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# HYPERURICEMIA IN GESTATIONAL DIABETES MELLITUS: A CROSS-SECTIONAL STUDY

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## ABSTRACT

**Introduction:** Gestational diabetes mellitus (GDM) has become more common and a cause of poor maternal and fetal outcomes for last few years. Literature has stated that GDM is related to elevated serum uric acid levels that can ultimately lead to unfavorable circumstances. The aim of the present study is to determine the frequency of hyperuricemia among patients with gestational diabetes.

**Objective:** To determine the frequency of hyperuricemia among women with gestational diabetes.

**Study Design and settings:** It was a cross-sectional study, conducted at the Department of Obstetrics and Gynecology, Liaquat University Hospital Hyderabad / Jamshoro.

**Duration:** The duration of this study was seven months from 7th August 2023 to 7th February 2024.

**Material and Methods:** The patients aged 16-45 years presenting with gestational diabetes were enrolled in the study. Informed consent was taken from the patient/caretaker after explaining the risks and benefits of the study. The outcome variable, i.e. hyperuricemia, was assessed. The collected data was entered and analyzed by using SPSS v. 17 and appropriate statistical tests were applied.

**Result:** In this study, we enrolled 150 women presenting with gestational diabetes. The mean age of women was 27.25 ± 4.48 years. The mean duration of GDM was 8.25 ± 2.55 weeks, and the mean uric acid level was 6.57 ± 2.59. Moreover, the frequency of hyperuricemia among women with gestational diabetes was 70 (46.67%).

**Conclusion:** This study highlights the high prevalence of hyperuricemia among women with gestational diabetes, emphasizing the need for monitoring uric acid levels, especially in women with associated risk factors.

## Introduction:

Diabetes is defined as raised blood glucose levels caused by failure of insulin secretion or due to abnormalities of biological function [1]. Gestational diabetes mellitus (GDM) is defined as intolerance of glucose which starts or first becomes detectable during pregnancy [2]. The prevalence of (GDM) is increasing globally and has been estimated that the total prevalence of GDM reaches almost 23.78% [3].

Research indicates that women with GDM have a substantially increased risk of developing T2DM, with some studies reporting a 7-fold higher risk compared to women without GDM [4]. Literature has proved a greater incidence of obesity and type II among the offsprings born to diabetic mothers. Compared to normal controls, children of diabetic women are more likely to have elevated blood insulin levels and glucose intolerance [5]. A study conducted by Silverman et al., have revealed that the children belonging to age group between 10 to 16 years, have a prevalence of about 19.3% of impaired glucose tolerance which is suggestive of a long-standing complication of diabetes in their mothers [6].

Elevation of uric acid, which is thought to be the outcome of purine metabolism, has been linked to a number of complications during pregnancy. Raised levels of serum uric acid can trigger inflammatory process by releasing inflammatory mediators bringing upon the oxidative stress with generation of reactive oxygen species [7]. These species are a potential cause of free radical injury that can culminate in insulin resistance [8]. The end product of purine catabolism is uric acid, which has a reciprocal relation with insulin resistance and hyperuricemia especially in pregnancy despite of increased glomerular filtration rate (GFR) [9].

One of the problems in treating hyperuricemia during pregnancy is that there is no universally recognized description of the condition during pregnancy. According to the American College of Rheumatology, hyperuricemia occurs when blood serum uric acid levels are more than 7 mg/dl [10]. A higher incidence of diabetic complications could be an outcome of hyperuricemia's potential to elevate the risk of blood glucose levels during pregnancy [11]. Hyperuricemia in GDM is associated with adverse maternal and fetal outcomes. A meta-analysis has shown a positive correlation between maternal hyperuricemia and pregnancy induced hypertension leading to eclampsia, low birth weight or small for gestational age babies [12].

According to the earlier research, hyperuricemia may be a novel feature in GDM that has a negative impact on pregnancy outcomes for a variety of ethnicities. These variations may result in different risks for GDM among ethnic populations, and we were unable to locate any Pakistani research on the association between GDM and hyperuricemia. This idea guided the current study's design, which aims to determine the prevalence of hyperuricemia in women with GDM to assist in appropriate management and to produce regional information that can be compared to the global literature to look for any variances.

## Material and methods:

This cross-sectional study was conducted at the department of Gynecology & Obstetrics in Liaquat University Hospital Hyderabad / Jamshoro. Duration of study was from 7th August 2023 to 7th February 2024. Keeping an anticipated prevalence of hyperuricemia in gestational diabetes mellitus 46% [13], at 95% confidence interval and 5% margin of error, the sample size was calculated to be 150 ladies with gestational diabetes mellitus. The p-values was kept at $\leq$ 0.05. Non probability consecutive sampling technique was acquired to collect the data.

The pregnant women in age group between 16 to 45 years, having a gestational age of more than 24 weeks and confirmed on their history as last menstrual period, whether primiparous or multiparous, and diagnosed with gestational diabetes mellitus based on oral glucose tolerance test (OGTT), attending the department of Obst and Gynae at Liaquat University Hospital Hyderabad were included in the study.

All those patients who were not willing to give their consent, suffering from any autoimmune disorder, pre-existing diabetes mellitus, gout or chronic renal diseases were excluded from the study. Also, women receiving diuretics, steroids or uric acid lowering therapies were also not included in the present investigation.

After getting the ethical approval from the institutional review board and CPSP, the subjects were recruited under the strict supervision of a consultant gynecologist with an experience not less than three years. After getting the informed consent from the recruited patients with GDM, they were evaluated for raised serum uric acid levels. The 2c.c blood samples were drawn and collected in a 5c.c sterilized syringe and were sent immediately at the laboratory for the biochemical analysis. The results were supervised by a senior biochemist with an experience of no less than three years. The hyperuricemia was labeled in those samples where serum uric acid level was greater than 6mg/dl. The data of all patients were analyzed in SPSS version 17.00. Frequencies and percentages were computed for variables including booking status (booked or un-booked), parity (primiparous or multiparous), residence (urban or rural), multiple pregnancy, anemia, obesity, hypertension, pre-eclampsia, smoking, and hyperuricemia. Means and standard deviations (SD) were calculated for quantitative variables such as maternal age, gestational age, duration of GDM, and serum uric acid levels. The quantitative variables such as maternal and gestational age, duration of GDM and serum uric acid level were expressed as mean ± S.D. the chi square test was applied for categorical variables and significance was kept at p-value $\leq 0.05$.

**Results:**

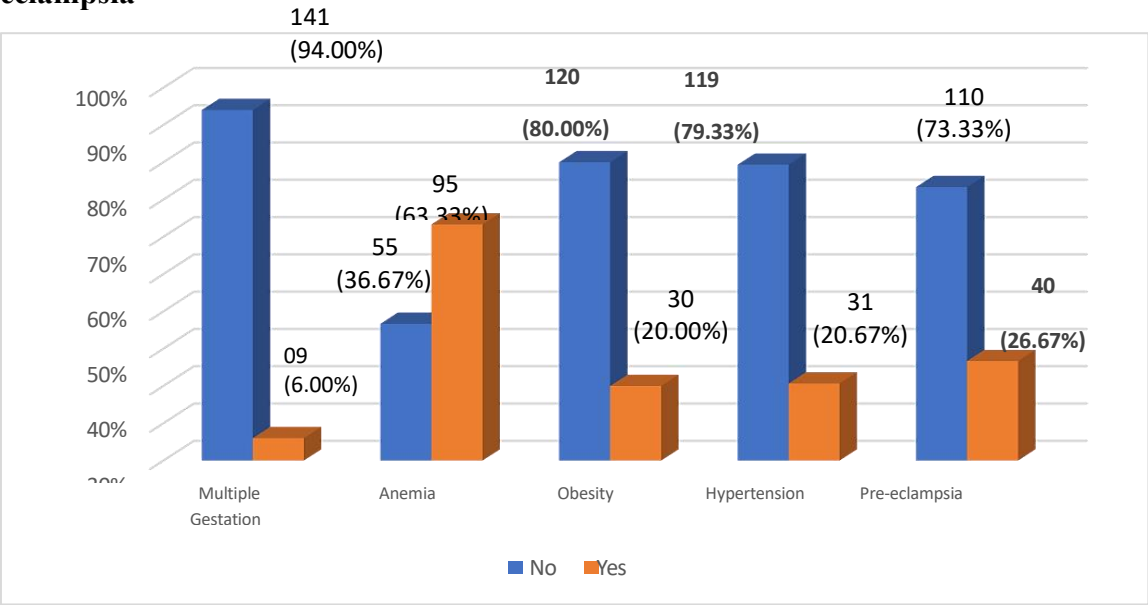
In the current investigation, 150 pregnant women with GDM were recruited. Their mean age was recorded to be 27.25 ± 4.48 years. The mean duration of GDM was 8.25 ± 2.55 weeks, while the mean serum uric acid level was 6.57 ± 2.59 (table-1).

**Table 1: Distribution of Age, duration of GDM and uric acid level of study population**

| Variable | Mean (SD) | Median (IQR) |
|---|---|---|
| Age (Years) | 27.25 ± 4.48 | 27 (23-31) |
| Duration of GDM (Weeks) | 8.25 ± 2.55 | 9 (6-10) |
| Uric Acid Level | 6.57 ± 2.59 | 5.76 (4.5-8.78) |

Additionally, 63 women (42%) were booked, 89 (59.33%) were primiparous, and 9 (6%) had multiple pregnancies. Anemia was present in 95 women (63.33%), obesity in 30 (20%), hypertension in 31 (20.67%), and pre-eclampsia in 40 (26.67%). Moreover, 28 (18.67%) women were smokers, while the frequency of hyperuricemia among women with GDM was found to be 70 (46.67%) (Figure-1).

**Figure 1: Distribution of multiple gestation, anemia, obesity, hypertension and pre-eclampsia**




Following that, table 2 displays the distribution of hyperuricemia according to age, residence, booking status, parity, multiple gestation, anemia, obesity, hypertension, pre-eclampsia, smoking, and the duration of GDM.

**Table 2: Stratification of hyperuricemia with respect to age, residence, booking status, parity, multiple pregnancy, anemia, obesity, hypertension, preeclampsia, smoking and duration of GDM.**

| Independent Variables | | Hyperuricemia | | p-value |
|---|---|---|---|---|
| | | No n(%) | Yes n(%) | |
| Age (Years) | <30 | 50 (62.5) | 46 (65.71) | 0.682 |
| | ≥30 | 30 (37.5) | 24 (34.29) | |
| Residence | Urban | 54 (67.5) | 46 (65.71) | 0.817 |
| | Rural | 26 (32.5) | 24 (34.29) | |
| Booking | Un-booked | 45 (56.25) | 42 (60) | 0.642 |
| | Booked | 35 (43.75) | 28 (40) | |
| Parity | Primpara | 46 (57.5) | 43 (61.43) | 0.625 |
| | Multipara | 34 (42.5) | 27 (38.57) | |
| Multiple Pregnancy | No | 75 (93.75) | 66 (94.29) | 0.890 |
| | Yes | 5 (6.25) | 4 (5.71) | |
| Anemia | No | 26 (32.5) | 29 (41.43) | 0.258 |
| | Yes | 54 (67.5) | 41 (58.57) | |
| Obesity | No | 64 (80) | 56 (80) | >0.99 |

| | | | | |
|---|---|---|---|---|
| | Yes | 16 (20) | 14 (20) | |
| HTN | No | 64 (80) | 55 (78.57) | 0.829 |
| | Yes | 16 (20) | 15 (21.43) | |
| Preeclampsia | No | 60 (75) | 50 (71.43) | 0.622 |
| | Yes | 20 (25) | 20 (28.57) | |
| Smoking | No | 64 (80) | 58 (82.86) | 0.654 |
| | Yes | 16 (20) | 12 (17.14) | |
| GDM Duration (Weeks) | ≤8 | 42 (52.5) | 32 (45.71) | 0.407 |
| | >8 | 38 (47.5) | 38 (54.29) | |

**Discussion:**

Gestational diabetes mellitus (GDM) is the most widespread complication come across in pregnancy, affecting the health and well-being of a great number of pregnant women globally [14]. It was formally defined by Wender-Ożegowska et al., as high blood glucose levels first diagnosed during pregnancy [15]. GDM is associated with several maternal and fetal complications, including preeclampsia, polyhydramnios, increased chances of cesarean section and induction of labor, congenital malformations, fetal macrosomia, birth asphyxia, respiratory distress syndrome, premature birth, neonatal metabolic complications, neonatal jaundice, and death [16, 17]. Numerous conventional influencing factors have been pointed out resulting in the development of GDM, including maternal obesity, advanced maternal age, family history of type II diabetes mellitus or a previous history of GDM [18]. However, several new risk factors have also been identified. Various biochemical abnormalities in early pregnancy can lead to the development of GDM at later stages of the pregnancy [19].

Raised serum uric acid, also known as hyperuricemia, has now been considered as one of the critical predisposing factors for elevated insulin resistance and GDM. Hyperuricemia has been regarded as a marker and predictor for the development of diabetes mellitus and metabolic syndrome in the future [20]. It is caused by a disturbance in uric acid metabolism i-e either increased production or decreased excretion. Various researches have revealed that hyperuricemia is associated with obesity, hypertension, hyperinsulinemia, and hyperlipidemia, signifying it could be a part of metabolic syndrome [21].

Nguyen et al., in their investigation reported hyperuricemia among pregnant women as 20.3% [22]. In contrast, the present study reported hyperuricemia in 70 (46.67%) women with gestational diabetes. The significant differences between the studies may be due to differences in study populations, geographic localizations, diagnostic standards, and procedural disparities. The variability in stated prevalence rates could be explained by differences in the number of samples tested, timing of testing, and participant variables (e.g., age, BMI, and comorbidities). Moreover, the higher prevalence detected in the current study could be an attribute to regional or population-specific factors that affect uric acid levels, such as dietary factors, lifestyle differences, or genetic predilections. It is also likely that different diagnostic procedures or cut-off points for hyperuricemia might be a reason of discrepancies between studies.

The current study revealed anemia was present in 95 women (63.33%) who had gestational diabetes with hyperuricemia. This could be result of oxidative stress, persistent low-grade inflammation as well as metabolic

abnormalities all of which could lead to vascular endothelial dysfunction resulting in impaired erythropoiesis. The similar findings were reported by Ahmed et al., they found that women with GDM had a higher prevalence of anemia, suggesting inflammation and metabolic derangements as potential contributing reasons [23].

This study offers valuable insight into the prevalence of hyperuricemia among women with gestational diabetes (GDM), an important component of maternal health. The sample size of 150 women has substantiated statistical strength to the findings, enhancing the generalizability of the results. The detailed demographic and clinical data collected provides a comprehensive overview of the factors influencing hyperuricemia in this population. A better understanding of the risk factors related to raised uric acid levels is made possible by stratifying hyperuricemia according to the variables. This insight can be used to recognize at-risk populaces and guide focused therapies.

Despite its strengths, this study has few limitations. The cross-sectional design confines the ability to establish causal relationships between hyperuricemia and gestational diabetes. Additionally, the study was conducted in a single center, and most of the participants were from urban areas, which may not be demonstrative of rural populations. The lack of a control group of pregnant women without gestational diabetes limits the ability to directly compare the prevalence of hyperuricemia in this specific cohort. Including a more diverse sample from both urban and rural areas, along with a control group of women without gestational diabetes, would allow for more comprehensive comparisons. Further research could also explore the long-term implications of hyperuricemia in women with gestational diabetes, including its potential impact on postpartum health and future cardiovascular risk.

**Conclusion:**

In conclusion, this study reveals a noteworthy prevalence of hyperuricemia among women with gestational diabetes and proposes that numerous demographic and clinical factors may influence its manifestation. The findings highlight the need to monitor uric acid levels in women with gestational diabetes, especially those with risk factors like obesity, hypertension, and pre-eclampsia. Early identification of women at increased risk for hyperuricemia could allow timely interventions and potentially better maternal and fetal consequences in gestational diabetes.

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