# TO MEASURE THE FREQUENCY OF GESTATIONAL DIABETES MELLITUS IN PATIENTS WITH RAISED SERUM URIC ACID LEVEL IN FIRST TRIMESTER OF PREGNANCY

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## ABSTRACT

***Objective:*** To determine the frequency of gestational diabetes mellitus in pregnant patients having increased serum uric acid level in first trimester of pregnancy.

***Study Design:*** Descriptive case series study.

***Place and Duration of Study:*** This study was conducted at Pak Emirates Military Hospital Rawalpindi for a period of 6 month, from Jul 2015 to Jan 2016.

***Material and Methods:*** All 140 pregnant women in their first trimester with increased serum uric acid level (cut off value >4mg/dl) were included in the study according to inclusion criteria (antenatal women with gestational amenorrhea of less than 13 weeks, age 20 to 40 year, parity 0 to 8) and exclusion criteria (pregestational diabetes, hypertension, renal disease, liver disease, multiple gestations, gout, drugs which increases uric acid excretion, past history of gestational diabetes mellitus, history of good size baby in previous pregnancies). Sampled patients were followed up in OPD, at 24 weeks of gestation, 75g OGTT was performed to diagnose GDM with cut off value: fasting blood sugar level of >92 mg/dl, 1 hour after breakfast >180mg/dl, 2 hours after breakfast >155mg/dl. Sampling technique was no probability consecutive sampling.

***Results:*** Frequency and percentage was observed for two groups (presence or absence) of gestational diabetes mellitus (GDM). Eighty one patients (57.9%) had positive (yes) gestational diabetes mellitus, while remaining 59 patients (42.1%) had Negative (no) gestational diabetes mellitus. Gestational diabetes mellitus has the prevalence rate between 50-51% among population with high serum uric acid. To determine the frequency of GDM in the population having high serum uric level, we applied one sample t test (one sided test). The hypothesis of our one sample test was H0: $P \leq P_0$, H1: $P > P_0$ where $p_0$ was anticipated population proportion. We find that the prevalence rate of GDM in the population having high serum uric acid is between 50-51%.

***Conclusion:*** It is suggested that levels of uric acids in serum must be monitored routinely during first antenatal care visit. Uric acid levels in serum should be monitored routinely during the first antenatal care visit. Frequency of GDM is also linked with higher number of parity.

**Keywords:** Frequency, Gestational diabetes, Hyperuricemia, Low birth weight.



## INTRODUCTION

In pregnancy, uric acid is correlated with insulin resistance. Serum uric acid is higher in first trimester in women diagnosed with GDM as compared to women without GDM[1].

Gestational diabetes mellitus is an illness distinct as any type of glucose intolerance which is developed for the first time in pregnant women. GDM is characterized by higher level of insulin resistance and abnormality in secretion of insulin. Essentially, pregnancy acts as metabolic stress test and bares the causal insulin resistance and dysfunctionality of beta cell. GDM is also linked with multiple complications (Maternal and fetal), mainly macrosomia[2,3].

Studies have indicated that there is an increase in propensity for higher and unbalanced free radical production, which can cause to trigger membrane harm in patients with GDM and other side effects related to oxidative imbalance. Altered prostaglandin biosynthesis is believed to be the main effect of increased presence of Reactive oxygen species in GDM. Abnormal biosynthesis of prostaglandin may be

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the main cause in development of GDM related embryopathy[4-6].

Hyperuricemia in first trimester was linked with higher possibility of developing GDM. The possibility of having GDM was 3.25 times greater if uric acid levels in first trimester remain in 4th quartile. Although, there is a strong relation of raised uric acid levels in the body with the body mass index, the possibility of having GDM remained elevated among pregnant women with raised level of uric acid in 1st trimester independent of BMI. The rationale of our study was to determine frequency of GDM in pregnant population with high serum uric acid level in first trimester of pregnancy[7].

## MATERIAL AND METHODS

It is a descriptive case series study conducted at: Pak Emirates Military Hospital Rawalpindi from: 11th Jul 2015 to 11th Jan 2016. All 140 pregnant women in their first trimester with increased serum uric acid level (cut off value >4mg/dl) were included in the study according to inclusion criteria (Antenatal woman's with gestational amenorrhea of less than 13 weeks, Age 20 to 40 year, Parity 0 to 8) and exclusion criteria (Pregestational diabetes, Hypertension, Renal disease, Liver disease, Multiple gestations, Gout, Drugs which increases uric acid excretion, Past history of gestational diabetes mellitus, History of good size baby in previous pregnancies). Sampled Patients were followed up in OPD, at 24 weeks of gestation, 75g OGTT was performed to diagnose GDM with cut of f value : fasting blood sugar level of >92 mg/dl, 1 hour after breakfast> 180mg/dl, 2 hours after breakfast >155mg.

All data was entered and analyzed using SPSS version 17. Descriptive statistics were calculated for both qualitative and quantitative variables. For qualitative variables like gestational diabetes mellitus, frequency and percentage were calculated. For quantitative variables like age, parity, gestational age, uric acid levels and blood glucose levels mean and standard deviation will be calculated. Qualitative variables were presented through tables and charts. Effect modifiers like age, gestational age, parity were controlled by stratification. Post stratification Chi-square test was applied. A *p*-value <0.05 was taken as significant.

## RESULTS

Study population included 140 pregnant females with increased serum uric acid level in their first trimester. Mean ± SD was recorded for Blood Sugar Fasting 101.31 ± 21.08. Mean ± SD was recorded for Blood sugar after one hour 177.05 ± 37.552. Mean ± SD was recorded for blood sugar after two hour 153.16 ± 31.65 (table-I).

We find that the prevalance rate of gestational diabetes mellitus among the population having high serum uric acid is between 50-51%.

The GDM percentage of Nulliparous is 6 (25%) out of 24 (17.1%), multiparous 62 (62.6%) out of 99 (70.7%) and grand multiparous 13 (16.64%) out of 17 (12.1%). Chi square test had applied to test the relation between parity and gestational diabetes mellitus In this study, there is link between gestational diabetes mellitus and equality and *p*-value 0.001 which is less than 0.05 (table-II). Stratification according to age and gestational age is given in table-III & IV.

## DISCUSSION

Previously, studies have indicated a link between hyperuricemia and GDM[8,10]. This study also supported this association. In our study, we observed that uric acid ≥4 mg/dl initially in pregnancy is connected with an increased possibility of developing gestational diabetes. In our study we determined that concentration of uric acid in first trimester of pregnancy is same as that of earlier; however, to our knowledge there are no prior reports of the connection between first trimester uric acid and Gestational Diabetes Mellitus among low risk women[11].

In the first trimester, levels of uric acid are roughly equal to pre-conception levels. The pregnant women with increased uric acid levels in first trimester may be regarded as at higher

risk of developing GDM independent of BMI and are predisposed to metabolic syndrome. Normally, there is a decrease in uric acid levels in early pregnancy, also implies that pregnant women with raised uric acid levels may have reduced adaptation to pregnancy. This poor adaptation like abnormal placentation may place them at higher risks for GDM.

Katherine *et al*[11] showed uric acid levels >3.6 mg/dl are linked with 3-fold higher possibility of developing GDM. Yoo *et al*, also reported about connection between raised uric acid and insulin resistance among non-pregnant women and blamed hyperuricemia as an element of risk for type 2 diabetes mellitus[12].

Hyperuricemia being the independent

**Table-I: Descriptive statistics of the study population.**

| Variables | N | Minimum | Maximum | Mean | SD |
|---|---|---|---|---|---|
| Age | 140 | 20 | 40 | 31.04 | 4.842 |
| Parity | 140 | 0 | 8 | 2.71 | 2.140 |
| Serum uric acid | 140 | 4.1 | 8.6 | 5.310 | 0.9091 |
| BSF | 140 | 62 | 183 | 101.31 | 21.080 |
| After one hour | 140 | 107 | 301 | 177.05 | 37.552 |
| After two hour | 140 | 94 | 247 | 153.16 | 31.650 |
| Gestational Age | 140 | 8 | 13 | 9.99 | 1.269 |

**Table-II: Relational between parity and gestational diabetes mellitus.**

| Parity groups | GDM | | Total | *p*-value |
|---|---|---|---|---|
| | No | Yes | | |
| Nuliparous-Parity equal to 0 | 18 | 6 | 24 | 0.001 |
| Multiparous-Parity equal to 1-5 | 37 | 62 | 99 | |
| Grand-multiparous - parity more than 5 | 4 | 13 | 17 | |
| Total | 59 | 81 | 140 | |

**Table-III: Frequency distribution of age groups among study population.**

| Age groups | Frequency | Percentage |
|---|---|---|
| Less or equal to 30 years of age | 65 | 46.4 |
| More than 30 years of age | 75 | 53.6 |
| Total | 140 | 100.0 |

**Table-IV: Frequency distribution of gestational age among study population.**

| Gestational age groups | Frequency | Percentage |
|---|---|---|
| Less or equal to 10 weeks | 87 | 62.1 |
| More than 10 weeks | 53 | 37.9 |
| Total | 140 | 100.0 |

As hyperuricemia has a relation with insulin resistance precedes type 2 diabetes development in non-pregnant women, hence it was assumed that elevated blood levels of uric acid in first trimester would be related with development of GDM[10].

The current study also established the fact and endorsed the previous studies that there is a robust connection between raised levels of uric acid in first trimester with higher risk of having GDM, where 57.9% of pregnant women with uric acid concentration > 4mg/dl developed GDM.

indicator of cardiovascular disease[13], is closely linked with insulin resistance. The data obtained from cross sectional as well as cohort studies have confirmed that raised uric acid levels being the independent risk factor DM[14,15].

In another study, it was observed that multiparous were 8.29 fold more expected to develop GDM than nulliparous. The chances for a parous woman for developing GDM inflate from 2% to 21% when age changes from 20 years to 40. Maternal age confounding effect may be attributed to higher incidence of GDM among

grand multiparous women[16]. 44.3% of multiparous women with raised levels of uric acid in serum, have GDM.

Wolak *et al*, observed that levels of uric acid at the highest quartile in initial 20 weeks during pregnancy are linked with GDM development and mild preeclampsia[17]. Usually, levels of uric acid in early pregnancy and in mid-trimester fall below normal levels and in late pregnancy, uric acid levels are restored to normal levels. If there are some preexisting metabolic imbalances in pregnancy where women have hyperuricemia, they may have poor physiological adaptations. It may predispose the pregnant women to problems like GDM and preeclampsia[18].

The present study is important in the aspect that it sets a cut-off serum uric acid level in pregnant women of 4 mg/dl responsible for GDM development. Therefore, it is strongly recommended to monitor the levels of uric acid in serum during first trimester of pregnancy so early diagnosis may be possible and treatment could be started in time. As, early diagnosis and management is important in avoiding adverse fetal and maternal complications.

## CONCLUSION

High uric acid correlates in assessing pregnant women in first trimester to predict gestational diabetes mellitus development. Frequency of GDM is significantly increased in patients with first trimester hyperuricemia and with high number of parity as well. Certain parameter of biochemical origin such as uric acid levels in serum may be helpful in determining and predicting complications like GDM. Early diagnosis is important in changing the outcome of complications and it may also help clinicians to better understand the condition and in proper management of condition like GDM. Timely diagnosis will help in improving health of quality of life of GDM women and offspring. Therefore, it is highly recommended to monitor serum uric acid levels in first antenatal care visit.

## CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

## REFERENCES


1. Weisz B, Cohen O, Homko CJ, Schiff E, Sivan E. Elevated serum uric acid levels in gestational hypertension are correlated with insulin resistance. Am J Perinatol 2005; 22: 139-44.
2. Mahalakshmi MM, Bhavadharini B, Kumar M, Anjana RM, Shah SS, Bridgette A, et al. Clinical profile, outcomes, and progression to type 2diabetes among Indian women with gestational diabetes mellitus seen at a diabetes center in south India. Indian J Endocrinol Metab 2014; 18(3): 400-6.
3. Amini E, Sheikh M, Hantoushzadeh S, Shariat M, Abdollahi A, Kashanian M. Maternal hyperuricemia in normotensive singleton pregnancy a prenatal finding withcontinuous perinatal and postnatal effects, a prospective cohort study. BMC Pregnancy and Childbirth 2014; 18(14): 104.
4. El-Gharib MN, Mahfouz A, Morad MA, Farahat MA. Prediction of gestational diabetes by measuring first trimester maternal serum uric acid concentration. J Basic Clin Reprod Sci 2013; 2(1): 27-31.
5. Modan M, Halkin H, Karasik A, Lusky A. Elevated serum uric acid - A facet of hyper- insulinaemia. Diabetologia 1987; 30: 713–8.
6. Adeniji1 AO, Oparinde DP. The profiles of lipid peroxidation and anti-oxidant activities in gestational diabetes mellitus & normal pregnancies in Nigerian population. Open J Obs Gyn 2013; 3(6): 5.
7. Gungor ES, Danisman N, Mollamahmutoglu L. Relationship between serum uric acid, creatinine, albumin and gestational diabetes mellitus. Clin Chem Lab Med 2006; 44: 974–7.
8. Rajakumar SA, Thirumal R, Usha V, Rontgen R. Co-Relation between first trimester Uric acid concentration and development of gestational diabetes mellitus. J Evol Med Dent Sci 2014; 3(2): 266-71.
9. Kodama S, Saito K, Yachi Y, Asumi M, Sugawara A, Totsuka K, et al. Association between serum uric acid and development of type 2 diabetes. Diabetes Care 2009; 32: 1737-422009.
10. El-Gharib MN, Mahfouz AE, Morad MA, Farahat MA. Pre-diction of gestational diabetes by measuring first trimester maternal serum uric acid concentration. Clin Reprod Sci 2013; 2: 27-31.
11. Katherine SL, Catovr J, Provins T, James MR, Robin EG. Elevated first-trimester uric acid concentrations are associated with the development of gestational diabetes mellitus. Am J Obstetrics Gynecology 2009; 2014(4): 402-5.
12. Yoo TW, Sung KC, Shin HS, Kim BJ, Kim BS, Kang JH, et al. Relationship between serum uric acid concentration and insulin resistance and metabolic syndrome. Circ J 2005; 69: 928-33.
13. Tsouli SG, Liberopoulos EN, Mikhailidis DP, Athyros VG, Elisaf MS. Elevated serum uric acid levels in metabolic syndrome: An active component or an innocent bystander? Metabolism 2006; 55: 1293-301.
14. Nakanishi N, Okamoto M, Yoshida H, Matsuo Y, Suzuki K, Tatara K. Serum uric acid and risk for development of hypertension and impaired fasting glucose or Type II diabetes in Japanese male office workers. Eur J Epidemiol 2003; 18: 523-30.
15. RasikaC, Samal S, Ghose G. Association of elevated first trimester serum uric acid levels with development of GDMJ Clin Diagn Res 2014; 8(12): 1-5.
16. Al-Rowaily, Abolfotouh. Predictors of GDM in high parity community in Saudi Arabia. Eastern Mediterranean Health J 2010; 16: 6.
17. Talya W, Ruslan S, Arnon W. High uric acid level during the first 20 weeks of pregnancy is associated with higher risk for gestational diabetes mellitus and mild pre-eclampsia 2012; 31(3): 307-15.
18. Kishk EA. Uric acid concentrations, insulin resistance and pregnancy outcome in obese and non-obese pregnant women. Med J Cairo Univ 2011; 79(2): 19-125.