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Lamellar Body Count in Diabetic Pregnancies with Good Glycemic Control

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Abstract

Objective: To evaluate the influence of diabetes with strict glycemic control on fetal lung maturity in pregnancies by using lamellar body counts (LBC).

Methods: Twenty-two diabetic and 53 non-diabetic pregnant women were conducted to the study. The glucose levels were strictly controlled and kept within normal ranges in all the diabetic women. The mean LBC, the rate of low LBC, the rate of neonatal intensive care unit stay (ICU), the rate of respiratory need and the pregnancy outcome were compared between the diabetic and non-diabetic groups. LBC was accepted as low when it was fewer than 50,000/microl. The relation of low LBC with gestational age, presence of diabetes, administration of antenatal steroid, cord blood PH, base deficit, neonatal intensive care unit stay and need of respiratory support were analyzed.

Results: The mean age of women, characteristics of pregnancy and pregnancy outcome, antenatal corticosteroid administration rate, rate of neonatal intensive care unit stay and respiratory need were similar in the groups. The mean LBC and the rate of low LBC were also similar in the groups. There was no statistically significant relation between the risk of low LBC and the presence of diabetes, antenatal corticosteroid administration, cord blood PH, base deficit and need of respiratory support. The independent predictor of low LBC was found as the low gestational age (OR=0.693, 95% CI: 0.49-0.98, P=0.038). The relation of low LBC with the increased stay in neonatal intensive care unit became insignificant when its effect was analyzed together with the gestational age (OR=9.2; 95% CI: 0.947-88.95, p=0.056).

Conclusion: Lamellar body count, thus fetal lung maturity and the neonatal outcome was not altered in diabetic pregnancies with good glycemic control. The only independent predictor of low LBC was low gestational age.

Keywords: Lamellar body count, diabetes, lung maturity.

İyi glisemik kontrollü diyabetik gebelerde lamellar cisim sayımı

Amaç: Diyabetik gebelerde iyi glisemik kontrollün fetal akciğer matüritesi üzerine etkisini değerlendirmek.

Yöntem: Yirmi iki diyabetik ve 53 non-diyabetik gebe kadın prospektif olarak çalışmaya alındı. Tüm diyabetik olgularda sıkı glisemik kontrol yapıldı ve kapiller kan glikoz düzeyleri normal aralıklarda tutuldu. Ortalama lamellar cisim sayısı, düşük lamellar cisim sayısı oranları, yenidoğan yoğun bakım ihtiyacı oranları, ventilatör desteği ihtiyacı oranları ve gebelik ve neonatal sonuçlar diyabetik ve non-diyabetik gebeler arasında karşılaştırıldı. Lamellar cisim sayısı 50,000/microl'nin altında olan değerler "düşük lamellar cisim sayısı" olarak kabul edildi. Düşük lamellar cisim sayısı ile gebelik haftası, diyabet varlığı, antenatal kortikosteroid uygulanması, kord kanı pH, kord kanı baz açığı, yenidoğan yoğun bakım ihtiyacı ve ventilatör ihtiyacı arasındaki ilişki incelendi.

Bulgular: Olguların yaş ortalamaları, gebelik özellikleri ve gebelik sonuçları, antenatal kortikosteroid uygulanma oranları, yenidoğan yoğun bakım ihtiyacı oranları ve ventilatör desteği ihtiyacı oranları iki grupta benzerdi. Düşük lamellar cisim sayısı ile diyabet varlığı, antenatal kortikosteroid uygulanması, kord kanı pH ve kord kanı baz açığı ve solunum desteği arasında istatistiksel olarak anlamlı bir ilişki bulunmadı. Düşük lamellar cisim sayısı ile gebelik haftası arasında anlamlı bağımsız bir ilişki izlendi (OR=0.693, %95 CI: 0.49-0.98, P=0.038). Artmış düşük lamellar cisim sayısı riski ile artmış yenidoğan yoğun bakım ihtiyacı arasında anlamlı bir ilişki tespit edildi, ancak bu ilişkinin gebelik haftası ile birlikte incelendiğinde önemsizleştiği izlendi (OR=9.2; %95 CI: 0.947-88.95, p=0.056).

Sonuç: Bu çalışmada iyi glisemik kontrol yapılan gebelerde lamellar cisim sayısının, dolayısıyla fetal akciğer matüritesi ve neonatal sonuçların değişmediği bulundu. Bu olgularda düşük lamellar cisim sayısınınn sadece gebelik haftası ile ilişkili olduğu saptandı.

Anahtar Sözcükler: Lamellar cisim sayısı, diyabet, akciğer maturasyonu.

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Introduction

Diabetes mellitus with unfavorable maternal and fetal outcomes, is the most important endocrinology-metabolic disorder that can complicate pregnancy. The most important complications of diabetes in pregnancy are macrosomia (27%), prematurity (21%) and perinatal mortality (2.7%).[1] In a study of high risk pregnancies the rate of Respiratory Distress Syndrome (RDS) was found as 44.2% of which 17.4% belonged to diabetic pregnancies.[2] After Gluck and Kulovich showed that the diabetes delayed fetal lung maturation, the timing of delivery became an important problem in the management of pregnant women with diabetes.[3,4] Therefore in diabetic pregnancies, to determine the timing of delivery, biochemical evaluation of the fetal lung maturity became the main clinical management, especially when the gestational age cannot be determined.

To determine the fetal lung maturity several biochemical tests like lecithin/sphingomyelin ratio,[3] phosphatidyl glycerol,[4] foam stability test,[5] OD650[7] and lamellar body count (LBC)[8] can be used. The accuracy of lecithin/sphingomyelin or phosphatidyl glycerol in determining fetal lung maturity is high.[9,10] However these tests are technically complex and costly tests and therefore cannot be performed in most of the centers. LBC has cost advantage and technically simple that can be performed by all the centers that can do the cell counting.[11] In addition LBC was shown as accurate as the commercial phospholipid analysis in predicting the fetal lung maturity.

The aim of the current study is to determine the impact of diabetes on fetal lung maturity in diabetic pregnancies with good glycemic control compared to non-diabetic pregnancies, via lamellar body count in amniotic fluid.

Methods

Between the dates January 2010 and September 2010, diabetic pregnant women treated and followed-up in the Obstetrics and Gynecology and Endocrinology clinics of Inonu University School of Medicine were conducted prospectively to our case control cohort study without randomization. Healthy pregnant women with no medical condition who were followed-up for antenatal care by the obstetrics policlinic were conducted to the study as the control group. A power analysis was performed by using the data reported in the publications and necessary sample size in each group was found as 22 when the desired significance level was set at .05 (α) and power was set at 0.8 (1-β). Therefore 22 and 53 cases were enrolled to diabetic and non-diabetic groups, respectively.

Blood glucose levels of diabetic pregnant women were measured via a capillary blood glucose monitorization system (glycometer). To meet the desired glycemic goals, cases were treated with either case specific diabetic diet or insulin when the diabetic diet was not sufficient. The treatment goal were to meet the capillary blood glucose levels of ≤95 mg/dl on fasting, ≤120 mg/dl on 2nd hour postprandial and >60 mg/dl (3.3 mmol/l) on all occasions.[13] Therefore a good glycemic control was accomplished with keeping the glucose levels within the objective ranges.

From each case a 2 ml of amniotic fluid and 1 ml of cord blood was collected to EDTA containing test tube and heparin washed syringe, respectively. Amniotic fluid was collected with a syringe before amniotic membrane was ruptured to prevent blood contamination. Amniotic fluid samples were analyzed without centrifugation with a cell counter (Coulter LH 780 Hematolgoy Analyzer, Beckman, CA-USA) for platelet number and therefore for the LBC. Cord blood was analyzed with a blood gas analyzer ((Rapidlab 348, Siemens, Deerfield-USA) for pH and base deficit. All of the newborns were examined by a pediatrician and were hospitalized to neonatal intensive care unit if needed. The cut off value of LBC in predicting fetal lung maturity was found as ≥50,000 /microl in recent studies.[1] Therefore we accepted the LBC values under 50,000 /microl as "low LBC".

The mean maternal age, gestational age, gravidity (G), parity (P), abortus (A), live (L), rate of corticosteroid administration, mean LBC, rate of low LBC, mean birth weight, need for neonatal intensive care unit stay, need for ventilator support, mean cord blood pH and mean base deficit were compared between the diabetic and non-diabetic groups. In all cases the relation of the low LBC with gestational age, presence of gestational diabetes mellitus, administration of antenatal steroid, cord blood PH, base deficit, neonatal

intensive care unit stay, need of respiratory support were analyzed.

Statistical Analysis

The data was analyzed using the Statistical Package for Social Sciences soft-ware 15.0 (SPSS, Inc., Chicago, IL, USA). The mean values were compared with the Mann Whitney-U test and the rates were compared with the Pearson chi-square test. Binomial regression analysis was conducted to find out the relation of low lamellar body count with gestational age, presence of gestational diabetes mellitus, administration of antenatal steroid, cord blood PH, base deficit, neonatal intensive care unit stay, need of respiratory support. The related factors were re-analyzed in multinomial regression analyses to find out the independently related factor.

Results

The mean age of women, characteristics of pregnancy and pregnancy outcome other than birth weight, antenatal corticosteroid administration rate, rate of neonatal intensive care unit stay and respiratory need were similar in the diabetic and non-diabetic groups. The mean birth weight was significantly greater in diabetic group compared to non-diabetic group (3005.9±589.1 gr and 2625.3±720.9 gr, P=0.023). The mean LBC and the rate of low LBC were similar in the diabetic and non-diabetic groups (Table 1). We did not find a significant relation between the risk of low LBC and the presence of diabetes, antenatal corticosteroid administration, cord blood pH, base deficit and need of respiratory support. The risk of low LBC decreased with increasing gestational week (OR=0.597; 95% CI: 0.443-0.806, p=0.001). The low LBC was also related with the increased stay in neonatal intensive care unit (OR=30.2; 95% CI: 3.7-246.8, P=0.001). However the relation of the latter became insignificant when its effect was analyzed together with the gestational age, in the multinomial regression analysis (OR=9.2; 95% CI: 0.947-88.95, p=0.056). The independent predictor of low LBC was found as the low gestational age (OR=0.693, 95% CI: 0.49-0.98, P=0.038).

Discussion

In our study, we found that LBC, low LBC ratio and neonatal results were similar in diabetic patients with good glycemic control and normal control subjects. Although the mean gestational age was similar to non-diabetic group and the fasting and postprandial blood glucose levels were kept below the cut off levels, the mean birth weight was significantly greater in diabetic group compared to non-diabetic group. However none of the cases had birth weight greater than 90th percentile according to the gestational age. In our

Table 1. Characteristics of pregnancy and pregnancy outcome.

	Diabetics (n=22)	Non-diabetics (n=53)	P
Age (year)	32.6±6.1	30.3±6.2	0.148
G	3.1±2.4	2.8±1.8	0.881
P	1.7±1.9	1.4±1.4	1
A	0.5±0.9	0.3±0.7	0.388
Live	1.3±1.6	1.4±1.4	0.389
Gestational age (week)	37.0±2.2	36.2±3.4	0.431
Corticosteroid administration rate (%)	13.6	17	0.719
LBC microl.	67,140±54,412	67,720±58,384	0.705
Low LBC rate (%)	59.1	54.7	0.728
Birth weight (gr)	3005.9±589.1	2625.3±720.9	0.023
Cord blood PH	7.28±0.08	7.32±0.07	0.067
Cord bloodbase deficit	-4.7±5.2	-5.2±3	0.518
Neonatal intensive care unit stay (%)	27.3	17	0.310
Respiratory need (%)	4.6	7.6	0.635

Data is given in mean±standard deviation or percentage.

clinic fasting blood glucose levels are kept at or below 95 mg/dl and postprandial 2nd hour blood glucose level are kept at or below 120 mg/dl. However HAPO study found the fetal weight and macrosomia risk increased with increasing blood glucose levels even for the levels below the cut off values.[14] Therefore the finding of us and HAPO study support the need of a re-evaluation of cut off values for blood glucose levels in diabetic pregnancies with further studies.

It is known that diabetes mellitus can worsen neonatal results, delay fetal lung maturation and increase RDS risk.[3 4,15,16] However it was previously shown that the increase in risk was due to high maternal glucose level and in diabetic pregnant women with good glycemic control the perinatal and neonatal risks were similar to non-diabetic pregnant women.[17] High RDS incidence in diabetic pregnancies was shown to be decreased with advanced neonatal care, accurate calculation of fetal age with early fetal ultrasonography and good glycemic control.[18] It was found that, especially good glycemic control in diabetic patients equalized the RDS frequency with normal pregnancies.[19] However fetal lung maturation can delay in diabetic pregnancies with bad glycemic control.[20]

Lamellar body count became popular because of its technical ease, low cost, fast result, and accurate prediction of fetal lung maturity.[11] However in different studies different cut-off values were used to determine fetal lung maturity. Although in Dubin et al.'s study it was shown that the fetal lung was mature for LBC >26,000/microl, Lewis et al. found that LBC >32,000/microl predicted a mature L/S ratio and PG levels in 99% of cases.[8,11] The reason of different cut-off values may be different cell counting devices used in these studies. Askwod et al. documented in 1993 that in a series of 247 cases whose LBC were higher than 48,000/microl none of infants developed RDS.[21] Also in recent studies the fetal lung was assumed as mature, in pregnancies with amniotic fluid LBC more than 50,000/microl.[1] Because of these recent literatures we took 50,000/microl as cut-off value for our study.

In our study we found that low LBC ratio was found similar both in diabetic and non-diabetic pregnant women. We found the low LBC risk increased with the decreasing gestational week and was related to increased neonatal intensive care unit stay. However when the data was controlled for the gestational age, the relation between the low LBC and the neonatal intensive care unit stay disappeared. Also no relationship was found between low LBC risk and the presence or absence of diabetes in both diabetic patients with good glycemic control and non diabetic patients. This finding proved that the need for neonatal intensive care unit was related to the deceasing gestational age and showed that the fetal lung maturity in diabetics with good glycemic control was similar to non-diabetics. Gluck et al. also showed that the fetal lung maturity occurred in similar gestational ages in diabetic pregnants with good glycemic control and non-diabetic pregnants.[3]

Conclusion

In the current study lamellar body count, thus fetal lung maturity and the neonatal outcome was found not altered in diabetic pregnancies with good glycemic control. The only independent predictor of low LBC was low gestational age. With concordance to prior literature adequate glucose control seems to lower the risk of fetal pulmonary immaturity to that seen in the non-diabetic population. With the current data, in euglycemic, metabolically controlled diabetic patients fetal lung maturation is not delayed and therefore routine fetal lung maturation testing might be abandoned in term pregnancies of diabetic mothers.

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