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# Effect of Antenatal Betamethasone and Dexamethasone on Maternal Blood Glucose Levels, Fetal Movement, Nst Parameters, and Umbilical Artery Doppler

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## ABSTRACT

**Background:** The rationale of the study is to establish the time duration of recovery of disturbed sugar values and NST parameters following steroid administration and which drug has a lesser rate of hyperglycemia and lesser disturbance of DFMC and NST parameters, so as to advocate better drugs for fetal lung maturity. This study aims to compare the changes in maternal serum glucose levels, daily fetal movement count, NST parameters, and umbilical artery doppler following Betamethasone and Dexamethasone administration in antenatal women.
**Subjects and Method:** The study design is a prospective observational cohort study. 100 pregnant patients, were recruited into 2 equal groups who received Betamethasone and Dexamethasone in Obstetrics & Gynaecology department, MLN Medical College, Prayagraj. The independent variables are Age, Gravidity, and BMI while the dependent variables are postprandial blood sugar values, Daily Fetal Movement Count, Fetal Heart Rate, Non-Stress Test Parameters, and Doppler Flow Velocimetry of the Umbilical artery. Categorical variables were compared using the Chi-square test, while, for continuous variables T-test was used. Study instruments include Glucometer, Cardiotocography, and Ultrasound.
**Results:** Significant changes in the glycemic profile and fetal movements were noted. The mean ± SD glucose rise after 24 hrs in Group A (Mean= 140.10; SD= 35.90) and group B (Mean= 113.26; SD= 27.90), with $p<0.001$. 54% and 24% women perceived reduced fetal movements ($p = 0.002$) while 14% and 12% women had reduced variability on NST ($p = 0.766$) in Group A and Group B respectively, with 66.6% and 85.71% showing reduced flow on Doppler.
**Conclusion:** Antenatal Betamethasone as well as Dexamethasone administration causes significant changes in maternal hyperglycemia, FHR, and DFMC at 24hrs while changes were non-significant in NST parameters and Doppler. Maternal hyperglycemia resolved within 72hrs with a resolution of decreased fetal movement perception. Umbilical artery flow decreased 24 hrs following steroid administration with more profound changes with betamethasone.

**Keywords:** Betamethasone, Dexamethasone, hyperglycemia, fetal heart rate, variability.

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## BACKGROUND

Administration of synthetic Corticosteroids in pregnancy is common practice in obstetrics to reduce the incidence/severity of hyaline membrane disease, respiratory distress syndrome, necrotizing enterocolitis, and intraventricular hemorrhage in neonates. Usually, two doses of 12 mg of Betametha-

sone, separated by 24 h or four doses of 6 mg of Dexamethasone separated by 12 hr are administered intramuscularly (Brownfoot et al., 2013).

Current recommendations from the National Institute of Health (2020) and the American College of Obstetricians and Gynaecologists (2020) are to administer corticosteroids in pregnancies between 24-34 weeks gestation deemed at risk for preterm delivery. Additionally, the current Green-top guidelines in the year 2021 and ACOG the in year 2020 also support the administration of steroids even after 34 weeks when delivery is planned electively by caesarean at 38+6 weeks of gestation. The recommended optimal time for best results is administration 48 hours prior to elective birth.

Steroid administration has an impact on glucose homeostasis and may induce clinically significant hyperglycaemia in women with diagnosed Diabetes Mellitus or even without gestational diabetes. The NICE guideline recommends that diabetic women receiving steroids should have additional insulin according to an agreed protocol. The National Indian guidelines on indoor management of diabetes recommend a 20-30% increase in the dose of insulin on the following 2-3 days of steroid administration(Bajwa et al., 2010).

Another bothersome impact of steroid administration includes altered fetal movements in pregnant women creating a lot of panic and inappropriate clinical decisions. Steroids have been related to transient reduction in fetal body and breathing movements and a decrease in the short-term variability (STV) in computerized cardiotocography (cCTG). In a small proportion of cases such profound depressive effects on fetus may persist up to 3 days after its administration that can be misinterpreted as a sign of brain hypoxia. It is still unclear why only some fetuses exhibit a reduced heart rate variability following steroids administration and others do not (Abbasalizadeh et al., 2013).

There is paucity of data on effect of steroids on glucose homeostasis in non-diabetic pregnant women because only few small studies with small number of subjects exist in the literature regarding this (Kakoulidis et al., 2020).

This study aims to evaluate and compare blood sugar changes, fluctuations in DFMC and CTG parameters along with diastolic flow in umbilical artery doppler in patients with abnormal NST findings for a period of three days, following antenatal betamethasone and dexamethasone administration in nondiabetic pregnant women.

## SUBJECTS AND METHOD

**1. Study Design**

The design in this study is prospective observational cohort study. This study was conducted at the Department of Obstetrics & Gynaecology, Swaroop Rani Nehru Hospital, Moti Lal Nehru Medical College, Prayagraj (U.P.) from December 2020-August 2021.

**2. Population and Sample**

The design in this study is prospective observational cohort study. This study was conducted at the Department of Obstetrics & Gynaecology, Swaroop Rani Nehru Hospital, Moti Lal Nehru Medical College, Prayagraj (U.P.) from December 2020-August 2021.

**3. Study Variables**

The independent variables are Age, Gravidity, BMI while dependent variables are Postprandial blood sugar values, Daily Fetal Movement Count, Fetal Heart Rate, Non-Stress Test Parameters and Doppler Flow Velocimetry of Umbilical artery.

**Criteria for Selection of Cases-**

All antenatal women aged 20-40 years of GA between 28-39 weeks with live fetus.

**Criteria for Exclusion of Cases-**

All antenatal women with: Pre-Diagnosed

diabetes, Pre-existing adrenal or pancreatic dysfunction, Evidence of infection, Patients in active labor, Patients with chronic kidney disease, Those who required immediate termination of pregnancy.

**4. Operational Definition of Variables**

**Blood Sugar Values:** Baseline post prandial blood sugars were estimated before steroid administration and reassessed on day 2, 3 and 4. Blood sugar values >140mg/dl were considered as clinically significant hyperglycaemia.

**Daily Fetal Movement Counts:** Patients were instructed to count fetal movement starting from arbitrary time in the morning and continued for 12 hrs. Reduced fetal movement was considered as <10 in 12 hours.

**Non-Stress Test Parameters:** NST was recorded for fetal heart rate, variability, presence of acceleration or decelerations. Reactive: 2 or more accelerations of 15bpm persisting for 15 seconds in the span of 20 minutes.

**Non-reactive**: Baseline oscillation of less than 5 bpm and/or absent accelerations/ presence of decelerations in extended NST i.e., 40 mins to avoid false positivity because of fetal sleep cycles.Daily Fetal Movement Counts and NST were recorded on day 1, 2, 3 and 4 NST was done on the days of steroid administration.

**Doppler flow velocimetry** of umbilical artery to see the diastolic flow in the patients with abnormal NST findings.

**5. Study Instruments**

**Glucometer:** Capillary postprandial blood sugar values were recorded using glucometer.

**Cardiotocography:** Cardiotocography strips were interpreted visually.

**Ultrasound:** Pulse Wave Doppler after real-time colour flow localization of the umbilical artery.

**6. Data analysis**

Analysis was done using Statistical Package for Social Sciences (SPSS) v. 26.0 (IBM Inc., Armonk, NY, USA). Data were shown as mean± standard deviation or as number (percentage). Categorical variables were compared using the Chi-square or Fisher exact test. Between-group comparison of continuous variables was undertaken using T-test for parametric analysis. p-values were calculated and p values <0.05 were considered as statistically significant.

**7. Research Ethics**

This research was conducted after approval from institutional ethics committee and taking informed consent from the patients. During the conduct of study, confidentiality and safety of the patients were maintained.

## RESULTS

**1. Analysis Univariat**

Shows distribution of age groups, gravida and BMI which were comparable in both the groups with non-significant differences (with p value >0.05).

**Table 1. Distribution of Cases Based on Age & Body Mass Index**

| Variables | Group A | | | | Group B | | | |
|---|---|---|---|---|---|---|---|---|
| | Mean | SD | Min. | Max. | Mean | SD | Min. | Max. |
| **Age Groups** | | | | | | | | |
| <25 Years | 22.4 | 1.50 | 20 | 24 | 22.68 | 2.16 | 17 | 24 |
| 25-30 Years | 27.44 | 1.88 | 25 | 30 | 27.34 | 1.85 | 25 | 30 |
| >30 Years | 34.12 | 1.88 | 32 | 37 | 35.0 | 1.41 | 34 | 36 |
| **BMI(kg/m²)** | | | | | | | | |
| <24.9 | 22.05 | 1.88 | 18.5 | 24.5 | 21.56 | 2.02 | 18 | 24.5 |
| 25 – 29.9 | 27.19 | 1.79 | 25 | 29 | 26.78 | 1.18 | 25 | 28 |
| ≥30 | 31.0 | 0 | 31 | 31 | 30.85 | 1.06 | 30 | 32 |

**Tabel 2. Distribution of Case Based on Gravidity**

| Variable | Group A | | Group B | |
|---|---|---|---|---|
| | Frequency | Percentage | Frequency | Percentage |
| **Gravida** | | | | |
| Primi | 11 | 22 | 19 | 38 |
| 2 | 19 | 38 | 13 | 26 |
| 3 | 15 | 30 | 10 | 20 |
| 4 | 5 | 10 | 8 | 16 |

**2. Analysis Bivariat**

**a. Changes in Mean Blood Glucose Levels Following Betamethasone And Dexamethasone Administration**

As shown in Table 3, Mean Blood Glucose levels raised at 24 hrs and then gradually returned to baseline after 72 hrs. The rise in blood glucose was significantly more ($p < 0.05$) at 24 hrs that too more in group A after Betamethasone injection.

**Table 3. Changes in Mean Blood Glucose Levels Following Betamethasone And Dexamethasone Administration**

| Variables | Group A | | Group B | | p |
|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | |
| Baseline Blood Glucose (mg/dl) | 95.42 | 23.37 | 102.66 | 22.31 | 0.116 |
| Blood Glucose At 24 HRS (mg/dl) | 140.10 | 35.90 | 113.26 | 27.90 | <0.001 |
| Blood Glucose At 48 HRS (mg/dl) | 114.36 | 27.83 | 118.88 | 30.82 | 0.443 |
| Blood Glucose At 72 HRS (mg/dl) | 105.24 | 26.83 | 107.06 | 26.98 | 0.736 |

**Table 4. DFMC and FHR Following Betamethasone and Dexamethasone Administration at 24, 48, and 72**

| Variables | Group A (n=50) | | Group B (N=50) | | p |
|---|---|---|---|---|---|
| | Frequency | % | Frequency | % | |
| **DFMC** | | **At 24 Hours** | | | |
| Poor | 27 | 54.0 | 12 | 24.0 | 0.002 |
| Good | 23 | 46.0 | 38 | 76.0 | |
| | | **At 48 Hours** | | | |
| Poor | 10 | 20 | 5 | 10 | 0.161 |
| Good | 40 | 80 | 45 | 90 | |
| | | **At 72 Hours** | | | |
| Poor | 1 | 2 | 0 | 0 | 0.312 |
| Good | 49 | 98 | 50 | 50 | |
| **FHR** | | **At 24 Hours** | | | |
| Within Range (110-160/min) | 50 | 100 | 50 | 100 | <0.001 |
| Outside Range (<110 or >160/min) | 0 | 0 | 0 | 0 | |
| | | **At 48 Hours** | | | |
| Within Range(110-160/min) | 50 | 100 | 50 | 100 | <0.001 |
| Outside Range (<110 or >160/min) | 0 | 0 | 0 | 0 | |
| | | **At 72 Hours** | | | |
| Within Range(110-160/min) | 50 | 100 | 50 | 100 | <0.001 |
| Outside Range (<110 or >160/min) | 0 | 0 | 0 | 0 | |

**b. DFMC and FHR Following Betamethasone and Dexamethasone Administration at 24, 48, and 72 Hours.**

In both the groups DFMC was significantly adversely affected at 24 hrs ($p < 0.05$) that gradually recovered after 72 hrs. Poor DFMC was more common with Betamethasone than Dexamethasone; 54% vs 24%. Though FHR remained within range amongst all the patients in both the groups (Table 4).

**Table 5. NST parameters in Group A and Group B At 24, 48 and 72 Hours.**

| Variables | Group A (n=50) | | Group B (n=50) | | p |
|---|---|---|---|---|---|
| | Frequency | % | Frequency | % | |
| **NST** | | **At 24 Hours** | | | |
| Normal | 29 | 58 | 34 | 68 | 0.298 |
| Abnormal | 21 | 42 | 16 | 32 | |
| | | **At 48 Hours** | | | |
| Normal | 36 | 72 | 43 | 86 | 0.085 |
| Abnormal | 14 | 28 | 7 | 14 | |
| | | **At 72 Hours** | | | |
| Normal | 45 | 90 | 49 | 98 | 0.093 |
| Abnormal | 5 | 10 | 1 | 2 | |
| **Variability** | | **At 24 Hours** | | | |
| Present | 43 | 86.0 | 44 | 88.0 | 0.766 |
| Reduced | 7 | 14.0 | 6 | 12.0 | |
| | | **At 48 Hours** | | | |
| Present | 46 | 92 | 48 | 96 | 0.400 |
| Reduced | 4 | 8 | 2 | 4 | |
| | | **At 72 Hours** | | | |
| Present | 48 | 96 | 50 | 100 | 0.152 |
| Reduced | 2 | 4 | 0 | 0 | |
| **Acceleration** | | **At 24 Hours** | | | |
| Absent | 7 | 14.0 | 6 | 12.0 | 0.764 |
| Present | 43 | 86.0 | 44 | 88.0 | |
| | | **At 48 Hours** | | | |
| Absent | 5 | 10 | 3 | 6 | 0.459 |
| Present | 45 | 90 | 47 | 94 | |
| | | **At 72 Hours** | | | |
| Absent | 2 | 2 | 1 | 2 | 0.555 |
| Present | 49 | 98 | 49 | 98 | |
| **Deceleration** | | **At 24 Hours** | | | |
| No | 43 | 86.0 | 46 | 92.0 | 0.525 |
| Present | 7 | 14.0 | 4 | 8.0 | |
| | | **At 48 Hours** | | | |
| No | 45 | 90 | 48 | 96 | 0.238 |
| Present | 5 | 10 | 2 | 4 | |
| | | **At 72 Hours** | | | |
| No | 47 | 94 | 50 | 100 | 0.078 |
| Present | 3 | 6 | 0 | 0 | |

**c. NST parameters in Group A and Group B At 24, 48 and 72 Hours.**

Although majority of patients in both the groups had normal NST as shown in Table 5 but, though statistically non-significant (p >0.05), a major proportion showed abnormal NST at 24 hrs; 42% vs 32% and the abnormal NST recovered gradually with only 10% in group A vs 2% in group B. Again, the abnormality was greater in group A in terms of reduced variability, absence of acceleration n presence of deceleration, statistically non-significant differences were observed in both the groups at 24 hours showing gradual recovery by 72 hours. The proportion of abnormal findings were again more in group A.

**d. Doppler Flow Velocimetry of Umbilical Artery in Patients with Abnormal NST In Group A and Group B At 24, 48 And 72 hours.**

Among patients with abnormal NST findings, Table 6 shows Doppler flow velocimetry of the umbilical arteries at 24, 48 and 72 hours. In Group A, at 24 hours, 21 patients had abnormal NST findings, 14.3% had reduced diastolic flow in umbilical artery while 16 patients had abnormal NST findings, 6.25% had reduced diastolic flow in umbilical artery in Group B. Although none of the patients had reduced diastolic flow on doppler velocimetry at 72 hours in both the groups.

**Table 6. Doppler Flow Velocimetry of Umbilical Artery in Patients with Abnormal NST In Group A and Group B At 24, 48 And 72 hours.**

| Patients with Abnormal NST | Diastolic Flow in Umbilical Artery At 24 Hours | | Diastolic Flow in Umbilical Artery At 48 Hours | | Diastolic Flow in Umbilical Artery At 72 Hours | |
|---|---|---|---|---|---|---|
| **Group A (n=40)** | | | | | | |
| At 24hrs - 21 patients | Reduced (%) | Normal (%) | Reduced (%) | Normal (%) | Reduced (%) | Normal (%) |
| At 48hrs - 14 patients | | | | | | |
| At 72 hrs - 5 patients | 3 (14.3%) | 18 (85.7%) | 0 | 14 (100%) | 0 | 5 (100%) |
| **Group B (n=24)** | | | | | | |
| At 24hrs - 16 patients | Reduced (%) | Normal (%) | Reduced (%) | Normal (%) | Reduced (%) | Normal (%) |
| At 48hrs - 7 patients | | | | | | |
| At 72hrs - 1 patient | 1 (6.25%) | 15 (93.75%) | 0 | 7 (100%) | 0 | 1 (100%) |

**e. Line diagram showing blood glucose levels after Dexamethasone administration at 24, 48 and 72 hours.**

Figure 1 shows the rise in blood glucose levels (y-axis) of subjects (x-axis) receiving Dexamethasone (Group B). Line diagram of baseline blood glucose levels almost corresponded to levels after 72 hours although raised blood sugar values are observed following its administration at 24 and 48 hours.

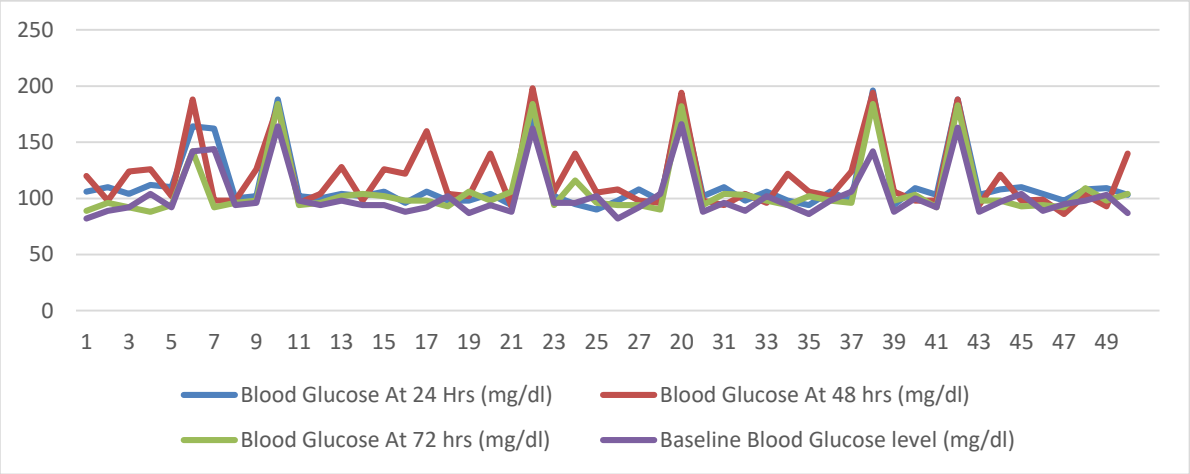


**Figure 1. Line Diagram showing Blood Glucose levels after Dexamethasone administration at 24, 48 and 72 Hours.**

**f. Line diagram showing blood glucose levels after Betamethasone administration at 24, 48 and 72 hours.**

Figure 2 shows the fluctuations in the blood glucose levels at 24, 48 and 72 hrs (y-axis) of subjects (x-axis) after Betamethasone administration (Group A). The line diagram of baseline blood glucose levels almost corresponded to levels at 72 hrs although the fluctuations at 24 hrs were more profound in Betamethasone group.

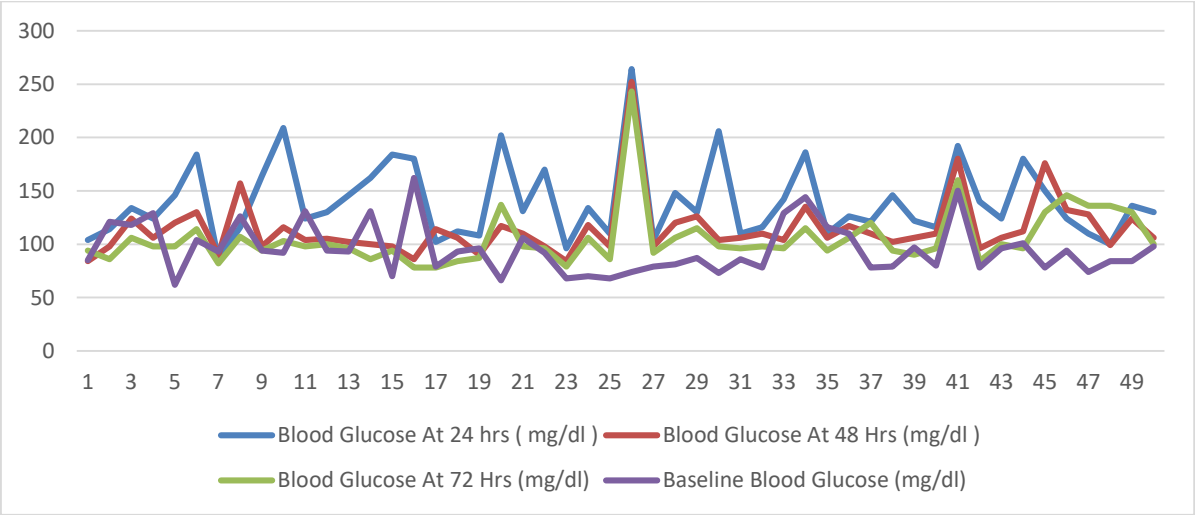


**Figure 2. Line Diagram showing Blood Glucose levels after Betamethasone administration at 24, 48 and 72 Hours.**

## DISCUSSION

Preterm delivery causes 7%-10% of complications and sometimes is the cause of permanent disability and death. The diabetogenic potential of steroids leads to transient hyperglycaemia on antenatal administration even in non-diabetic pregnant women because of additive effect on obvious insulin resistance caused by pregnancy. The period of persistence of hyperglycaemic state is dictated by the half-lives of these drugs; i.e. 11 hours for betamethasone, about twice as

long as 5.5 hours for dexamethasone (Tamez-Pérez, 2015).

In our study, since the distribution of demographic variables were comparable in both the groups, their effect on glucose tolerance were nullified and rise in blood sugar levels could be exclusively owed to corticosteroids administered. Raised blood sugar levels were demonstrated in significant proportion of patients after 24 hrs of steroid administration in both the groups but was more profound with betamethasone. The raised levels gradually reached to pre administration state after 72 hours.

A similar outcome of increase in maternal blood sugar values following antenatal steroid was noted with the study (Yun et al., 2012) following Dexamethasone administration. Although these levels normalized within 3-4 days, its clinical implication lies in the fact that screening women for GDM during the time span of 3-4 days after corticosteroid coverage may give false positivity. Secondly, maternal hyperglycemia may stimulate fetal pancreas to secrete more insulin in response to glucose excursion in fetus as a reflection of maternal hyperglycemia. So, preterm delivery within 3-4 days after steroid coverage puts additional risk for neonatal hypoglycaemia and warrants special care.

The effect of steroids on fetal movements, fetal heart rates and variability in NST is again a bothersome consequence creating a lot panic amongst patients as well as doctors and sometimes may also lead to unnecessary preterm deliveries. Poor fetal movements were significantly more frequent in betamethasone group because Betamethasone has been shown to induces more profound suppression of fetal breathing, limb and trunk movements, resulting in decreased biophysical profile scores. The findings of our study as well as other study conducted (Wahby et al., 2017), demonstrate that these fetal effects after steroid coverage are only transient and they need only a careful surveillance of the fetus till recovery that usually occurs after 24-48 hours. Additionally, these poor NSTs may be followed by a Doppler USG and Biophysical profile for more assurance.

Although both the steroids significantly lower the severity, frequency or both of respiratory distress syndrome, intracranial hemorrhage, necrotizing enterocolitis and death in preterm. Recommendations to choose dexamethasone over betamethasone is documented based on the fact that dexamethasone has better outcomes in reducing IVH, lesser rates of hyperglycemia, lesser disturbances of DFMC and NST, having been found none of the supply problems of betamethasone and is over 20 times cheaper per 24-mg course.('Committee Opinion No. 713: Antenatal Corticosteroid Therapy for Fetal Maturation', 2017)

We also observed the Doppler USG parameters of patients with reduced variability on NST, although the Doppler study can help differentiate fetal hypoxia from the corticosteroid-induced decreased BPP score, future studies are needed to confirm the role of Doppler velocimetry and prevent unnecessary preterm deliveries when the BPP score decreases after corticosteroid administration. Though we did not observe in our study, researchers have also shown improved maternal uterine artery, fetal MCA, descending aorta and umbilical artery blood flows, 24 h after Dexamethasone administration (Elwany et al., 2018) and the beneficial effect is consistent regardless of the gestational age and fetal weight.

Corticosteroid administration before anticipated preterm birth is one of the most important antenatal therapies available to improve newborn outcomes recommended for women at risk of preterm labour including those with ruptured membrane

and multiple gestations. Transient hyperglycemia and fetal depression may be observed in some cases requiring only a careful follow-up. Although, currently there is paucity of recommendations to follow after steroid administration as well as no standards of care exist for women having post steroid hyperglycemia, and no level of blood glucose is defined to warrant starting therapy; awareness of these drug-induced effects is essential to prevent over diagnosis of GDM, futile interventions and unnecessary iatrogenic delivery of preterm foetuses. Dexamethasone may be chosen over betamethasone as dexamethasone is found to be more cost effective, easily available and has less detrimental effects on fetus as compared to Betamethasone.

## AUTHOR CONTRIBUTION

Dr. Vidhi Singh collected the data. Dr. Amrita Chaurasia collaborated to analyze the data. All authors read and approved the final manuscript.

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## CONFLICT OF INTEREST

There is no conflict of interest in this study.

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