Analysis of Effects of Most Influential Risk Factors on Gestational Diabetes Mellitus

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Abstract
The prevalence of Gestational Diabetes Mellitus (GDM) is consistently on the increase among pregnant women in the Indian subcontinent. Discriminant Analysis (DA), a statistical technique was applied on primary data to identify the risk factors which are most significant for gestational diabetes. Overweight/obesity and advancing maternal age have had, in particular, a profound impact on both fetal and maternal complications connected with GDM. The objective of this paper was to examine the individual association between two of the study variables namely pre-pregnancy maternal Body Mass Index (BMI) and maternal age with the development of GDM by classifying the pregnant women based on these factors. Moreover, there has been no consensus on the age above which there is significantly increased risk of GDM. The results of this study showed that pregnant women aged above 30 years are at increased risk of developing gestational diabetes and thus the age threshold for increased risk of GDM was determined. Hence for selective screening in clinical practice, maternal age of 30 years and above should be embraced in view of the increased risk for the development of GDM.

Keywords: Gestational Diabetes Mellitus, Discriminant Analysis, Risk Factors, Association, Body Mass Index, Obesity, Maternal age

Análisis de los efectos de los factores de riesgo más influyentes en la diabetes mellitus gestacional
Resumen
La prevalencia de la Diabetes Mellitus Gestacional (DMG) está constantemente en aumento entre las mujeres embarazadas en el subcontinente indio. Discriminant Analysis (DA), una técnica estadística aplicada a los datos primarios para identificar los factores de riesgo más significativos para la diabetes gestacional. El sobrepeso / la obesidad y el avance de la edad materna han tenido, en particular, un profundo impacto en las complicaciones tanto fetales como maternas relacionadas con la DMG. El objetivo de este trabajo fue examinar la asociación individual entre dos de las variables de estudio, es decir, el índice de masa corporal (IMC) materno antes del embarazo y la edad materna con el desarrollo de DMG al clasificar a las mujeres embarazadas según estos factores. Además, no ha habido un consenso sobre la edad por encima de la cual existe un riesgo significativamente mayor de DMG. Los resultados de este estudio mostraron que las mujeres embarazadas mayores de 30 años tienen un mayor riesgo de desarrollar diabetes gestacional y, por lo tanto, se determinó el umbral de edad para un mayor riesgo de DMG. Por lo tanto, para el cribado selectivo en la práctica clínica, la edad materna de 30 años o más debe ser adoptada en vista del riesgo incrementado para el desarrollo de DMG.

Palabras clave: diabetes mellitus gestacional, análisis discriminante, factores de riesgo, asociación, índice de masa corporal, obesidad, edad materna

1. Introduction

Gestational Diabetes Mellitus is characterized by carbohydrate intolerance of varying severity with onset or first recognition during pregnancy [11]. It generally develops after 28 weeks of pregnancy and in most cases vanishes following the birth of the infant. However, women who have GDM are more likely to develop type2 diabetes later in life. The cumulative incidence of future diabetes extends from 2.6% to 70%, with the greatest increase in risk in the first 5 years after a pregnancy with GDM and a plateau in risk after a decade [7]. The neonatal or fetal death rate in the infants of women with GDM or type2 diabetes is more than that of non-diabetic women. Risk of developing GDM is worsened by acquiring excess weight during inter-pregnancy and growing maternal age. Excessive infant weight during birth in the current pregnancy and inflated pre-pregnancy weight in the mother have been connected with recurrent GDM [6]. BMI is the strongest anthropometric measure related with the development of type2 diabetes and GDM in women. It is found that 50% to 75% of obese women who have a history of GDM develop type2 diabetes [4]. Shoulder dystocia, failure during labour induction, malpresentation and failure to progress in the first stage of labour are some of the vital complications in overweight women during labour. While it is known that advancing maternal age influences the likelihood of development of GDM in women of all racial origins, the most at risk at the youngest age are the South Asian women. A non-white woman between 25 and 29 years of age has a risk of developing GDM that is identical to a forty year old white European woman and at
least 3 to 4 times higher than a 20-24 year old white European woman [10]. GDM is however a treatable condition and to allow effective treatment, early identification of GDM is essential.

The aim of this article is to determine the most influential risk factors of GDM using Discriminant Analysis, one of the popular statistical techniques and thereafter to analyze the association and the effects of two of the risk factors, namely pre pregnancy BMI and age of the pregnant woman with the development of gestational diabetes.

2. Methodology

In biomedicine models, one of the most commonly accepted statistical techniques extensively implemented is Discriminant Analysis. As it can be utilised easily and studied and can also yield coefficients like probability ratio to express each predictor variable’s impact on the model, it is very often adopted in medical fields [6,9,12].

The principal objective of Discriminant Analysis is to forecast group membership from a predictors set where logistic discrimination allows predicting a discrete outcome such as group membership from a set of dichotomous, discrete or continuous variables [5]. It is basically a multivariate method which segregates different sets of observation values and assigns fresh observation values to already defined sets. Based on the population size, the statistical problem is to build a classification function. The score of the discriminant function can be obtained with the help of unstandardized discriminant function scores and raw scores.

To maximize the differences between the two groups, the discriminant function coefficients are chosen, which have mean zero and standard deviation one. For each group the mean discriminant function coefficient known as centroids can be found which are generated by the discriminant function brought down from the starting independent variables. The differences in the location of these centroids indicate the dimensions along which the groups differ. Through their capacity to exactly discriminate every data point to their derived groups, the utility of these functions can be reviewed. When the classification functions are ascertained groups are then differentiated. In order to achieve this purpose, from the linear discriminant functions, the classification functions are acquired.

The classification function coefficient $C_j$ whose sample sizes are all equal for the jth group, $j = 1...k$ is given by:

$$C_j = c_{j0} + c_{j1} x_1 + c_{j2} x_2 + ... + c_{jp} x_p$$

where $c_{j0}$ is a constant and $x$ stands for the raw scores of each predictor. If $M$ denotes mean column matrix for group $j$ and $W$ denotes within-group variance-covariance matrix, $c_{j0} = (-1/2) C_j M_j$.

When the size of the sample is unequal in every group, if in group $j$, size is denoted by $n_j$ and $N$ denotes the entire size of the sample, then $C_j$ is as follows:

$$C_j = c_{j0} + \sum_{i=1}^{p} c_{ji} x_i + \ln \left( \frac{n_j}{N} \right)$$

$$\text{Eq. (2)}$$
In Multivariate Analysis of Variance (MANOVA), the independent variables are the groups and the dependent variables are the predictors whereas the independent variables are the predictors and the dependent variables are the groups in DA. To identify the variables contributing to the discrimination between groups, several variables are generally involved in a study. The process of testing significance of a set of discriminant functions in Discriminant function analysis is computationally similar to that of MANOVA. There is a matrix of total variances and covariances and in the same way a matrix of pooled within-group variances and covariances exists. To determine whether there are any significant differences with regard to all variables between groups, the two matrices are collated using multivariate F tests. The multivariate test is first performed and if found statistically significant, the variables which have significantly different means across the groups are identified.

3. Data Collection
Primary data was collected from a multi-specialty hospital in Chennai, Tamil Nadu, India using past patient records. The patient data sets of 336 records, which had 148 patients pregnant for the first time, each consisting of ten parameters was collected from the records of outgoing patients between January and December 2013. The study variables were selected based on consultation with gynaecologists and also considering the various factors that are relevant medically for a woman who is pregnant to develop GDM. Of the ten parameters, three include common details like BMI and age of the patient and history of diabetes in family amongst relatives of first degree. Details on previous pregnancy namely child born weighing above 3.8kg, presence or absence of GDM, the demise of a child within 5 months, a baby’s birth which has flaws in major organs like the heart or brain, the birth of an infant that has died in the womb strictly after having survived through at least 5 months of pregnancy are included in five other variables [15]. Particulars on history of infections and syndrome of polycystic ovaries are revealed in the remaining two variables.

The information on the statistics of the records from history of the multi-gravida patients is shown in Figure 1 by means of a graph. It was observed that the age of the pregnant ladies on an average was 27.76 years while average BMI of the patients was 25.34. The prevalence rate of GDM was found to be an alarming 34.52% in this study.

4. Results and Discussion
To determine most significant parameters of GDM, Discriminant Analysis model was implemented using version 20 of SPSS, namely the Statistical Package for Social Sciences for Windows.
In DA, Wilks' lambda is applied by the mean differences ANOVA F test. Lambda value lies between 0 and 1, wherein 0 indicates that the group means differ and a value of 1 indicates that all means of the group are equal [17]. Hence an independent variable will contribute more to the discriminant function as the lambda value gets smaller for the variable. Thus the significance of the contributions of the variables is revealed through the Wilks' lambda’s F test. Corresponding to each discriminant function, the Pearsonian correlations of all the variables are depicted by the structure matrix table in SPSS, which are known as discriminant loadings or correlations or structure coefficients.

The significance of discriminant analysis was indicated using Wilk’s Lambda test. From table 1, it is inferred that pre pregnancy body mass index, diabetes history in family and presence or absence of GDM history were the variables which were the most influential with GDM occurrence since they had the least p values [14]. Moreover, large infant delivery, age and infections in the past were the variables with 5% level of significance whereas the variable history of miscarriage had 1% level of significance.

4.1 Overweight and Obesity
Quetelet index or the Body Mass Index is a number calculated using the height and mass (weight) of a person. The BMI is defined as the body mass divided by the square of the body height, and is widely expressed in units of kg/m2, resulting from height in meters and mass in kilograms. The National Institute of Health and The World Health Organization (WHO) categorize BMI as follows: a body mass index of 18.5 kg/m2 as underweight, a BMI of 18.5–24.9 kg/m2 as normal weight, a body mass index of 25–29.9 kg/m2 as overweight, and a BMI of 30 kg/m2 and above as obesity. Obesity is classified further into class I (30–34.9 kg/m2), class II (35–39.9 kg/m2), and class III (>40 kg/m2).

Obesity and overweight are excessive or abnormal fat accumulation which may possibly damage health. Men generally tend to have less body fat than women and it is extensively agreed that men with more than 30% fat of the body and women with more than 25% body fat are termed obese. Obesity has become a pandemic in recent times. In the year 2000, the WHO assessed that as many as three hundred million among the human community around the world were medically obese. Infertility and various other pregnancy complications are related to overweight and obesity. Moreover, it is in particular connected with GDM, which worsens the risk of these complications. As the existence of obesity is very much on the rise, so is the number of women who are obese and overweight in the reproductive age. Among all categories of age, the mean body mass index is booming and women begin pregnancy with higher weights. It is saddening that with every pregnancy, women are more prone to retaining their weight gained during gestation. The risk of GDM rises substantially when pregnancy is entered with obesity or when gestational weight gain is excessive. Literature survey done between the years 1975 and 2015 on the
relation of GDM with pregnant woman’s weight gain during pregnancy period, pre-pregnancy body mass index and nutritional prevention strategies imply that maternal obesity obtained from pre-pregnancy body mass index is associated with a larger chance of development of GDM. 

According to literature, one of the main reasons behind an increased risk of GDM is high maternal BMI. Chu et al. concluded that GDM risk increases with increasing pre-pregnancy BMI using meta-analysis evaluating the quantity of GDM risk among women having higher body mass index [2]. Lowering the risk of type2 diabetes in women at high risk can be managed with an increase in physical activity and weight loss, inclusive of individuals with history of GDM, reveal several randomized trials [16, 20]. Hence, to the extent that pre-pregnancy obesity and overweight can result in GDM, lowering pre-pregnancy weight in these women ought to lower diabetes associated harmful outcomes of pregnancy. Maintaining this loss of weight beyond pregnancy should reduce risk of type2 diabetes for women in future [1]. Thus a healthy lifestyle and weight loss go a long way in reducing the risk of GDM thereby preventing type2 diabetes.

To evaluate the percentage of GDM cases that could possibly be averted if all women who are obese or overweight had a risk of GDM identical to that of women of normal weight,. One of the objectives of this article was to review the evidence regarding the relation between obesity and GDM and to determine the percentage of GDM attributable specifically to obesity and overweight with regard to several BMI categories as a means of understanding the possible effects of weight management on the prevalence of GDM in a better way.

Classification of non-GDM and GDM patients based on pre-pregnancy BMI is shown in Figure 2. It was seen that no pregnant woman developed GDM in the underweight (<18.5 kg/m²) category. In the normal weight (18.5-24.9 kg/m²) category, 34 out of 152 women had GDM thereby implying 22.37% of the normal weight population had GDM. 141 pregnant women were present in the overweight (25-29.9 kg/m²) category, of which 57 had GDM, which means 40.43% of the overweight pregnant women had GDM. 20 out of 29 women namely an astonishing 68.97% of the pregnant women had GDM in the obese class 1 (30-34.9 kg/m²) category. Finally, 5 out of the 7 pregnant women who belonged to the obese class 2 (35-39.9 kg/m²) category developed GDM. Of the total 336 records, 116 pregnant women had GDM of which 57 of them belonged to the overweight BMI category. In other words, 49.14% or almost half of the GDM patients were overweight. Moreover, 82 out of the 116 GDM patients belonged to the overweight/obese category, which means a staggering 70.69% of the GDM patients were either overweight or obese. Therefore, a BMI of 25 or higher was
found in more than 70% of all women with GDM, while the rest had normal BMI.

4.2 Advancing Maternal Age
Maternal age of a woman is said to be advanced when she gives birth at the age of over 35. It has clearly been a growing trend in recent years and is well known to be associated with gestational diabetes as the pancreas becomes less effective in everyone as they get older. Despite the wealth of evidence about the importance of risk factors, in particular older maternal age, for the development of GDM [13,19], there is little published information about how these risk factors interact to influence an individual’s risk of GDM. Presently, the National Institute for Health and Clinical Excellence (NICE) in the United Kingdom advocates a diagnostic test for GDM in pregnant women with traditional risk factors like body mass index (BMI) >30 kg/m2, racial origin with a high prevalence of diabetes, previous history of GDM or delivery of a macrosomic baby and family history of diabetes. Maternal age has not been included as one of the screening criteria because the increase in maternal age over recent years would have resulted in offering a diagnostic test to a high proportion of the pregnant population [18].

There is a wealth of literature confirming a strong positive correlation between maternal age and the development of GDM. Research proves that the risks associated with pregnancy and childbirth was higher in advanced maternal age than in younger expectant mothers [3, 8]. The current study aims to examine the individual association between maternal age with the development of GDM and their interaction and also to determine the age threshold for increased risk of GDM in India. The pregnancies were categorized according to maternal age namely <20 years, 20–24 years, 25–29 years, 30–34 years, 35–39 years, and >=40 years. Prevalence of GDM was calculated for each maternal age group.

![Figure 3: Classification of GDM Based on Maternal Age](chart)

The rates of prevalence of GDM and non-GDM in the study population according to the maternal age groups are shown in Figure 3. All the 4 pregnant women in the less than 20 years category had no GDM. In the 20 – 24 years category, 18 out of 73 women had GDM, which means 24.66% of this category population had GDM. There were 154 pregnant women aged between 25 and 29 years, of which 46 had GDM, thereby implying a similar 29.87% belonging to this category had GDM. A staggering 45.88% of the pregnant women aged between 30 and 34 years had GDM, the reason being 39 out of 85 in this category had GDM. 11 out of the 17 pregnant women, namely 64.71% in the 35 – 39 years category had GDM. Lastly, only three pregnant women belonged to the 40 years and above category, of which two had GDM. Of the total records, 116 pregnant women had GDM of which 39 of them belonged to the 30 – 34 years category. In other words, 33.62% of the GDM
patients were aged between 30 and 34 years. 46 of the 116 GDM patients, i.e., 39.66% belonged to the 25 – 29 years category. Moreover, 85 out of the 116 pregnant women who had GDM belonged to the 25 – 34 category. In other words, 73.28% of all women with GDM were aged between 25 and 34 years.

Because nearly 70% of the pregnant women were less than 30 years of age, without significantly compromising on the rate of diabetes detection, the intent was to determine if glucose screening could be eliminated in patients <30 years of age. If this could be done, it would have a significant economic impact on our prenatal costs. However, 55.17% of gestational diabetic women would have been missed had the less than 30 year age group not been screened. Only 15.52% of the women with gestational diabetes were less than 25 years and this group made up about 22.92% of the patient population. These findings, coupled with the reported low risk of gestational diabetes in young women, provide a rational basis for not screening women less than 25 years for gestational diabetes.

In this analysis, it was estimated that only 27.71% of women aged less than 30 years developed GDM whereas greatest risks associated with age were detected among mothers aged 30 onwards as 49.52% of women aged 30 and above had GDM. Thus, women aged 30 and above had nearly double the risk of women aged below 30 for developing gestational diabetes. The study found that, compared with the younger cohort of mothers aged 20 to 29, those aged 30 and over have higher risks and that the risk increases with age and the differences between these groups were highly significant.

5. Conclusion
The retrospective study has demonstrated strong interactions between two of the most significant risk factors identified using discriminant analysis namely advancing maternal age and pre-pregnancy BMI on the development of GDM. Apart from ascertaining the fact that GDM risk substantially increases with rising maternal BMI, through this article it has been estimated that a bewildering 70.69% of GDM cases were attributable to obesity and overweight alone, thereby proving that preventing GDM depends on preventing obesity in young women. Moreover, maternal age also has a strong influence on the well-being of mothers, their infants and the entire health system. Increasing birth rates among women who are in their thirties and forties are believed to persist in the forthcoming years. The findings in this study demonstrate that GDM risk becomes significantly and progressively high from 30 years onwards as 49.52% of women aged 30 and above had GDM. This study recommends the use of age 30 years as the cutoff for screening in clinical practice and the observation that maternal age 30 years is the factor most predictive of GDM.

The increasing prevalence of obesity and advanced maternal age and related conditions such as GDM and type2 diabetes are already bringing in change in the predictions of the medical care cost in the future. Hence among women of reproductive age, efforts to promote recommended levels of physical activity and healthy eating habits should be strengthened as lifestyle interventions designed to reduce weight have the capacity to lower GDM risk. Increased physical activity in women who are sedentary and pledging preference over wholesome and healthful food choices rather than
junk food would bring about finer pregnancy outcomes for both the baby and the mother. The above analysis can help public health officials estimate the potential effects of prevention interventions on GDM prevalence rates. Also, the message for obstetricians in India is to routinely screen antenatal women for GDM as early in pregnancy as possible for pregnant women aged 30 years onwards. Women in view of postponing starting a family or contemplating pregnancy at 30 years or over should find the information beneficial.

6. References

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