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**ORIGINAL ARTICLE**

# Association of Gestational Diabetes with Parental Diabetic Mellitus and Impaired Glucose Tolerance: A Cross-Sectional Study

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## ABSTRACT

**Aim:** To determine the association of gestational diabetes with parental diabetic mellitus and impaired glucose tolerance
**Study design**: A cross-sectional study
**Place and Duration:** This study was conducted at Jahra Hospital Kuwait from February 2021 to February 2022
**Methodology:** This study includes 100 women with gestational diabetes. They were aged 35 (±5) years. They were tested by fasting plasma glucose (fpg). There were 61 women who either had diabetes or fasting hyperglycemia (fpg = >5.4 millimole/l). A total of 35 women had their parents alive. Of these 35 women's parents, 14 women's parents agreed to test their metabolism. Their metabolism was tested by CIGMA (continuous infusion of glucose with model assessment).
**Results:** Among those 14 families, 7 probands had diabetes and the other 7 had impaired glucose tolerance (IGT). The women were aged 36 (±4) years with a BMI of 27 (±5) kilograms/m2. The parents were aged 63 (±5) with a BMI of 30 (±5) kilograms/m2. The presence of glucose intolerance defined their affection status (an age and obese matched population with fpg or post-infusion attained plasma glucose levels greater than 3 standard deviation). Among those 14 families, 5 probands did not have any parent affected, which represents 35.7%, 3 probands had both parents affected, which represents 21.4%, and 6 probands had only 1 parent affect, which represents 42.9%. Only 3 of proband's parents were affected by diabetes as explained by WHO criteria.
Practical implication This paper outlines some of the growing evidence showing pregnant women with gestational diabetes mellitus are more likely to give birth to diabetic mothers. These preliminary findings' are provocative implications to encourage additional research.
**Conclusion:** In conclusion, examining women with gestational diabetes, who have both parents available for this research, helps to find probands with IGT or diabetes. Those who had neither parents impacted with diabetes nor IGT were representing a significant portion which was much the same as elementary families of NIDDM.
**Keywords:** diabetes mellitus, gestational diabetes, parents, impaired glucose tolerance

## INTRODUCTION

Non-insulin-dependent diabetes mellitus (NIDDM) is likely to affect in females with gestational diabetes later in life. Fifty percent of these women develop NIDDM within 25 years [1] It is found that thirty percent of women, who develop NIDDM in their middle ages, had gestational diabetes due to glycosuria or hyperglycemia [2]. Due to the women with gestational diabetes, researchers get the opportunity to research diabetes at an early stage [3]. These women are mostly overweight and have high insulin resistance as well as impaired beta cell [5]. These faults are much alike to those which were found in the 1st-degree folks of NIDDM patients [4,6,7]

It has been restricted to research on patients with NIDDM because it was difficult to identify elementary families which have both parents alive and ready for research [8]. Twenty patients with NIDDM from elementary families were identified by Cook et al. in order to determine the prevalence of NIDDM in the parents as well as the evident pattern of inheritance [9]. Among 14 elementary families, 7 probands had diabetes while the other 7 had glucose intolerance. 1/3rd (37.5%) of the diabetic patients did not have any parents affected. This implies that either the disease is polygenic or a significant amount of diabetes is of environmental origin, with diabetic factors inherited from both parents who may or may not be necessarily diabetic themselves. Because the participants with diabetes had an average age at observation of forty years and their parents were in their seventh to the tenth decennary, there was an unavoidable potential bias.

We evaluated those females who had gestational diabetes and whose parents were affected with impaired glucose tolerance or mild diabetes and were likely to later develop diabetes in their lives. If we examine these individuals at a starting stage, it is possible that their parents may be alive and would be ready for research. This research would be conducted in order to assess the pattern of inheritance of diabetes.

## METHODOLOGY

This study was approved by the Research and Ethics Committee. Consent was taken from every patient. This study includes 100 women with gestational diabetes. They were selected from the registrations of women with gestational diabetes, regardless of their diabetic family history. The mean age of these women was 36 (±4) years. They were examined during their pregnancy when gestational diabetes developed. A total of 50 women were facing their first pregnancy, 20 women were facing their second pregnancy and 30 women were facing their third or subsequent pregnancy. When 2 or more venous plasma glucose concentrations were equivalent to normal upper limits or exceeding them, gestational diabetes was labelled. A seventy-five grams (glucose tolerance test) GTT was conducted at 27-33 weeks of pregnancy to determine the normal upper limits. The upper limits were as follows: <5.7, <11.5, <8.9, <7.4 millimole/l. During pregnancy.A total of 48 women were given insulin.

The fasting plasma glucose (fpg) and body mass index (BMI) were examined to assess their obesity. The patients who had fasting hyperglycemia( > 5.4 millimole/l) were picked for further research if both of their parents were alive. It was found that every proband had fastinghyperglycemia as well as gestational diabetes. The HOMA model was used to measure beta-cell function using fasting glucose and C-peptide concentrations in all participants. It also includes those who were on insulin therapy [10, 11]. Using the HOMA model, the participants' C-peptide concentrations and glucose was assessed using a mathematical model. The mathematical model included insulin interactions and body's glucose, which assumes equimolar insulin production as well as C-peptide production. The model examines the extent of resistance of insulin and beta-cell dysfunction likely to arise in the participants' fasting glucose and C-peptide levels.

CIGMA (continuous infusion of glucose with model assessment) test was carried out on probands' parents who were

available for research [12]. In this test, 5 milligrams of glucose was continuously infused. Metropolitan Life Insurance tables were used to take ideal body weight [13]. An intravenous cannula was heated and was slided into the back of the hand or the wrist to take blood samples. A total of 3 samples were taken at 5-minute intervals. Fasting plasma glucose (fpg) was considered to be the mean glucose concentration. The samples taken at 50 and 55 minutes were considered as mean plasma glucose while samples taken at 60 minutes were considered as achieved plasma glucose (apg). The CIGMA test was carried out on thirty participants. Among those thirty participants, 12 were not diabetic, 12 had NIDD APG and 6 had impaired glucose tolerance. This CIGMA study gave a coefficient of variation of 5 percent [14]. Table No. 2 and 3 shows a Z score that is the fpg and apg in terms of standard deviation. Patients with NIDDM were detected according to the WHO criteria (fpg < 7.7 millimole/l) [15]. The impaired glucose tolerance and NIDDM also defined the status of affection.

GTT was not performed in 7 parents that were elderly. Fpg and HbA1C were acquired and 3 parents were treated with insulin who had diabetes. The other 4 parents who did not have diabetes were having a chronic disease which lowered the CIGMA. They were also examined with a fpg and HbAIC. If the fpg was >2 SD higher than the mean normal value for the patient's age and obesity level, it was considered as impacted.

A Cobas MIRA centrifugal analyzer was used to measure plasma glucose along with a hexokinase method. The Bio-Rad DIAMAT was used to measure HbA along with the ion-exchange high- performance liquid chromatography. The parents without diabetes had ages ranging from 63 (±5) years. The data is expressed in terms of SD.

## RESULTS

Overall, 100 women who had developed gestational diabetes for the first time in their pregnancy were selected for this research. There were 61 women who either had diabetes or fasting hyperglycemia (fpg > 7.7 millimole/l). Out of 61 women, 26 women and out of 39, 18 women had one or both of their parents died (with or without fasting hyperglycemia). Overall, 44 women had either one or both of their parents died. Only thirty-five women's both parents were living with an fpg < 5.4 millimole/1. Among these 35 women, 14 women's parents agreed to get examined. During the pregnancy in which gestational diabetes was identified, 10 of the probands were given insulin, while 4 were given only a restricted diet. A total of 7 probands had diabetes and among those, 5 were treated with insulin. On CIGMA testing, 6 probands were found to be affected with impaired glucose tolerance while 1 proband, who had a BMI of 41 kg, had an fpg of 6.2 millimole/l but a normal sigma achieved plasma glucose. Clinical characteristics of the probands are shown in Table No. 1.

Out of 14 probands' parents, 4 were affected with diabetes out of which, 3 were under insulin treatment. 21 out of 24 patients who did not have diabetes were ready to go under an infusion test. Fasting plasma glucose was used to assess the affection status. There were 5 probands whose parents were affected with neither impaired glucose tolerance nor NIDDM. There were 3 probands whose both parents were impacted by IGT. The probands with 1 or more impacted parents and those without affected parents were diagnosed with gestational diabetes at similar ages. Clinical details of parents are shown in Tables No. 2 and 3.

Table 1: Clinical characteristics of the probands

| | Diabetic Status | | Current Status | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Age | Treatment | Age | Treatment | BMI | Glycemic Status | Beta-cell | Affected |
| 1 | 27 | Insulin | 33 | - | 25 | FH | 70 | 0 |
| 2 | 24 | Insulin | 32 | Insulin | 24 | D | 9 | 0 |
| 3 | 23 | Diet | 36 | Insulin | 26 | D | - | 0 |
| 4 | 31 | Insulin | 40 | Insulin | 26 | D | 72 | 0 |
| 5 | 21 | Insulin | 34 | Diet | 21 | D | 105 | 0 |
| 6 | 25 | Insulin | 45 | - | 27 | FH | 81 | 1 |
| 7 | 22 | Insulin | 30 | Diet | 27 | D | 54 | 1 |
| 8 | 31 | Insulin | 42 | - | 26 | FH | 53 | 1 |
| 9 | 19 | Insulin | 34 | Insulin | 30 | D | 48 | 1 |
| 10 | 33 | Diet | 34 | - | 43 | FH | 115 | 1 |
| 11 | 26 | Diet | 28 | - | 24 | FH | 51 | 1 |
| 12 | 22 | Insulin | 34 | Insulin | 23 | D | 20 | 2 |
| 13 | 36 | Diet | 39 | - | 25 | FH | 91 | 2 |
| 14 | 31 | Insulin | 38 | - | 29 | FH | 78 | 2 |

FH: Fasting hyperglycemia D: Diabetes

Table 2: Parents who were unaffected

| | Gender | BMI | Age | fpg | apg | HbA (%) | fpg Z | apg Z | Glycemic status |
|---|---|---|---|---|---|---|---|---|---|
| 1 | M | 31 | 62 | 4.9 | 8.9 | 5.6 | 0.4 | 0.4 | N |
| | F | 33 | 61 | 5.0 | 8.1 | 5.7 | 0.06 | -1.2 | N |
| 2 | M | 26 | 59 | 4.9 | 7.2 | 4.9 | 0.4 | -0.7 | N |
| | F | 25 | 58 | 4.9 | 7.4 | 5.2 | 0.4 | -0.9 | N |
| 3 | M | 25 | 62 | 5.2 | 9.4 | 4.9 | 1.1 | 0.8 | N |
| | F | 49 | 56 | 4.7 | 7.0 | 5.8 | -0.4 | 0.02 | N |
| 4 | M | 27 | 66 | 5.5 | 8.6 | 5.7 | 1.4 | 0..1 | N |
| | F | 26 | 65 | 4.7 | 8.7 | 5.4 | 0.4 | -0.2 | N |
| 5 | M | 33 | 55 | 4.9 | - | 5.2 | 1.2 | - | N |
| | F | 23 | 48 | 4.9 | 9.9 | 5.2 | 1.8 | 0.1 | N |

M: Male N: Normal
F: Female

Table 3: One or more affected parents

| | Gender | BMI | Age | fpg | apg | HbA (%) | fpg Z | apg Z | Glycemic status |
|---|---|---|---|---|---|---|---|---|---|
| 6 | M | 31 | 75 | 5.9 | 8.9 | 5.9 | 2.8 | 0.4 | IGT |
| | F | 28 | 66 | 5.2 | 9.1 | 5.2 | 1.9 | 1.4 | N |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| 7 | M | 32 | 56 | 5.5 | 11.0 | 4.8 | 1.4 | 2.4 | IGT |
| | F | 20 | 49 | 4.9 | 10.0 | 5.9 | 0.6 | 0.6 | N |
| 8 | M | 31 | 62 | 11.1 | - | 8.1 | 10.9 | - | D |
| | F | 32 | 61 | 5.8 | 9.3 | 6.4 | 1.6 | 0.9 | N |
| 9 | M | 24 | 63 | 4.9 | 8.7 | 6.4 | 0.6 | 0.5 | IGT |
| | F | 26 | 69 | 5.9 | 9.9 | 5.4 | 2.4 | 1.4 | N |
| 10 | M | 33 | 66 | 5.0 | 8.9 | 5.9 | 1.6 | 1.6 | N |
| | F | 26 | 54 | 4.9 | 10.9 | 4.8 | 3.0 | 2.8 | IGT |
| 11 | M | 27 | 48 | 7.5 | - | 7.2 | 6.8 | - | N |
| | F | 26 | 46 | 4.7 | - | 5.3 | -0.4 | - | D |
| 12 | M | 28 | 65 | 9.9 | 16.0 | 6.2 | 10.0 | 7.6 | D |
| | F | 32 | 64 | 17.9 | - | 11.1 | 29.9 | - | IGT |
| 13 | M | 28 | 67 | 6.2 | 10.1 | 5.9 | 3.7 | 2.7 | IGT |
| | F | 28 | 62 | 5.9 | 8.9 | 7.5 | 2.8 | 1.5 | IGT |
| 14 | M | 32 | 72 | 6.3 | 10.6 | 7.5 | 4.0 | 1.9 | D |
| | F | 28 | 69 | 5.2 | - | 5.9 | 1.7 | - | |

M: Male D: Diabetes IGT: Impaired glucose tolerance
F: Female N: Normal

## DISCUSSION

A poor yield makes it difficult to identify 2 generation elementary families suitable for genetic investigation through probands with NIDDM. Only 127 families were available for examination in a study in Oxfordshire [16]. In this research, probands with gestational diabetic history were involved who later developed impaired glucose tolerance or NIDDM which was found out after retesting. These patients are examined at an early stage because it is possible that their parents may be alive and would be ready for research. A significant number of probands were affected with gestational diabetes in the 1st or 2nd pregnancy. The mean age at which they were examined was 38 years, 10 years after gestational diabetes was diagnosed. Sixty-one percent of the patients were either affected by impaired glucose tolerance or diabetes. Therefore, it was a high risk that they would be affected with diabetes. Only a few of the women had both of their parents alive. The final yield of probands was 34.9%. The proportion of children with living parents might have been higher if the families of gestational diabetic individuals had been characterized closer to the time of the first diagnosis. Probands with fasting hyperglycemia were likely to decrease in number. Forty percent of the 35 possible probands were accessible and agreed to be examined as a family, showing twenty-three percent of those with FH. This is a great yield as compared to the yield told in the Oxfordshire study [17]. Those with diabetic parents are more likely to participate in the research. In any case, such a notion is unlikely, given that there was dissimilarity in the proportion of participants who were now normoglycemic versus those who had fasting hyperglycemia.

The pattern of affection in the parents of the probands with the gestational diabetes is much the same as that reported in the parents of participants with NIDDM, with a significant fraction having neither parent affected by diabetes nor impaired glucose tolerance [18]. The lack of affection in parents above the age of 60 years is consistent with polygenic inheritance or environmental causes of diabetes. If we talk about probands' parents where only one parent was affected, 4 out of 5 were impacted with IGT. This data is much the same as the data for families with NIDDM patients. There were 3 probands whose both of the parents were affected. This is much the same to the NIDDM individuals whose both parents were affected. This is a higher incidence than would be expected by chance with a dominant model. Some people with gestational diabetes in their 20s share characteristics with those with early-onset diabetes in their late 30s, and it is likely that both affected parents received a "double gene dose" that resulted in premature presentation [19].

Impaired beta-cell function was observed in probands with gestational diabetes which was similar to that found in the NIDDM patients' first-degree relatives [20]. Diabetes was early detected that may be due to insulin resistance which was linked with pregnancy and the testing for hyperglycemia. Their pathophysiology is similar to those having NIDDM. This is not surprising given that thirty percent of women with diabetes at an average age of 52 years have previously had a pregnancy with probable diabetes.

## CONCLUSION

In conclusion, examining women with gestational diabetes, who have both parents available for this research, helps to find probands with IGT or diabetes. Those who had neither parents impacted with diabetes nor IGT were representing a significant portion which was much the same as elementary families of NIDDM.

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