ORIGINAL RESEARCH

Study of Maternal Blood Glucose Levels and Blood Count after Betamethasone Therapy in Preterm Pregnancy

Shaziya Azmathulla[1], Nandini Gopalakrishna[2], Jessica Celilna Fernandes[3], Kogali Suresh Shrichetan[4]

Received on: 03 April 2023; *Accepted on:* 17 August 2023; *Published on:* 04 December 2023

Abstract

Background: Premature birth is one of the largest problems in obstetrics today and the most significant cause of neonatal morbidity and mortality. An important complication of preterm birth is respiratory distress syndrome. Corticosteroids to the mother will help in accelerating the fetal lungs maturity. This study was undertaken to evaluate the blood sugar changes and white cell count in the mother, respectively, following antenatal corticosteroids.

Objectives of the study: To evaluate changes in blood glucose levels, total leukocyte count, and differential count following betamethasone therapy in preterm labor.

Materials and methods: A prospective cohort study was performed in women at 28–34 weeks of gestation with preterm labor receiving betamethasone. Fasting and postprandial blood sugar glucose values were obtained on days 2, 4, and 6 after betamethasone therapy from the day of admission. Total count (TC) and differential count (DC) were also measured on day 2 and day 4 from the day of admission.

Results: In this study, FBS started rising from day 2 of betamethasone, with 93% having increased blood sugar. There was a significant change in FBS levels ($p < 0.001$) and PPBS levels (<0.001) following antenatal steroid therapy. Corticosteroid induced a significant neutrophilia and lymphocytopenia on day 2 following administration.

Conclusion: Betamethasone resulted in an acute rise in fasting blood sugar and postprandial blood sugar, and leukocytosis is expected to peak in 24 hours, and the magnitude is small.

Keywords: Betamethasone, Corticosteroids, Fasting blood glucose, Hyperglycemia, Postprandial blood glucose.

Journal of South Asian Federation of Obstetrics and Gynaecology (2023): 10.5005/jp-journals-10006-2355

Introduction

Preterm labor and birth are the leading explanation for perinatal mortality and morbidity.[1] The incidence of preterm labor is 6–15%. One of the most common complications with preterm birth is respiratory distress syndrome (RDS). It causes a significant burden on the economy throughout the world as it is expensive to look after premature babies.[2] Preterm birth can be defined as birth between the age of viability and 37 weeks of gestation. In many developed countries, and officially, records state all births with birth weight of more than 500 gm as viable. The period of viability varies in different countries from 20 to 28 weeks, depending on the facilities available for the newborn and the likelihood of survival. There is growing evidence that cervical insufficiency and infections play a serious role within the pathogenesis of spontaneous preterm labor.[3]

Preterm labor is known as a syndrome initiated by multiple mechanisms, including infection or inflammation, uteroplacental ischemia or hemorrhage, uterine overdistension, stress, and other immunologically mediated processes.[4]

One of the important antenatal therapies available to improve the neonatal outcome is corticosteroid administration before anticipation of preterm birth.[5] The greatest benefit was seen between 1 and 7 days after corticosteroid administration. Doubling the dose did not further improve the outcome, and there was no increased risk of infection for the mother or baby.[6] In the fetus, the most important role of corticosteroids is pulmonary maturation, thereby decreasing the risk of respiratory distress in premature infants. They also play a vital role in fetal brain development by initiating terminal neuronal maturation, remodeling of axons and dendrites, and affecting cell survival.[7,8] Other beneficial effects on other organs such as kidneys, liver, heart, adipose, and thyroid tissue all contribute to improving postnatal adaptation.[9,10]

The antenatal corticosteroids on initiation are known to increase white blood cells. Leukocytosis in healthy, noninfected pregnant women is anticipated to peak at 24 hours after administration, and the magnitude of increase is small.[11]

One of the main common side effects in pregnancy of steroids is the tendency to cause hyperglycemia. This is seen in patients with a history of gestational diabetes mellitus, family history of diabetes, abnormal fasting glucose, and impaired glucose tolerance.[12]

[1–4]Department of Obstetrics and Gynaecology, MS Ramaiah Medical College, Bengaluru, Karnataka, India

Corresponding Author: Nandini Gopalakrishna, Department of Obstetrics and Gynaecology, MS Ramaiah Medical College, Bengaluru, Karnataka, India, Phone: +91 9480059850, e-mail: nandinigopalakrishna@gmail.com

How to cite this article: Azmathulla S, Gopalakrishna N, Fernandes JC, *et al*. Study of Maternal Blood Glucose Levels and Blood Count after Betamethasone Therapy in Preterm Pregnancy. J South Asian Feder Obst Gynae 2023;15(6):675–678.

Source of support: Nil

Conflict of interest: None

Objectives

To evaluate changes in blood glucose levels, total leukocyte count, and differential count following betamethasone therapy in preterm labor.

Materials and Methods

This was a prospective study, approved by the Ethical Committee of MS Ramaiah Medical College. The objective of our study was to evaluate changes in the blood sugar levels, total leukocyte count, and differential count following betamethasone therapy in preterm labor. The participants were all antenatal women between 28 and 34 weeks of gestation judged to be at risk of preterm delivery and admitted at Ramaiah Hospital, Bengaluru, from November 2018 to May 2020.

The sample size was 73. All patients with singleton pregnancy, preterm premature rupture of membranes, and with preeclampsia were included.

The exclusion criteria were patients with diabetes on insulin therapy, GDM, those who were in active labor, those who had features of chorioamnionitis, features of sepsis, and those patients who were already on corticosteroids, beta-sympathomimetics, and preexisting adrenal or pancreatic dysfunction.

The data collection and the mode of sample collection were done after the patients fulfilled the criteria. It was a prospective cohort study that was conducted to estimate the changes in blood glucose levels, total count (TC), and differential count (DC) in antenatal women of 28–34 weeks of gestation admitted to Ramaiah Hospital with preterm labor. After the selection of the patient and taking the detailed maternal history, blood sugar levels, TC, and DC were done.

EDTA-K3 venous blood sample (3 mL) was collected from each subject, mixed gently, and was sent within 30 minutes of collection for laboratory investigation.

Total count (TC) and DC were performed as part of complete blood count between 28 and 34 weeks of gestation by automated blood cell counter Beckman Coulter.

Fasting and postprandial blood sugar were done by the hexokinase method. The first dose of betamethasone 12 mg intramuscularly was given, followed by a second dose of injection, betamethasone 12 mg intramuscularly was given after 24 hours of the first dose. Samples of fasting and postprandial blood sugar were done on days 2, 4, and 6 from the day of admission. Total count and DC were done on days 2 and 4 from the day of admission.

The statistical analysis was done by quantitative variables, which were summarized using descriptive statistics such as mean and standard deviation (min–max). The entire qualitative variable was presented using frequency and percentage. The mean comparison of blood sugar levels between the variable days will be compared using repeated measurement of ANOVA or Friedman's test. Chi-square test were used to find the association between categorical variables.

The following was considered as significance:

+ means (p value: $0.05 < p < 0.10$), *moderately significant (p value: $0.01 < p < 0.05$), **strongly significant (p value: $p < 0.001$). The statistical software, namely IBM SPSS Statistics 22, was used for the analysis of the data, and Microsoft word and excel have been used to generate graphs, tables, etc.

Table 1: Sugar values and mode of treatment following antenatal corticosteroids

	Days	*Median (Q1, Q3)*	*Min*	*Max*	*p-value*
FBS RBS	Day 0	89 (81, 106)	61	213	<0.0001
	Day 2	126 (120, 134)	77	250	
	Day 4	98 (94, 108)	79	138	
	Day 6	94 (90, 101)	74	120	
PPBS RBS	Day 0	89 (81, 104)	61	213	<0.0001
	Day 2	140 (130, 150)	88	262	
	Day 4	116 (104, 125)	88	168	
	Day 6	106 (98, 118)	82	189	

Results

Among the patients studied, 44% were between 26 and 30 years and 34% were between 18 and 25 years indicating that 78% were below 30 years. About 45% of the patients had a BMI of 25–29.9 kg/m^2. Primigravidae accounted for 47% and gravida 2 accounted for 33%.

In this study, 42% had threatened preterm and steroid was given, 32% had PPROM and steroid was given, and the remaining 26% received steroid and had a combination of the above complaints. All these patients received antenatal corticosteroids due to various causes. In 95% of the patients, the RBS was <140 mg%, and in 5%, it was between 140 and 200 mg%.

The TLC was between 4,000 and 11,000 in 42% of the patients and between 11,000 and 16,000 in 48% of the patients. In 3%, it was more than 20,000 cells/cumm.

In this study, on day 2, 55% had FBS of 121–140 mg/dL, 7% had FBS of 121–140 mg/dL on day 4, and none had high FBS on day 6. In this study, MNT was advised for patients whose FBS was >105 mg/dL and PPBS >120 mg/dL and <140 mg/dL. Insulin was started in those patients whose FBS >140 mg/dL.

The PPBS was between 140 and 200 mg/dL in 53% on day 2, and 8% had PPBS between 140 and 200 mg/dL on day 4. Only 3% had PPBS >200 mg/dL.

Following corticosteroids, 80% were euglycemic, 8% were started on MNT, and 12% were started on insulin.

In pregnancy, the main cause of preterm labor is genital tract infection, and hence, all the patients were started on antibiotics after sending the investigations.

p-value is < 0.0001 by Friedman test, which is significant.

We have used the Friedman test, which indicates that there is a significant difference over the time period, $p < 0.0001$.

The median value of FBS on day 2 was 126, which was increased from the day of admission, and on day 4, it decreased to 104%, and on day 6, it decreased to 94%.

We have used the Friedman test, which indicates that there is a significant difference over the time period, $p < 0.0001$.

The median value of PPBS on day 2 was 140, which was increased from the day of admission, and on day 4, it decreased to 116%, and on day 6, it decreased to 106%.

Thus, there was a significant increase in the FBS and PPBS levels following, antenatal steroid therapy.

In this study, among the 73 patients studied, 9 patients were started on insulin, and 6 patients were on MNT (Table 1).

p-value is < 0.0001 by Friedman test, which is significant.

We have used the Friedman test, which indicates that there is a significant difference over the time period, $p < 0.0001$.

Table 2: Final results of total leukocyte count

	Days	*Median (Q1, Q3)*	*Min*	*Max*	*p-value*
TLC	Day 0	11,700 (9,500, 14,000)	5,100	21,500	<0.0001
	Day 2	15,000 (12,100, 17,000)	6,800	23,400	
	Day 4	12,400 (10,500, 14,600)	4,900	20,600	

The median value of TLC on day 0 was 11,700, and on day 2, it increased to 15,000, and on day 4, it decreased to 12,400 (Table 2).

p-value is < 0.0001 by Friedman test which is significant.

We have used the Friedman test, which indicates that there is a significant difference over the time period, $p < 0.0001$.

The median value of neutrophils on day 0 was 74, and on day 2, it increased to 80, and on day 4, it decreased to 75.

The median value of lymphocytes on day 0 was 17, and on day 2, it decreased to 15, and on day 4, it was 18.

Discussion

Preterm labor and preterm birth are the leading causes of perinatal morbidity and mortality. The incidence of preterm labor is 5–10%. Antenatal steroids can be lifesaving in preterm babies and are commonly used in women who are at risk of preterm birth.[13]

Respiratory distress syndrome is the primary cause of early neonatal death. The use of steroids has enhanced pulmonary maturation and decreased the incidence of RDS. Steroids also decrease the incidence of intraventricular hemorrhage and necrotizing enterocolitis, thereby decreasing neonatal mortality.

Pregnancy is considered a diabetogenic state owing to the increased levels of human placental lactogen, cortisol, and other hormones. Hence, the impact of betamethasone on glucose values was a concern. In this study, we planned to analyze the degree of increase in FBS and PPBS following betamethasone therapy.

Administration of steroids increases the number of circulating white blood cells by causing leukocyte extravasation from bone marrow and decreasing the rate at which the cells are removed from the blood vessels. This physiologic response can pose a challenge if there is an associated infection causing leukocytosis. Our study aimed to know the degree of leukocytosis following corticosteroid administration and the time taken for the leukocyte to return to normal.[14–16]

In our study, booked patients were 53% and unbooked were 47%. The socioeconomic status of the majority of the patients was upper-middle and upper-lower according to Kuppuswamy classification. The mean age group in our study was 27.7 years ± 4.8 SD, which was similar to the study done by Sheldon et al.[15] and Star et al.[16]

The mean body mass index of the women in our study was 27.22, which was similar to the study by Langen et al.,[17] whereas Jolley et al. reported a mean BMI of 33.9 ± 7.1 SD.

In our study, 47% were primigravida, and 33% were gravida 2, which was similar to the study done by Renuka S et al. About 53% were between 32 and 34 weeks of gestation, whereas Renuka et al. reported 50% between 32 and 34 weeks of gestation.

In this study, the mean FBS was 127 ± 22 on day 2, decreased to 101 ± 11.8 on day 4, and it was 95.7 ± 9.2 on day 6. In the study done by Sheldon et al., the mean FBS was 108.5 ± 15.6 on day 2, decreased to 86.3 ± 10.5 on day 4, and it was 88 ± 12.6 on day 6.

In this study, FBS started rising from day 2, with 93% having increased values and reaching the normal range on day 3. On day 4, 64% had increased FBS and 43% continued to have increased FBS, which was similar to the study by Renuka S et al. In the study done by Lee et al.,[18] FBS and PPBS were elevated on day 2, then falling by days 4 and 5.

In this study, the mean PPBS was 142.7 ± 25.9 on day 2, decreased to 116 ± 16 on day 4, and it was 110 ± 19.4 on day 6. In the study done by Sheldon et al., the mean PPBS was 130.4 ± 29.8 on day 2, decreased to 111.7 ± 19.5 on day 4, and it was 119.6 ± 26.3 on day 6.

In our study, PPBS started rising from day 2 with 56% having increased sugar values and reaching normal range on day 3. On day 4, 8% had increased PPBS, and on day 6, 9% had increased PPBS.

In a study by Beena et al., 54% had increased PPBS on day 2, and on day 4, 21% had increased sugars, and on day 6, it was not recorded.

In this study, the baseline WBC was 11.84 ± 3.4 (cells/mm^3), increased to 14.83 on day 2, and it was 12.59 ± 3.2 on day 4. This was similar to a study done by Denison et al. and Wallace et al.[13,14] In a study done by Vaisbuch et al.,[15] baseline WBC was 10.2 ± 2.82, increased to 13.32 on day 2, and on day 4, it was 11.4 ± 3.2.[15]

Summary and Conclusion

Betamethasone therapy in preterm gestation has an impact on maternal glucose levels. The degree and duration of hyperglycemia will help us to know whether the patient has developed gestational diabetes or not following steroid therapy. Hence, monitoring the sugar values is important following corticosteroid therapy. Betamethasone-induced hyperglycemia was clinically significant and required treatment. In our study, 20% had hyperglycemia, of which 12% were started on insulin, and 8% were started on medical nutrition therapy (MNT).[19–21]

This study showed that betamethasone administration can cause transient rise in WBC with neutrophilia and lymphocytopenia. The extent and the duration of these changes may be useful in guiding the clinical management of women who receive betamethasone. The increase was apparent on day 1 and returned to normal on day 3. If the WBC count remained elevated beyond day 3, the patient has to be monitored for signs of infection. Following steroid therapy, the increase in WBC count is 3300 cells/cumm, and this should not be mistaken for infection.[22,23]

Ethical Clearance

This study was approved by the Ethical Committee of Ramaiah Medical College.

Acknowledgment

The author would like to thank MS Ramaiah Medical College and Hospital.

Orcid

Nandini Gopalakrishna https://orcid.org/0000-0003-0701-1928

References

1. Arias F, Bhinde AG. Practical guide to high-risk pregnancy and delivery, a south Asian perspective. Preterm Birth. 4th edition, India. Elsevier Publications; 2015. pp. 135–137.
2. Sharma JB. Textbook of obstetrics. Preterm Labour. 2nd edition. Avichal Publication Company; 2020.

3. Misra R. Ian Donald's – Practical Obstetric Problems. Preterm Birth. 7th edition; 2014. pp. 409–410.
4. Romero R, Dey SK, Fisher SJ. Preterm labor: One syndrome, many causes. Science; 2014;345(6198):760–765. DOI: 10.1126/science.1251816.
5. American College of Obstetricians and Gynecologists' Committee on Practice Bulletins—Obstetrics. Practice Bulletin No. 172: Premature rupture of membranes. Obstet Gynecol 2016;128(4):el65–el77. DOI: 10.1097/AOG.0000000000001712.
6. Howie RN, Liggins GC. The New Zealand study of antepartum glucocorticoid treatment in lung development. In: Farrell PM (ed.) Biological and Clinical Perspectives Vol II. Academic Press; 1982. pp. 255–265.
7. Yehuda R, Fairman KR, Meyer JS. Enhanced brain cell proliferation following early adrenalectomy in rats. J Neurochem 1989;53(1): 241–248. DOI: 10.1111/j.1471-4159.1989.tb07320.x.
8. Meyer JS. Early adrenalectomy stimulates subsequent growth and development of the rat brain. Exp Neural 1983;82(2):432–446. DOI: 10.1016/0014-4886(83)90415-6.
9. Harris A, Seckl J. Glucocorticoids, prenatal stress and the programming of disease. Horm Behav 2011;59(3):279–289. DOI: 10.1016/j.yhbeh.2010.06.007.
10. Kemp MW, Newnham JP, Challis JG, et al. The clinical use of corticosteroids in pregnancy. Hum Reprod Update 2016;22(2): 240–259. DOI: 10.1093/humupd/dmv047.
11. Bauer ME, Price LK, MacEachern MP, et al. Maternal leukocytosis after antenatal corticosteroid administration: A systematic review and meta-analysis. J Obstet Gynaecol 2017;38(2):210–216. DOI: 10.1080/01443615.2017.1342614.
12. Hwang JL, Weiss RE. Steroid-induced diabetes: A clinical and molecular approach to understanding and treatment. Diabetes Metab Res Rev 2014;30(2):96–102. DOI: 10.1002/dmrr.2486.
13. Denison FC, Elliott CL, Wallace EM. Dexamethasone-induced leukocytosis in pregnancy. Br J Obstet Gynaecol 1997;104(7):851–853. DOI: 10.1111/j.1471-0528.1997.tb12035.x.
14. Wallace EM, Ekkel K, Cotter T, et al. Hematological effects of betamethasone treatment in late pregnancy. Aust N Z J Obstet Gynecol 1998;38(4):396–398. DOI: 10.1111/j.1479-828x.1998.tb03095.x.
15. Vaisbuch E, Levy R, Hagay Z. The effect of betamethasone administration to pregnant women on maternal serum indicators of infection. J Perinat Med 2002;30(4):287–291. DOI: 10.1515/JPM.2002.041.
16. Diebel ND, Parsons MT, Spellacy WN. The effects of betamethasone on white blood cells during pregnancy with PPROM. J Perinat Med 1998;26(3):204–207. DOI: 10.1515/jpme.1998.26.3.204.
17. Langen ES, Kuperstock JL, Sung JF, et al. Maternal glucose response to betamethasone administration. Am J Perinatol 2015;30(2):143–148. DOI: 10.1055/s-0034-1376387.
18. Lee SE, Park JS, Norwitz ER, et al. Measurement of placental alpha-microglobulin-1 in cervicovaginal discharge to diagnose rupture of membranes. Obstet Gynecol 2007;109(3):634–640. DOI: 10.1097/01.AOG.0000252706.46734.0a.
19. Cunningham FG, Gant NF, Leveno KJ. Williams's Obstetrics, Preterm. 25th edition. United States: McGraw-Hill Education; 2018. pp. 803–809.
20. Gardosi J. Customized fetal growth standards: Rationale and clinical application. Semin Perinatol 2004;28(1):33–40. DOI: 10.1053/j.semperi.2003.12.002.
21. Liggins GC, Howie RN. A controlled trial of antepartum glucocorticoid treatment for prevention of the respiratory distress syndrome in premature infants. Pediatrics 1972:50(4);515–525. PMID: 4561295.
22. Sakonidou S, Dhaliwal J. The management of neonatal respiratory distress syndrome in preterm infants (European Consensus Guidelines–2013 update). Arch Dis Child Educ Pract Ed 2015;100(5): 257–259. DOI: 10.1136/archdischild-2014-306642.
23. Fernandes SF, D'Cunha RJ, D'Almeida J. A study on the effect of antenatal corticosteroids on glycemic response in preterm patients. J South Asian Federation Obstet Gynaecol 2022;14(2):148–151. DOI: 10.5005/jp-journals-10006-2016.