ORIGINAL RESEARCH

# Glucose Disposal Index Predicts Adverse Pregnancy Outcomes in Gestational Diabetes

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## ABSTRACT

**Objective** • To explore the prognostic significance of the Glucose Disposal Index (DI) concerning unfavorable pregnancy outcomes in mothers and newborns affected by Gestational Diabetes Mellitus (GDM).

**Methods** • Our investigation encompassed 75 GDM patients who received treatment at Anhui Mingguang People's Hospital between January 2019 and July 2023. Subjects were divided into two groups: those with adverse pregnancy outcomes (n = 18) and those without (n = 57). Between weeks 24 and 28 of gestation, all participants underwent a 75 g Oral Glucose Tolerance Test (OGTT), and relevant details such as height, weight, and complete pregnancy information were gathered. The Insulin Sensitivity Index (ISI) and the area beneath the insulin-to-glucose curve from 0 to 120 minutes (AUC_INS120/AUC_GLU120) were computed from the 75 g OGTT findings, and their multiplication was represented as DI. Comparisons between groups were made using *t* tests, Wilcoxon rank-sum tests, and $\chi^2$ tests. Binary logistic regression was applied to probe the relationship between DI and the risk of adverse pregnancy outcomes, and the Receiver Operating Characteristic (ROC) curve was employed to evaluate the predictive capacity of DI.

**Results** • Statistically meaningful differences in FPG, $HbA_{1c}$, and DI were noted between the groups ($P < .05$), whereas the difference in 2hPG was not significant ($P > .05$). Pearson correlation analysis revealed a negative correlation between DI and both FPG and $HbA_{1c}$ ($P < .05$). Multivariate logistic regression showed that DI (OR = 0.599) was a determining factor of adverse pregnancy outcomes ($P < .05$). The ROC curve disclosed an AUC of 0.837 for DI in forecasting adverse pregnancy outcomes (95% CI: 0.741-0.933), with a specificity of 82.10% and a sensitivity of 80.65% at the optimal threshold value of 2.1.

**Conclusion** • An elevation in DI among GDM patients is closely linked to a reduced risk of adverse pregnancy outcomes, corroborating DI's prognostic value for such outcomes in gestational diabetes. (*Altern Ther Health Med.* 2024;30(10):97-101).


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## INTRODUCTION

Gestational Diabetes Mellitus (GDM) is a form of diabetes that develops during pregnancy.[1] GDM occurs when the body's insulin production is unable to keep up with the increased demand caused by the pregnancy.[2] If left untreated, GDM can lead to complications for both the mother and the baby, including preterm birth, birth defects, and newborn hypoglycemia. Epidemiological data indicates that the prevalence of GDM has been increasing worldwide, likely due to factors such as obesity, sedentary lifestyle, and genetic predisposition.[3] The underlying physiological process of Gestational Diabetes Mellitus (GDM) is typified by a resistance to insulin and/or an insufficient corresponding insulin release.[1] This is particularly characterized by a significant decrease in insulin responsiveness during the latter stages of pregnancy in those with GDM, showing a decrease ranging from 60% to 70% compared to pre-pregnancy levels, and roughly 40% to 60% less than what is observed in standard pregnancies.[2] Concurrently, at an equivalent level of insulin sensitivity, GDM patients exhibit a 40% to 70% reduction in insulin secretion compared to healthy individuals.[3] Previous research has demonstrated that GDM patients have diminished insulin sensitivity, which is strongly associated with a higher risk of adverse pregnancy outcomes, including pre-eclampsia, neonatal hypoglycemia, and the need for cesarean section.[4] Insulin sensitivity and insulin secretion are mutually dependent factors in the development of GDM,[5] solely evaluating insulin sensitivity

may not adequately represent the comprehensive glucose disposal capacity of an individual.

In 1981, Bergman et al.[5] initially uncovered a hyperbolic connection between insulin responsiveness and the secretion of insulin, introducing the term "disposition index" (DI) to describe the multiplication of these quantitative measures. This index serves as an indicator of pancreatic β cell functionality, taking into account insulin sensitivity. Currently, there is limited research concentrating on the link between DI values and the likelihood of unfavorable results in expectant mothers. Therefore, we conducted a cohort study to examine the relationship between DI values and the likelihood of adverse pregnancy outcomes in women diagnosed with GDM. The objective of our study was to explore the predictive ability of DI for negative pregnancy outcomes in both mothers and newborns affected by GDM.

## METHODS

### Study Subjects

Our research encompassed 75 individuals diagnosed with Gestational Diabetes Mellitus (GDM) who underwent treatment at Anhui Mingguang People's Hospital from January 2019 to July 2023. All involved patients were briefed about the study's objectives and willingly signed the informed consent form. Ethical clearance for the research was granted by the institution's review board. Eligibility criteria included: (1) Being at least 20 years old; (2) Having a detailed electronic health record throughout pregnancy; (3) Undergoing a 75 g OGTT during weeks 24 to 28 of pregnancy. Those excluded from the study had: (1) Persistent renal or hepatic conditions; (2) Twin or higher-order pregnancies; (3) A diabetes diagnosis before becoming pregnant.

### General Information and Laboratory Biochemical Examination

For all participants, digital health records were established during their first appointment in the 6th week of gestation. These records incorporated vital data, including stature, body weight, gravidity, parity, and previous health conditions. Measurements for stature, body weight, and arterial tension were taken for each participant, leading to the computation of their Body Mass Index (BMI). After observing a fasting duration between 8 and 20 hours, blood specimens were drawn to determine Fasting Plasma Glucose (FPG), fasting insulin (FINS), and $HbA_{1c}$ levels. A 75 g OGTT was performed, with subsequent evaluations of glucose and insulin concentrations at 30-minute intervals up to 180 minutes after glucose intake. The Charisma 2000 biochemical autoanalyzer, utilizing the glucose oxidase technique (Shanghai Kehua China Bioengineering Co., Ltd., Shanghai, China), was employed for plasma glucose determinations. Meanwhile, the Cobas e 601 automatic analyzer, based on an electrochemiluminescence immunoassay (Roche insulin assay technique, Basel, Switzerland), was used for serum insulin evaluations.

### Calculation of DI

Based on the results of the 75g OGTT, the Insulin Sensitivity Index (ISI) was calculated using the steady-state model analysis method to evaluate insulin sensitivity.[7] The area under the curve for insulin relative to the area under the curve for glucose from 0 to 120 minutes (AUC_INS120/AUC_GLU120) was calculated using the irregular trapezoidal formula to assess insulin secretion function.[8] The ISI formula is given by ISI = M / [average glucose level × lg(average insulin level)],[7] where the average glucose and insulin levels are the mean concentrations at 0 min and 120 min during the OGTT. M denotes the glucose uptake rate, calculated as M = 75,000/120 + (FPG - 120 min glucose) × 1.15 × 180 × 0.19 × body weight/120.[9] DI is defined as the product of insulin secretion function and ISI, i.e., DI = ISI × AUC_INS120/AUC_GLU120.[5]

### Outcome Indicators

The primary outcome measures for our research encompass the combined endpoints of unfavorable pregnancy results, such as being Large for Gestational Age (LGA), undergoing a first-time cesarean delivery, developing pre-eclampsia, and experiencing early childbirth.[10] LGA is characterized by a neonatal weight that surpasses the 90th percentile, adjusted for gestational duration and sex.[11] A first-time cesarean delivery denotes a cesarean procedure during an initial pregnancy. Pre-eclampsia is identified by a systolic pressure ≥140 mmHg (1 mmHg = 0.133 kPa) or a diastolic pressure ≥90 mmHg, recorded twice with at least a 6-hour interval, coupled with proteinuria levels of ≥0.3 g/24 h or incidental proteinuria levels of ≥1+. Early childbirth is defined as childbirth occurring from 28 to 37 weeks of pregnancy. LGA, first-time cesarean delivery, pre-eclampsia, and early childbirth are considered secondary outcome events. Those GDM patients who encountered these events were grouped into the unfavorable pregnancy result category (n = 18), and others were classified into the favorable outcome category (n = 57).

### Statistical Analysis

Data were analyzed using Statistic Package for Social Science (SPSS) version 21.0 (IBM, Armonk, NY, USA). For normally distributed experimental data, measurements were expressed as $\bar{x} \pm s$, and paired $t$ tests were used for comparisons between groups. Count data were presented as numbers or rates, and the $\chi^2$ test was employed for group comparisons. Pearson correlation analysis was utilized to explore the relationship between DI and clinical indicators in patients. Factors found to be statistically significant in univariate analysis were included in multivariate analysis, conducted using a Logistic regression model. The Receiver Operating Characteristic (ROC) curve assessed the predictive value of relevant factors for adverse pregnancy outcomes, with $P < .05$ indicating statistical significance.

**Table 1.** Comparison of Basic Information Between the Two Groups

| Item | Adverse Pregnancy Group (n = 18) | Non-Adverse Pregnancy Group (n = 57) | $t/\chi^2$ value | *P* value |
|---|---|---|---|---|
| Age (years) | 33.98±1.57 | 33.57±1.70 | 0.908 | .367 |
| Pre-pregnancy BMI (kg/m²) | 23.74±0.68 | 23.86±0.75 | 0.604 | .547 |
| Gestational Age at Diagnosis (weeks) | 25.78±0.69 | 25.64±0.67 | 0.767 | .445 |
| Parity (number, %) | | | | |
| Primipara | 6 | 11 | 1.537 | .215 |
| Multipara | 12 | 46 | | |
| Family History of Diabetes (number, %) | 7 | 15 | 1.043 | .307 |

**Table 2.** Comparison of Laboratory Indicators Between the Two Groups

| Item | Adverse Pregnancy Group (n = 18) | Non-Adverse Pregnancy Group (n = 57) | $\chi^2$ value | *P* value |
|---|---|---|---|---|
| FPG (mmol/L) | 6.74±0.56 | 6.38±0.52 | 2.514 | .014 |
| 2hPG(mmol/L) | 8.59±0.67 | 8.42±0.64 | 0.972 | .334 |
| $HbA_{1c}$(%) | 7.24±0.56 | 6.75±0.43 | 3.910 | .000 |
| DI | 2.25±0.16 | 3.76±0.22 | 26.905 | .000 |

**Table 3.** Correlation Between DI and Patient Indicators

| Indicator | FPG | $HbA_{1c}$ |
|---|---|---|
| r | -0.623 | -0.636 |
| *P* value | 0.041 | 0.036 |

## RESULTS

### Comparison of Basic Information Between the Two Groups

A comparison of the basic information between the two groups revealed no statistically significant differences ($P > .05$). Refer to Table 1 for details.

### Comparison of Laboratory Indicators Between the Two Groups

A comparison of FPG, $HbA_{1c}$, and DI between the two groups revealed statistically significant differences ($P < .05$), whereas the comparison of 2hPG showed no statistically significant difference ($P > .05$). Refer to Table 2 for details.

### Correlation Between DI and Patient Indicators

Pearson correlation analysis found that DI was negatively correlated with FPG, $HbA_{1c}$, and E2 ($P < .05$). Refer to Table 3 and Figures 1-2 for details.

### Multivariate Linear Regression Analysis of Factors Influencing Adverse Pregnancy Outcomes

In the multivariate Logistic regression analysis, variables that were statistically significant in the univariate analysis were used as independent variables, with adverse pregnancy outcomes as the dependent variable (No=0, Yes=1). The results indicated that DI (OR=0.599) was a significant factor influencing adverse pregnancy outcomes ($P < .05$). Refer to Table 4 for details.

### Predictive Value of DI for Adverse Pregnancy Outcomes

Utilizing DI as the predictive variable and the occurrence of adverse pregnancy outcomes as the actual outcome, an ROC (Receiver Operating Characteristic) curve was constructed. The analysis revealed that the AUC (Area Under the Curve) for DI in predicting adverse pregnancy outcomes was 0.837 (95% CI: 0.741~0.933). With DI at the optimal cut-off value of 2.1, the specificity reached 82.10%, and the sensitivity was 80.65%. Refer to Figure 3 for details.

**Figure 1.** Correlation between DI and FPG

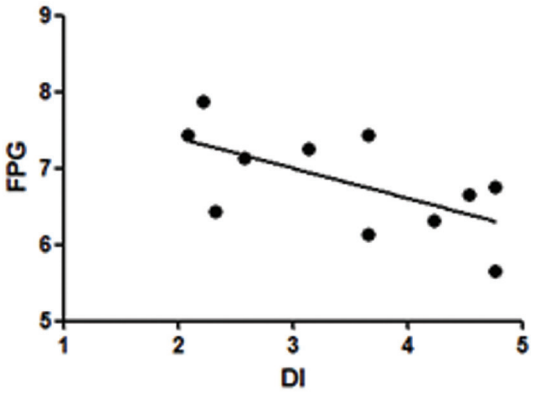



**Figure 2.** Correlation between DI and $HbA_{1c}$

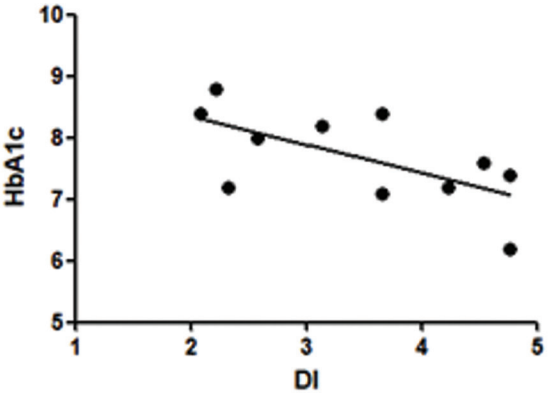
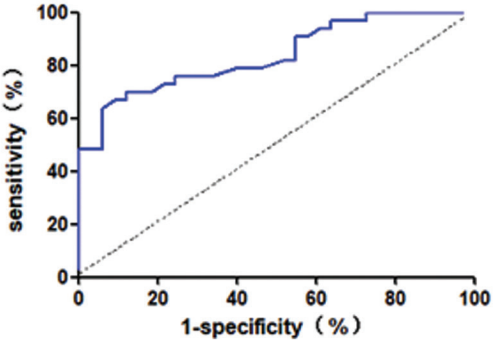



**Table 4.** Multivariate Linear Regression Analysis of Factors Influencing Adverse Pregnancy Outcomes

| Factor | *B* Value | *SE* Value | *Ward* Value | *OR* Value | *95%CI* | *P* value |
|---|---|---|---|---|---|---|
| DI | -0.508 | 0.136 | 14.417 | 0.599 | 0.462~0.781 | .000 |
| FPG | 0.473 | 0.582 | 0.642 | 1.554 | 0.502~5.012 | .422 |
| $HbA_{1c}$ | 1.108 | 0.609 | 3.116 | 3.002 | 0.874~10.115 | .078 |

**Figure 3.** ROC Curve for DI Predicting Adverse Pregnancy Outcomes



## DISCUSSION

Gestational Diabetes Mellitus (GDM) frequently affects women during their reproductive years, especially in the perinatal phase. Epidemiological data suggests that by 2018, GDM's prevalence in China had risen to 14.8%, with the numbers increasing each year.[12] Previous investigations have confirmed that elevated glucose levels in GDM patients are closely tied to an increased likelihood of unfavorable pregnancy results, such as early childbirth, preeclampsia, macrosomia, and postnatal metabolic issues like diabetes and metabolic syndrome.[13] Lately, the scientific community has delved into understanding the impact of different pathophysiological conditions in GDM patients on negative pregnancy results. An analysis involving 710 Chinese GDM patients found a significant correlation between the homeostasis model assessment for insulin resistance (HOMA-IR) and negative pregnancy results, especially gestational hypertension.[14] Yet, both insulin opposition and inadequate β-cell compensation play roles in GDM's onset, demonstrating a mutual and dynamic connection. Therefore, singular metrics that depict islet functionality, such as HOMA-IR, homeostasis model assessment (HOMA-β), and ISI, might not fully capture the glucose management capabilities of expectant mothers and their prognostic implications. The disposition index (DI), which accounts for both insulin responsiveness and release, depicts the β-cells' capacity to produce insulin amidst insulin opposition. The Disposition Index (DI) is a valuable parameter used to assess beta-cell function and insulin sensitivity in individuals at risk for diabetes and pregnancy complications. DI is calculated by multiplying the insulin sensitivity index (e.g., Matsuda Index or Homeostatic Model Assessment of Insulin Resistance) with the corresponding insulin secretion index (e.g., insulinogenic index or the ratio of insulin to glucose during oral glucose tolerance test). In our research, using DI metrics, we discerned a notable link between DI values and the likelihood of negative pregnancy results for GDM patients. Hence, tracking DI metrics could aid in pinpointing GDM patients more susceptible to pregnancy-related complications. The DI (Disposition Index) level provides a comprehensive reflection of the body's insulin sensitivity and insulin secretion function. Previous research has demonstrated that the DI level holds significant clinical importance in predicting the onset and progression of diabetes within a population.[15] Furthermore, a study that included 6,337 women with Gestational Diabetes Mellitus (GDM) revealed that incorporating the DI value of these women could enhance the predictive accuracy for adverse pregnancy outcomes, such as Large for Gestational Age (LGA), neonatal obesity, gestational hypertension, and neonatal hyperinsulinemia.[16] In another prospective cohort study involving 140 women with GDM, the DI level was identified as an independent risk factor for reduced glucose tolerance post-delivery (OR=0.20, 95% CI 0.04~0.70).[17] The findings of this study indicate that an elevated DI level is significantly associated with a decreased risk of composite endpoints, including LGA, primary cesarean section, preeclampsia, and preterm birth. These results further substantiate the correlation between DI levels and adverse pregnancy outcomes in women with GDM, providing additional evidence-based support.

Furthermore, our research pinpointed a notable association between the Disposition Index (DI) and the likelihood of unfavorable pregnancy results, particularly among females diagnosed with Gestational Diabetes Mellitus (GDM). This association might be attributed to the fundamental pathophysiological processes resulting in negative pregnancy events among those with GDM. A defining feature of GDM is persistently high blood sugar levels, originating from β-cell anomalies in situations of insulin opposition.[18] This dysfunction manifests as a lack of response to insulin, known as insulin resistance, coupled with inadequate compensatory insulin secretion in individuals with GDM. On a molecular level, insulin resistance often results from a failure in insulin signal transmission, leading to insufficient membrane transport of glucose transporter 4.[19] Compared to normal pregnancy, the glucose uptake rate stimulated by insulin in the GDM population is reduced by 54%,[20] resulting in a significant increase in blood sugar. This, in turn, exacerbates the burden on β-cells, ultimately leading to further dysfunction. The malignant cycle created by the interplay of chronic hyperglycemia, insulin resistance, and β-cell dysfunction may be a crucial underlying factor for adverse pregnancy outcomes in the GDM population.[21] The findings of this study indicate that adverse pregnancy outcomes in patients with gestational diabetes are associated with serum levels of $HbA_{1c}$, NSF-1, OB, and GLP-1. Through binary logistic regression analysis, DI was identified as an independent factor influencing adverse pregnancy outcomes in GDM patients. Additionally, this study delved into the diagnostic capability of DI in predicting adverse pregnancy outcomes in patients with GDM.

The strength of this study is rooted in the comprehensive medical history data, lending credibility to the conclusions. However, there are still certain limitations to consider. Firstly, the research only encompasses pregnant women treated at a single medical institution in China, raising questions about the generalizability of the findings to a wider population. Further research is needed to address this concern. Secondly, the study does not include information on lifestyle and socio-economic factors, leaving room for potentially confounding influences that have not been accounted for. Lastly, the calculation of the DI value in this study was derived from the OGTT test results, rather than employing the more precise and classical method of the glucose clamp technique. Despite this, the DI value's relative simplicity in acquisition makes it more accessible and easier to implement.

The DI has gained widespread attention in both diabetes and pregnancy-related research due to its ability to reflect both beta-cell function and insulin sensitivity. However, the current methods for measuring DI value remain complex and require sophisticated laboratory equipment, which limits their suitability for routine clinical practice. To address this issue, researchers have been exploring alternative, more practical approaches, such as simplified indices that can be easily calculated from readily available clinical data. These include the Stumvoll first-phase insulin secretion (IPS) index, the oral disposition index (DIo), and the Gutt Index, among others. These simpler indices may offer a more feasible and accessible alternative to the traditional methods of measuring DI value

and facilitate its integration into routine clinical care. In addition, novel measurement strategies such as continuous glucose monitoring (CGM) and mathematical models based on artificial neural networks (ANNs) have also been proposed to improve the accuracy and precision of DI estimation. These emerging technologies show great promise in advancing our understanding of glucose metabolism and its perturbations, as well as in informing personalized treatment decisions for patients with diabetes or at risk for diabetes.

Overall, the optimization and standardization of DI measurement, as well as the development of simplified clinical evaluation indicators, hold significant potential for improving the diagnosis, prediction, and management of diabetes and pregnancy complications. An important application of DI values in clinical practice is its utility in guiding the treatment and health management of patients with GDM.[22] The DI provides valuable insights into an individual's beta-cell function and insulin sensitivity, which are crucial factors in determining the appropriate therapeutic approach.[23] For patients with GDM, regular monitoring of DI values can help assess their response to interventions such as lifestyle modifications, dietary adjustments, and pharmacological therapies. A decreasing DI over time may indicate a decline in beta-cell function or worsening insulin resistance, prompting the need for intensifying treatment to achieve glycemic control.[23] Conversely, an increasing DI might suggest improved beta-cell function and enhanced insulin sensitivity, indicating a positive response to intervention. Furthermore, DI values can guide individualized treatment decisions. For instance, patients with GDM who have impaired beta-cell function but preserved insulin sensitivity may benefit from therapies that focus on enhancing insulin secretion.[24] On the other hand, those with reduced insulin sensitivity may require interventions that target improving insulin action. In addition to treatment guidance, DI values can also inform long-term health management strategies for women with a history of GDM. Individuals with lower DI values during pregnancy are at a higher risk of developing type 2 diabetes later in life. Therefore, postpartum follow-up and regular monitoring of DI values can help identify individuals who may require closer surveillance and preventive interventions to reduce their future diabetes risk. Overall, incorporating DI values into clinical practice for the management of GDM allows for personalized and targeted interventions, optimizing therapeutic outcomes, and reducing the risk of long-term complications.

In conclusion, this study discovered that an elevated DI level in patients with GDM is intimately associated with a decreased risk of adverse pregnancy outcomes, indicating that DI holds predictive value for such outcomes in gestational diabetes. The DI level, reflecting the functionality of islet β-cells after adjusting for insulin sensitivity, aids in identifying women at high risk of pregnancy complications within the GDM population. Future research should explore simplified clinical assessment methods for DI and conduct prospective observations of its variations in the clinical prevention and treatment of GDM. In summary, our study on the Disposition Index (DI) in Gestational Diabetes Mellitus (GDM) management had promising findings but several limitations. Future research should address these limitations through cross-institutional studies, consideration of lifestyle and socioeconomic factors, prospective designs, and comparative evaluations with established indices to enhance the robustness and applicability of DI values in clinical practice for GDM.

## ETHICAL COMPLIANCE

This study was approved by the ethics committee of Anhui Mingguang People's Hospital. Signed written informed consent was obtained from the patients and/or guardians.

## CONFLICT OF INTEREST

The authors have no potential conflicts of interest to report relevant to this article.

## AUTHOR CONTRIBUTIONS

BY and YY designed the study and performed the experiments, BY collected the data, YY analyzed the data, and BY and YY prepared the manuscript. All authors read and approved the final manuscript.

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