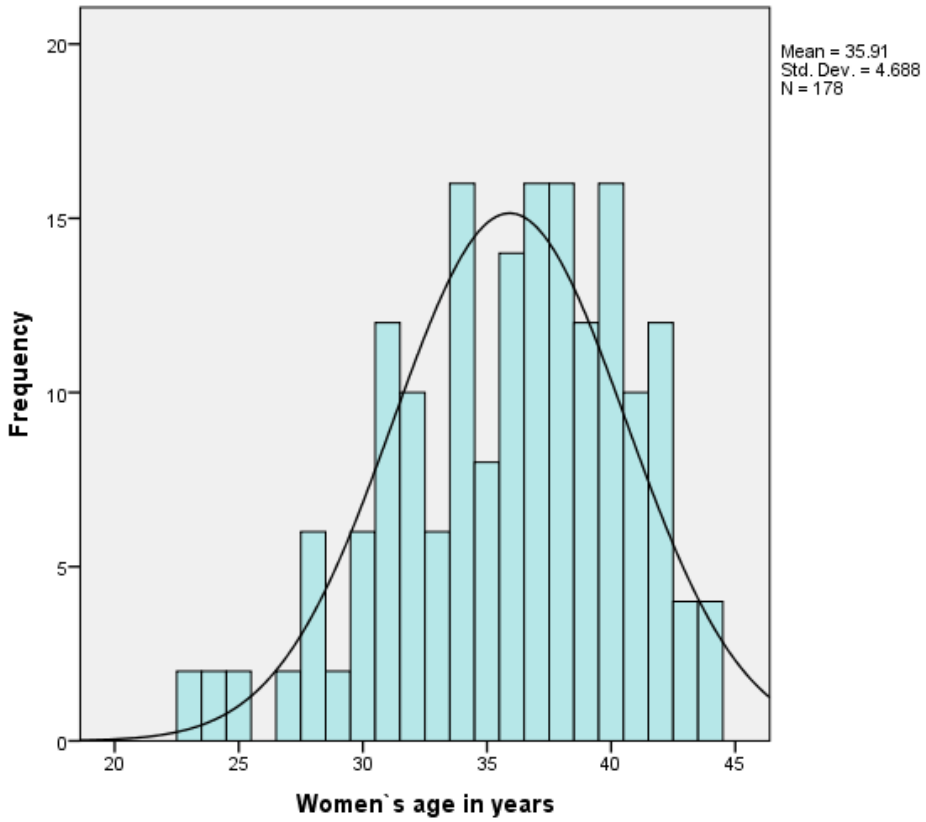

Figure 1: Age distribution of women diagnosed with gestational diabetes mellitus, Diabetic Center, Hera General hospital, Makkah, 2022

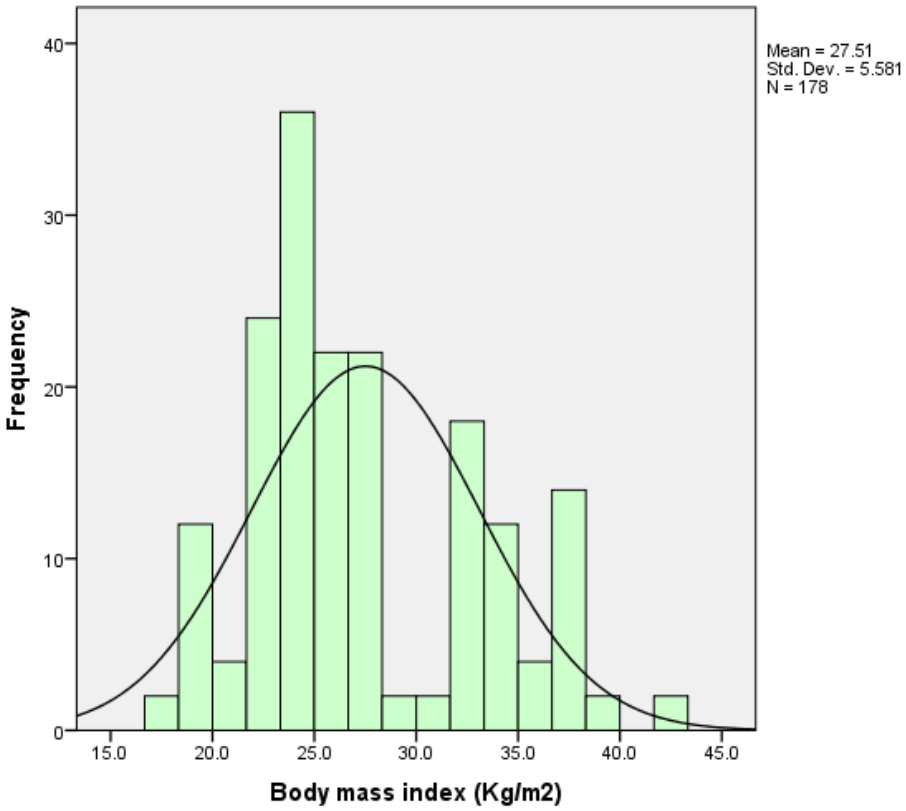

Figure 2: Body mass index of women diagnosed with gestational diabetes mellitus, Diabetic Center, Hera General hospital, Makkah, 2022

Family history of diabetes mellitus

As illstrated from Figure 3, family history of diabetes mellitus was reported by 40 women (22.5%).

Family history of gestational diabetes mellitus

Family history of gestational diabetes mellitus was observed among 36% of women diagnosed with gestational diabetes mellitus as shown in Figure 4.

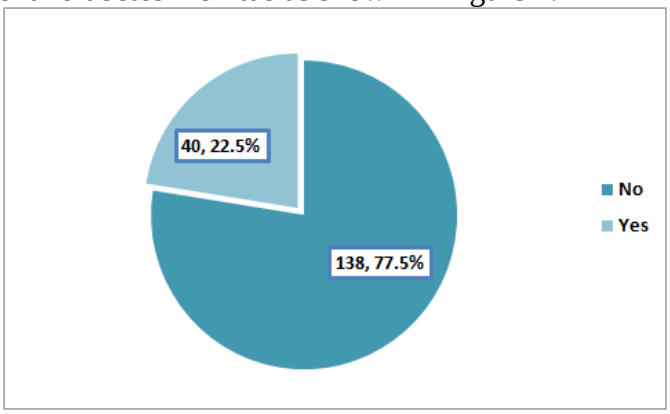

Figure 3: Family history of diabetes mellitus among women diagnosed with gestational diabetes mellitus, Diabetic Center, Hera General hospital, Makkah, 2022

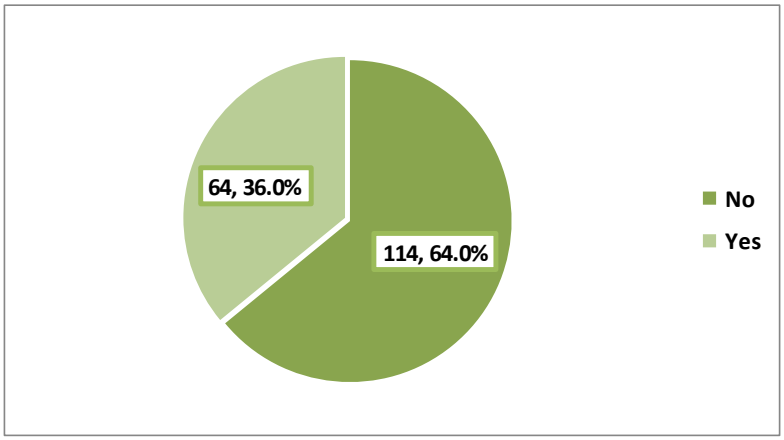

Figure 4: Family history of gestational diabetes mellitus among women diagnosed with gestational diabetes mellitus, Diabetic Center, Hera General hospital, Makkah, 2022

Number of previous attacks of gestational diabetes

Almost two-thirds (67.4%) of women had no previous attacks of gestational diabetes whereas 3.4% had three attacks or more. Table 1

Treatment of gestational diabetes

More than half of women with GDM (53.9%) were treated by lifestyle modification and diet whereas the remaining 46.1% were treated by insulin and diet. Table 2

Table 1: Number of previous attacks of gestational diabetes among the women diagnosed with gestational diabetes mellitus, Diabetic Center, Hera General hospital, Makkah, 2022

	Frequency	Percentage
None	120	67.4
Once	36	20.2
Twice	16	9.0
Three and more	6	3.4

Table 2: Treatment of gestational diabetes among the women diagnosed with gestational diabetes mellitus, Diabetic Center, Hera General hospital, Makkah, 2022

Variables	Frequency	Percentage
Lifestyle modification and diet	96	53.9
Insulin and diet	82	46.1

Incidence rate of overt diabetes

The incidence of overt diabetes among women with gestational diabetes, as indicated by positive OGTT test, was 27% as illustrated in Figure 5.

Body mass index was significantly higher among women who developed overt diabetes compared to those who did not develop overt diabetes (median "IQR" values were 32 "25-36.53" and 25.1 "23-28" Kg/m^2, respectively), $p<0.001$. Women with family history of diabetes were more likely to develop overt diabetes than their peers (40% versus 23.2%, p=0.035). Also women with family history of GDM were more likely to develop overt diabetes than their counterparts (37.5% versus 21.1%, p=0.018). Two thirds of womn with three or more previous GDM attacks compared to only 23.3% of those with no previous attacks had overt diabetes, p=0.016. Women

treated with insulin and diet were more likely to develop overt diabetes compared to those treated with lifestyle modifications and diet (39% versus 16.7%), p=0.001. Table 3

Multivariate logistic regression analysis revealed that with every increase in women`BMI by one kg/m^2, the risk of overt diabetes increased by 12% (Adjusted odds ratio "AOR"=1.12; 95% confidence interval "CI": 1.05-1.20, p=0.001). Compared to women with no previous attacks of GDM, those with two or three/more were at significant increased risk of GDM (AOR=3.74; 95% CI: 1.05-13.37, p=0.042 and AOR=7.31; 95% CI: 1.22-43.75, p=0.029), respectively. Women treated with insulin and diet were at almost four-folds risk of developing overt diabetes compared to those treated with lifestyle modifications and diet (AOR=3.72; 95% CI: 1.63-8.50, p=0.002). Table 4

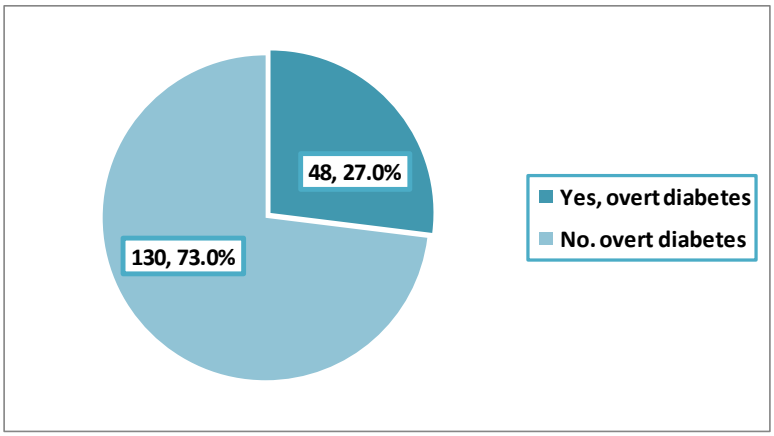

Figure 5: Incidence rate of overt diabetes in women diagnosed with gestational diabetes mellitus, Diabetic Center, Hera General hospital, Makkah, 2022

Table 3: Factors associated with overt diabetes in women diagnosed with gestational diabetes mellitus, Diabetic Center, Hera General hospital, Makkah, 2022

Variables	Overt diabetes		p-value
	No N=130 N (%)	**Yes** N=48 N (%)	
Age (years)			
Median (IQR)	36 (32-40)	37.5 (34-39.75)	
Mean rank	86.65	97.21	0.224*
BMI (Kg/m^2)			
Median (IQR)	25.1 (23-28)	32 (25-36.53)	
Mean rank	79.82	115.71	<0.001*
Family history of diabetes			
No (n=138)	106 (76.8)	32 (23.2)	
Yes (n=40)	24 (60.0)	16 (40.0)	0.035 [Fr]
Family history of GDM			
No (n=114)	90 (78.9)	24 (21.1)	
Yes (n=64)	40 (62.5)	24 (37.5)	0.018 [Fr]
Number of previous attacks of GDM			
None (n=120)	92 (76.7)	28 (23.3)	0.016 [Fr]
Once (n=36)	28 (77.8)	8 (22.2)	
Twice (n=16)	8 (50.0)	8 (50.0)	
Three or more (n=6)	2 (33.3)	4 (66.7)	
Treatment of GDM			
Lifestyle modification and diet (n=96)	80 (83.3)	16 (16.7)	
Insulin and diet (n=82)	50 (61.0)	32 (39.0)	0.001 [Fr]

IQR: Interquartile range GDM: Gestational diabetes mellitus
BMI: Body mass index
*Mann-Whitney test
[Fr]Chi-square test

Table 4: Predictors of overt diabetes among women with gestational diabetes: Results of multivariate logistic regression analysis

	Adjusted OR	**95% CI**	**p-value**
BMI (Kg/m^2)	1.12	1.05-1.20	0.001
Number of previous attacks of GDM			
None (n=120)	1.0		
Once (n=36)	1.05	0.39-2.82	0.925
Twice (n=16)	3.74	1.05-13.37	0.042
Three or more (n=6)	7.31	1.22-43.75	0.029
Treatment of GDM			
Lifestyle modification and diet (n=96)	1.0		0.002
Insulin and diet (n=82)	3.72	1.63-8.50	

OR: Odds ratio CI: Confidence interval

Terms of family history of diabtes and family history of gestational diabetes mellitis were removed from the final logistic regressin model (not significant)

DISCUSSION

Several international organizations such as the World Health Organization (WHO) 2013 [16], International Federation of Gynecology and Obstetrics (FIGO) 2015 [17], American Diabetes Association (ADA) 2020 [18] and Australasian Diabetes in Pregnancy Society (ADIPS) 2014[19] recommended classification of overt diabetes in pregnancy and gestational diabetes as two separate groups.

Overt diabetes represents a more severe form of hyperglycemia during pregnancy compared to gestational diabetes as it is usually associated with adverse maternal and fetal outcomes, and calls more aggressive management [20-22].

Kim, et al reported a great variability in the cumulative incidence of overt diabetes mellitus, 6 weeks to 28 years postpartum, ranging from 2.6 to 70% among women with GDM [14]. In Canada (2008), a large, population-based study showed a prevalence of 18.9% of overt diabetes after 9 years from the index pregnancy in women with previous gestational diabetes [23]. Wong et al revealed that 41% of women diagnosed with overt diabetes in pregnancy had normal glucose tolerance test performed 6-8 weeks postpartum while 38% expressed impaired fasting glucose or impaired glucose tolerance and 21% developed diabetes whereas among women with GDM, 74.9% had normal glucose tolerance, 22.8% had impaired fasting glucose or impaired glucose tolerance and only 2.3% had diabetes [24]. In the present study, the incidence rate of overt diabetes was 27% among women with GDM, which is within the range metioned by Kim, et a [14]. It has been suggested that diagnosis of overt diabetes early in the first trimester of pregnancy is predictive of postpartum diabetes and most likely reflect a state of undiagnosed pre-existing diabetes [19]. Goyal A, et al reported that a remarkable heterogeneity exists with regard to the postpartum glycemic status in patients with overt diabetes, related to the time of diagnosis of overt diabetes and the abnormal glycemic at diagnosis[25]. In the present study, unfortunately, we did not include the trimester of preganncy at which GDM was diagnosed.

In the present study, body mass index of women with gestational diabetes was a significant predictor for the development of postpartum overt diabetes mellitus as the risk increase by 12% with each unit of increase in the women BMI. The same has been observed by others [13, 26]. However, some outhors did not find an association between BMI of women with GDM and overt diabetes mellitus in postpartum period [27]. The association between women` body mass index and overt diabetes could be explained by low level of physical activity, and increased dietary fat which in turn adversely impact insulin resistance [28]. In the same context, studies have shown that progression to overt diabetes among women with GDM can be potentially preventable by lifestyle mofidications particularly in high-risk women [29].

In the present study, women treated with insulin and diet were at almost four-folds risk of developing overt diabetes compared to those treated with lifestyle modifications and diet. It had been reported by Diabetes Prevention Research Group that both lifestyle modifications was effective in postponing the progression from impaired glucose tolerance to overt diabetes mellitus in previous GDM women [15].

In the present study, women with more previous attacks of GDM were more likely to develop overt DM compred to others. The same has been observed by others [20, 28].

Limitations of the present study include mainly being a single center study which could impacts the generalizability of findings. Also, collection of data from electronic medical records is subjected to bias as it depends on the level of accuracy and completeness of data. However, the

study findings could be of benefit for identifying the rate of developing overt diabetes among patients with GDM, and detecting cases that need more consideration.

CONCLUSION AND RECOMMENDATIONS

Gestational diabetes in many cases progressed to overt diabetes. Therefore, identifying those at higher risk for both GDM and overt diabetes is very important, to reduce risks of morbidity and mortality associated with these two health problems. Women with gestational diabetes, who are obese, treated with insulin and hadf previous higher attacks of GDM wer more likely to develop overt diabtes. Based on the study`s findings, estimating the incidence rate of overt diabetes mellitus in women with GDM and identifying associated risk factors could be of great importance for effective screening and evidence-based disease management. Additionally, further larger study including women from other disciplines is recommended for better clarification and estimating the proper magnitude of these two health concerns.

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