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DETERMINING THE CRUCIAL RISK FACTOR OF GESTATIONAL DIABETES MELLITUS USING RECEIVER OPERATOR CHARACTERISTIC CURVE ANALYSIS

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Abstract

One of the common complications in the course of pregnancy namely Gestational Diabetes Mellitus (GDM) is indeed a major health issue that is generally disregarded and overlooked. The principal objective in the areas of promotion of health and prevention of disease is to determine the most influential risk factors for the illness. The most significant risk factors in diagnosing gestational diabetes were identified using Discriminant Analysis (DA). Further, the Receiver Operator Characteristic (ROC) curves for the most significant risk factors obtained from the DA method in discriminating gestational diabetes were drawn and analyzed and the areas under the corresponding curves were estimated and compared. It was established that pre-pregnancy BMI played the most vital and crucial role in the discrimination of GDM.

1. Introduction

Gestational diabetes mellitus is characterized as "any level of intolerance

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of glucose with beginning or first recognition during pregnancy" (Metzger and Coustan, 1998). When the placenta holds the developing fetus, GDM is brought about by the pregnancy hormones that are then generated. These hormones may meddle with the capacity of the mother to produce and utilize her insulin. Soon after delivery, generally, this type of diabetes departs yet women who have an incidence of GDM have a twenty to fifty percentage possibility of incidence of Type 2 diabetes. All over the globe, the incidence rates of gestational diabetes have been reported to have risen from 3% to 21% and as of late, it has been increasing hugely and rapidly. 16.2% of pregnant ladies were identified to have the occurrence of gestational diabetes in the urban population of Chennai, according to a random survey carried out (Seshiah et al. 2008).

After delivery, almost all ladies return to normal carbohydrate metabolism, nonetheless, a few with diagnosed gestational diabetes will have persistent glycemia which is abnormal. Be that as it may, women with the incidence of gestational diabetes in a prior pregnancy are definitely at greater risk of incidence of type 2 diabetes in the ensuing years of their lives (Kasper, 2005). Type 2 diabetes mellitus and GDM have numerous common regular hazard factors, which include obesity and overweight. Gestational diabetes is regarded by numerous individuals to be a predecessor of type 2 diabetes. In fact, with over half of GDM patients proceeding to inherit type 2 diabetes in 5 to 10 years after giving birth, the health impact of GDM is indeed long-term (Ghattu, 2007). More precisely, the cumulative occurrence of future diabetes varies between 2.6% and 70%, with the largest risk ascent in the initial 5 years following a pregnancy with gestational diabetes and during the following 10 years, a plateau in risk (Kim et al. 2002).

A risk factor is a condition, characteristic, or behavior that raises the possibility or likelihood of acquiring a disease or illness. Risk factors play a central part in prediction and prevention. Identification of possible risk factors of specific diseases helps guide diagnosis, therapy, or disease control. Considering the fact that nearly 40% of GDM patients can be translated to diabetes mellitus over the next following years, restricting or limiting these risk factors can reduce the increase of sugar levels during the pregnancy period. In consequence, the necessity to identify and review the most influential risk factors seems very essential and crucial for pregnant women.

The proposed study has implemented discriminant analysis to determine the risk factors which are most crucial for GDM. Furthermore, the variable that played the most crucial role in discriminating gestational diabetes patients was established using the ROC curve analysis by comparing the areas under ROC curves of the corresponding risk factors.

One of the sought-after and most universally accepted techniques executed and used enormously in biomedicine models is Discriminant Analysis (Mohamad et al. 2015, Majd et al. 2018). Ricciardi et al. (2020) presented a practical application of the conventional data mining techniques which could be utilized to assist medical professionals in coronary artery disease decision-making. Linear DA was applied two times using R statistical programming language and the Knime analytics platform in order to distinguish normal or pathological patients and the classification accuracies for both the methods were found commendable. Yanga et al. (2018) proposed a new nonlinear DA framework for diagnosis of illnesses utilizing Electronic Health Records data named Fisher's Wishart Discriminant Analysis (FWDA), formulated as a robust and faster nonlinear prediction model. FWDA implemented the adaptive Bayesian voting scheme to weighted-average the classification result to enable the nonlinear prediction. Besides, the experimental results on Electronic Health Records datasets revealed that the ensemble and downstream learning classifiers were clearly outperformed by FWDA. Kolisnyk et al. (2021) carried out research into the likelihood of enhancing the quality of telemedicine diagnostics, by employing an integrated approach to learn the importance of the parameters measured and justify the feasibility of their utilization in the detection of particular pathologies. The efficacy of this technique on detection of atopic dermatitis was considered.

By applying a linear DA of heart rate variability (HRV) indices, Shinba et al. (2021) attempted to substantiate the effectiveness of autonomic calculation in major depressive disorder (MDD) sick people by evaluating the achievability of their return to work after medical leave. By making use of the HRV indices of major depressive disorder persons from the earlier research work, a linear discriminant function was formulated to distinguish the unsuccessful reinstatement from the successful effectively, which was later examined on current MDD patients. The discriminant function showed the existence of high sensitivity rate thereby revealing that normal HRV was needed for an effective return to work and also that the DA of HRV indices played a significant role for coming back to work screening in MDD affected persons. Singh et al. (2021) proposed an effective classifier to formulate application-specific arrhythmia detection by implementing a hybrid approach consisting of Dual-tree complex wavelet transform double decomposition and linear discriminant analysis to contain a compact input electrocardiogram (ECG) feature dataset for classifier models such as k-nearest neighbor, extreme learning machine and support vector machine with efficient utilization of time. The desired accuracy and adequate computational time were achieved by the experimental outcomes and consequently, may be implemented for security and secrecy of human ECG as well for mobile e-health care system.

2. Methodology

Discriminant function analysis is utilized to identify the continuous variables which distinguish among two or more naturally transpiring groups. It is a multivariate method that distinguishes various sets of observation values and allots new values of observation to sets which are defined already. Depending on the size of the population, the statistical issue is to develop a classification or discriminant function. The discriminant function's score could be generated with the raw scores and the scores of the unstandardized discriminant function. To amplify the dissimilarity between the two categories or groups, the coefficients of the discriminant function are selected, whose average is equal to zero while one is the standard deviation. For every group, the average of the coefficients of discriminant function namely centroids may be evaluated which are produced by the discriminant function calculated from the initial predictor variables.

The features across which the categories vary are indicated by dissimilarity in the position of the centroids. By their efficiency to segregate each data point to their derived categories, the significance of the functions may be analyzed. Once the classification functions are established, the classes are later distinguished. In order to accomplish this objective, using the linear discriminant functions, the classification functions are derived.

For the j^{th} group, the classification function coefficient C_j, $j = 1, \ldots, k$ who have their sample sizes to be the same, is as follows:

$$C_j = c_{j0} + c_{j1}x_1 + c_{j2}x_2 + \ldots + c_{jp}x_p \tag{1}$$

where c_{j0} is a constant and x depicts the raw score for every input variable. For group j, let M denote the mean column matrix and W denote the variance-covariance matrix for within-group, $c_{i0} = (-1/2)C_i M_i$ (Poulsen and French, 2004).

When the sample size is not identical in each group and size is indicated as n_i in group j and N denotes the size of the total sample, C_j is then given by:

$$C_j = c_{j0} + \sum_{i=1}^{p} c_{j1}x_1 + \ln\left(\frac{n_j}{N}\right)_2 \tag{2}$$

Here C_j is the discriminant function and the c_{ji}'s are the coefficients or weights of the unstandardized discriminant for the corresponding variables. These c_{ji}'s amplify the distance between the averages of the dependent or condition variable. Standardized discriminant coefficients may likewise be utilized. Efficient input variables will in general have huge loads. This function must enhance and amplify the distance between the two groups, that is, bring forth an identity that has a powerful distinguishing capacity between the categories. Subsequent to utilizing a current set of information to evaluate the discriminant function and group cases, any new samples may then be distinguished. The quantity of categories is one greater than the quantity of discriminant functions. There is exclusively one function for the essential two group discriminant analysis.

Normalizing the predictors' guarantees that differences in scale between the factors are removed. When all predictors are normalized, absolute weights, that is, weights without the sign can be utilized to grade variables subject to their distinguishing capacity, the weight which is largest being connected with the strongest variable that discriminates (Cooley and Lohnes, 1971). The most dominant variable is declared to be the input variable that is connected to the dependent variable the most. Predictor variables with huge weights are those that provide mostly to distinguishing the categories.

A matrix of total covariances and variances exists. Likewise, a matrix of pooled within-group covariances and variances exists. These matrices are studied in comparison employing multivariate F tests to identify if there exists any significant dissimilarity subject to all predictor variables between the groups. Wilk's lambda, in addition, is utilized to examine the significant dissimilarity among the categories on the respective input parameters. It reveals the variables that provide a considerable quantity of forecasting to assist in distinguishing the classes. The smaller the values of Wilks' lambda, the higher the distinguishing power of the function. The multivariate test is first performed and only when found statistically important, continues to observe those variables which have significantly different averages over the categories.

3. Data Collection and Analysis

A hospital-based research was performed to select the risk factors in association with the development of GDM. Additionally, articles related to the incidence and the possible risk factors of GDM in India and Asia on the whole from 1993-2013 were studied and reviewed (Nanda et al. 2013, Cheung et al. 2001). Besides on consultation with the gynecologists, ten parameters made use of in the research work were identified on the basis of the numerous features which are medically appropriate for a pregnant lady to develop gestational diabetes.

The real-time data sets contain three hundred and thirty six records of pregnant women, where one hundred and eighty eight members were multi gravida women, each set consisting of ten parameters was gathered from the documents of outgoing patients at a Chennai multi-specialty hospital in India during one complete year from January to December 2013. The predictor variables selected for the proposed study that were found to be relevant medically are age, pre-pregnancy Body Mass Index (BMI), history of diabetes, history of GDM, history of miscarriage, delivery of large infant (> 3.8 kg), history of stillbirth, abnormal baby in previous pregnancy, history of polycystic ovary syndrome and history of infections. Of the ten input variables, only BMI and maternal age are continuous while the remaining are Boolean.

The phase of analysis of data is crucial since it transforms raw data into treasured and valuable insights which can be utilized to intensify and strengthen the study. Once the patterns and insights are uncovered from the data, the findings can be implemented in a finer perception of the research. The interpretation of data allocates an understanding and meaning to the analyzed information and identifies its implications and significance.

Amidst all the women who were pregnant, surprisingly more than half of the population chosen for the study had either both of their parents having diabetes or at least one of the two having diabetes, while the percentage of pregnant women who were free from parents who were diabetic was 45.2 (%). Women who have had GDM in any of their prior pregnancies were less than a quarter of the population in the study, which demonstrates that a little more than 80 percent of patients did not have any GDM history. Around ten percent of the pregnant women have given birth to a newborn weighing heavier than 3.8 kg in a prior pregnancy while the remaining ninety percent of the pregnant women did not give birth to a large infant.

Unbelievably, almost forty percent of the pregnant women had a miscarriage in a prior pregnancy whereas the remaining patients did not have any history of miscarriage. About three percent of the pregnant women in a prior pregnancy had given birth to an abnormal baby. The pregnant women who had an experience of stillbirth in a past pregnancy were a little more than four percent. The percentage of women who have had infections was nearly thirty while almost six percent of the pregnant women have had an issue of polycystic ovary syndrome.

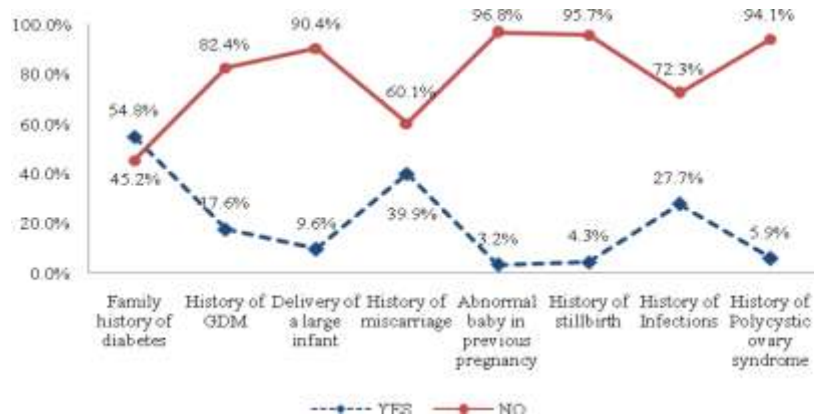


Figure 1. Summary of statistics of history of pregnant women for multi-gravida patients.

The details on the statistics of records comprising the history of the pregnant women is exhibited employing a graph in Figure 1. On an average, the maternal age of the patients was found to be 27.76 years whereas the mean BMI of the pregnant women was 25.34. Among the 336 pregnant women in the proposed work, 116 women were observed to have GDM while the remaining 220 women did not have any incidence of GDM. In other words, the rate of incidence of gestational diabetes was observed to be a daunting 34.04% in this study.

4. Results and Discussion

One of the principal objectives in the areas of prevention of disease and promotion of health is to determine the most influential risk factors for illness. Consequently, data and knowledge obtained about the significant risk factors can be shared, in the view and desire that individuals will utilize this information to transform their attitude and behavior to lessen the risk of their disease.

The risk factors of diabetes mellitus have extensively been in the process of investigation and review following examination have undergone in several research and studies. Nevertheless, not a sufficient amount of research has been carried out to inspect and explore the risk factors of GDM in pregnant ladies. Determination of the risk factors of GDM requires precise, sensitive, and unerring statistical tools. In this study, Discriminant Analysis was utilized to figure out the risk factors of GDM which were most influential. DA model was applied on the dataset of pregnant women and the outcomes were then studied by implementing Statistical Package for Social Sciences (SPSS) version 20.0.

4.1 Discriminant analysis for identifying most significant risk factors

Wilks' lambda is performed by the mean difference Analysis of Variance F test in DA. Wilks' Lambda test is used to examine which predictor variable contributes to the discriminate function, the maximum significance. Lambda value lies between zero and one, in which zero points out that the means of the group are different and one indicates that all averages of the class are identical. Thus a predictor variable will provide further to the discriminant function as the value of lambda decreases for the input parameter. In consequence, the importance of the attributions of the independent variables is shown by means of the Wilks' lambda's F test (Anderson, 2003). For every discriminant function, the Pearsonian correlation of every predictor variable is indicated in the table on structure matrix, called correlations or structure coefficients.

Table 1. Tests of Equality of Group Means.

Study Variable	F Value	Wilks' Lambda	PValue
Pre pregnancy body mass index	16.130	0.920	<0.001**
Abnormal baby in previous pregnancy	2.953	0.984	0.087
Infections (Urinary, Skin, Vaginal)	6.455	0.966	0.012*
Delivery of a large infant	6.657	0.965	0.011*
Age	5.850	0.970	0.017*
History of miscarriage	7.283	0.962	0.008**
History of GDM	95.894	0.660	<0.001**
History of polycystic ovary syndrome	2.190	0.988	0.141
History of stillbirth	3.030	0.984	0.083
Family history of diabetes	27.594	0.871	<0.001**

** represents 1% level of significance

* represents 5% level of significance

The importance of DA was revealed by making use of Wilk's Lambda test. Table 1 depicted that among all the predictor variables, diabetes history in the family, pre-pregnancy Body Mass Index and occurrence of GDM history were the parameters that were the most crucial with the development of GDM as they had the minimal values of p. Furthermore, the variables maternal age, large new born delivery in the past and infection history were significant at 5% level as their p values were in the range between 0.011 and 0.050 and the only predictor variable significant at 1% level was history of miscarriage with its p value lying in the range from 0.000 to 0.010.

Table 2. Canonical Discriminant Function Coefficients.

Variables	Unstandardized Coefficients	Standardized Coefficients
Age	0.041	0.156
Family history of diabetes	1.011	0.472
Pre-pregnancy body mass index	0.017	0.053
History of GDM	2.577	0.800
Delivery of a large infant	0.841	0.244
History of miscarriage	0.629	0.304
Abnormal baby in a previous pregnancy	0.830	0.145
History of stillbirth	-0.469	-0.094
Infections (Urinary, Skin, Vaginal)	0.707	0.313
History of Polycystic ovary syndrome	0.997	0.234
Constant	-3.199	

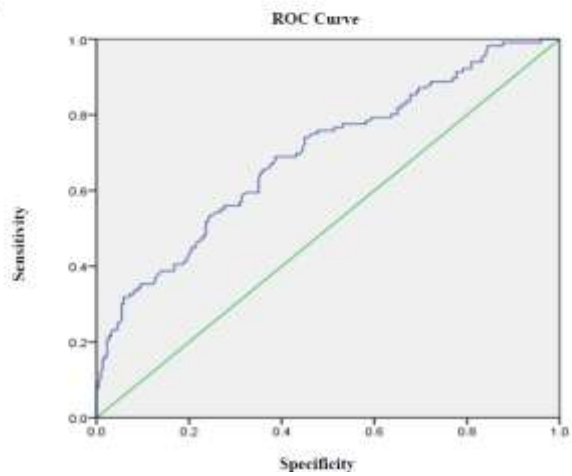
By making use of the structure matrix and the standardized coefficients, the discriminant functions are deciphered. Standardized beta coefficients are provided for all input ROC Curve variables in every discriminant function.

The greater the value of the standardized coefficient, the higher is the contribution of the corresponding variable to distinguishing the two classes. It is inferred from Table 2 that the predictor variable which played a vital role in distinguishing gestational diabetes patients from unaffected pregnant women was history of GDM. In addition, other variables which also contributed extensively to the discrimination were family history of infections, diabetes history and history of miscarriage.

4.2 Receiver operator characteristic curve analysis for two most significant risk factors

The area under the receiver operator characteristic curve (AUC) covers the entire region in the two-dimensional plane beneath the complete ROC curve. It designates and characterizes the association between two of the performance measures (1-specificity) and sensitivity. The area under Curve is the value of the average sensitivity for every conceivable specificity value. The ROC curve which has a bigger AUC is superior when compared with the ROC curve which has a smaller AUC (Hajian-Tilaki et al. 2013). It can assume values anywhere ranging from 0 to 1 because the x and y axes a like take values between 0 and 1. The nearer the area under the curve is to one, the larger the predominant ability of the predictor variable to discriminate between people with the disease and the normal people free from the disease. The line along the diagonal represents the receiver-operator characteristics curve of a random input variable and possesses an area under the curve of value 0.5 and is the pragmatic lower bound for the AUC of a prediction model. The random predictor is generally utilized as a baseline to check whether the considered model or variable is useful and effective. Owing to the fact that specificity and sensitivity do not rely upon the prevalence of disease, AUC likewise does not depend on disease occurrence. Consequently, analysis of the ROC curve has an advantage.

Two of the most significant risk factors identified in the previous section using the Discriminant Analysis model are pre-pregnancy BMI and age of the pregnant woman. The ROC curves for the two predictor variables are drawn, the corresponding areas under the curve are determined and consequently, their significance and contribution to distinguishing the group into GDM and non-GDM patients are examined, and finally, their performances are compared in this section.



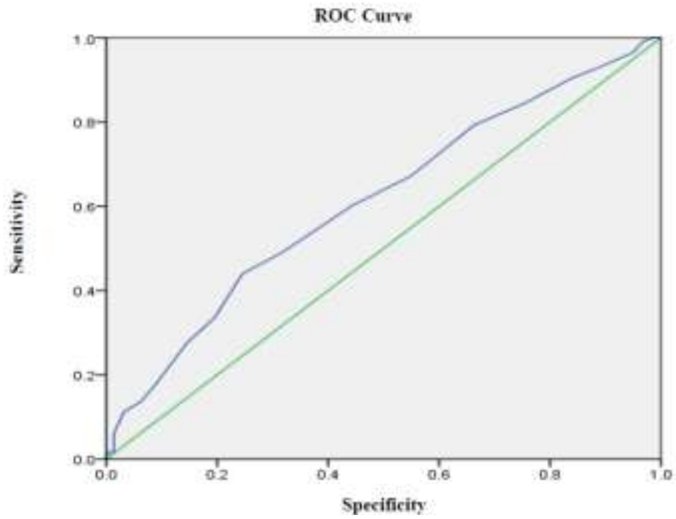
Diagonal segments are produced by ties

Figure 2. ROC curve for Pre-pregnancy Body Mass Index.

Table 3. Area Under the Curve for Pre-pregnancy Body Mass Index.

Test Result Variable(s): BMI				
Area	Std. Error	Asymptotic Sig.	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
0.695	0.031	0.000	0.635	0.755

Making use of the estimation of specificity and sensitivity of several cut-off values of pre-pregnancy BMI for detecting GDM, the relative empirical receiver-operator characteristics curve was drawn which is illustrated in Figure 2 by a nonparametric technique utilizing the SPSS software and the corresponding area under the curve for the predictor variable pre-pregnancy BMI is observed to be 0.695. (AUC=0.695, 95% confidence interval: 0.635-0.755, $p<0.001$) as depicted in Table 3. This ROC curve and the associated AUC demonstrate that pre-pregnancy BMI as a biomarker has considerable diagnostic power to distinguish gestational diabetes patients from normal pregnant patients.



Diagonal segments are produced by ties

Figure 3. ROC Curve for Age.

Table 4. Area Under the Curve for Age.

Test Result Variable(s): Age in years				
Area	Std. Error a	Asymptotic Sig[b]	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
0.612	0.033	0.001	0.548	0.676

Likewise, the empirical ROC curve for the age of the pregnant woman for diagnosis of gestational diabetes was drawn which is illustrated in Figure 3. From the above Table 4, we infer the area under the curve for the predictor variable age was noted to be 0.612.

(AUC=0.612, 95% confidence interval: 0.548-0.676, p<0.001). The ROC curve and the relative AUC similarly prove that maternal age also has the decent capability to distinguish the group under study.

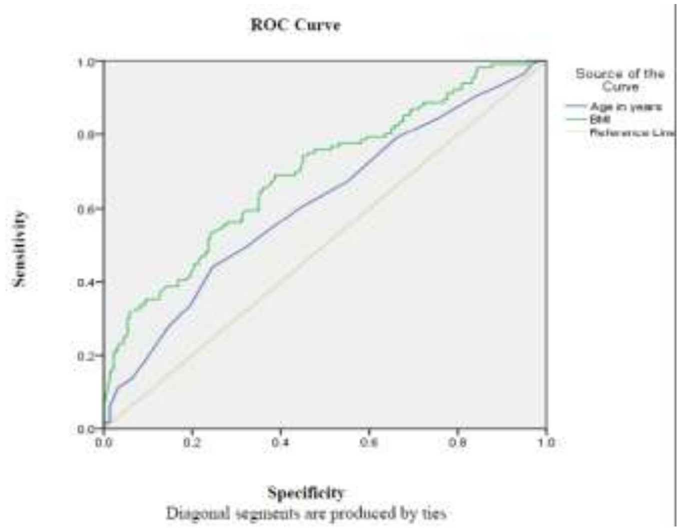


Figure 4. Comparison of ROC Curves for Age and BMI.

Table 5. Comparison of Area under the Curve for pre-pregnancy BMI and Age.

Test Result Variable(s)	Area Under Curve	Std. Error	Asymptotic Sig	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
Age	0.612	0.033	0.001	0.548	0.676
BMI	0.695	0.031	0.000	0.635	0.755

Since the area under the curve represents the mean value of sensitivity for every possible value of specificity, this measure index is particularly beneficial in a study of comparison of two independent variables (or prediction models). If two input variables are to be compared, then it is advisable to compare the complete ROC curve preferably at a specified point. The above graph and table illustrated, namely, Figure 4 and Table 5 demonstrate a comparative study of the significance of the performances of the two risk factors pre-pregnancy BMI and age on gestational diabetes and that pre-pregnancy BMI plays a more crucial and vital role than maternal age in the discrimination of GDM and non-GDM pregnant women.

5. Conclusion

In conclusion, of the 10 predictor variables that were considered in the study, seven were identified to be significant. Among these risk factors, pre-pregnancy BMI, the occurrence of gestational diabetes in a prior pregnancy, and history of diabetes in family were determined to be the risk factors that were the most influential for developing gestational diabetes using the Discriminant Analysis model. Additionally, ROC curves were drawn and the corresponding AUC were evaluated for two of the most significant risk factors identified, namely pre-pregnancy BMI and age of the pregnant woman and their comparison studied. It was observed that though both variables played vital roles in discriminating GDM and non-GDM patients, the role of the pre-pregnancy BMI predictor was greater and more crucial.

The upsurge of GDM has had a predominant rise during the years of late in terms of its prevalence. Screening provides a chance for avoiding complications of gestational diabetes. The suggestion of screening based on the identified order of these risk factors can diminish the cost and reduce stress among women who are pregnant. Moreover, it also makes detection of disease incidence faster. The medical management sectors can consider these recognized priorities through statistical techniques for the prevention of gestational diabetes in the future.

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