Correlation between Amniotic Fluid Optical Density (AFOD) and functional maturity status of the newborn at caesarean delivery in GDM.

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Abstract:

Objective: To observe the correlation between Amniotic Fluid Optical Density (AFOD) and functional maturity status of the newborn at caesarean delivery in 16 women with Gestational Diabetes Mellitus (GDM). Methods: Amniotic Fluid (A.F) samples were collected while doing caesarean sections around 38+wks CRL gestation. Uncentrifuged fresh AF samples were used for AFOD estimations with colorimeter at 650nm. HbA1c estimations were done for all women just before caesarean sections. These women received antenatal steroids as per the RCOG guidelines¹. Babies were evaluated for functional maturity status in terms of APGAR scores, development of RDS after 5mnts, adherence of vernix on skin surface, and color of the skin. Birth weights were recorded by electronic weighing machine. **Results:** Fourteen of these 16 women, were observed to have mature AFOD values (0.98±0.27), at different gestational ages (GA) ranging from 36w+6d to $39w+6d^{2,3}$. Twelve of these 14 women had good glycemic control with HbA1c values between 5.1 and 5.6.Two women had poor glycemic control with HbA1c values 7.0 and 7.1. All these babies were fully functionally mature, and their skin was mature pale brown in color with very little vernix, and none of them developed RDS. Birth weights ranged from 2.6kg to 3.9kgs. Two women had premature AFOD values (<0.40)^{2, 3}at 36w+6d and 40wks gestation. Their glycemic control was good with HbA1c values 5.4 and 5.6 respectively. Both these babies had plenty of vernix caseosa on skin surface, and developed severe RDS with in 5mnts after delivery which required invasive and noninvasive ventilation support and surfactant therapy. Conclusion: The concept of 'individual term for each fetus⁴ is also applicable in women with GDM. AFOD value 0.98 ± 0.27 assures functionally mature babies who do not develop RDS irrespective of GA and glycemic control. Babies born with AFOD values<0.40 are functionallypremature irrespective of GA and arelikely to develop RDS which may require ventilator support.

Key Words: Individual term for each fetus, Amniotic fluid optical density (AFOD), Gestational diabetes mellitus (GDM)

I. Introduction

The incidence of GDM is progressively increasing in proportion to the increasing global burden of GDM. This problem is growing in alarming proportions necessitating universal screening in south Asian countries like India⁵. Results from Amniotic Fluid Optical Density (AFOD) research indicate, fetuses attain completion of functional maturity at AFOD value 0.98 ± 0.28 , and go in for spontaneous labor at any time from 35w+d to 42w+d, indicating individual term for each fetus²,³,⁴. Babies can be functionally fully mature even at 35w+d gestation if AFOD value is 0.98 ± 0.28 . On the other hand babies can be functionally premature and develop RDS even at 40wks if AFOD value $<0.40^{2, 3, 6}$. Even in cases of GDM, it is not an uncommon observation to observe, few babies born around 37wks do not develop RDS, and few babies born even around 40wks develop severe RDS which may require ventilator support. Decision making regarding the time of delivery in pregnancies with GDM is a balancing act between unheralded fetal death on one side, and functional prematurity and development of RDS on the other side. Even though amniotic fluid L/S ratio estimation is the gold standard for lung maturity assessment, it is costly, cumbersome, time taking, and not available in every setting, and not being done regularly by everybody. On the other hand AFOD estimation is cheap, easily available in any setting, and the results can be obtained within few minutes and helps to make quick decisions. In this study we attempted to

explore the possibility of utilizing mature AFOD values for decision making regarding the time of delivery in pregnancies with GDM.

II. Methods

Sixteen singleton pregnant women with GDM who underwent first trimester scan for CRL gestational age estimation, and who underwent caesarean sections at around 38wks gestation as per the NICE guide lines⁷ and also for other different indications were included in this study. Informed and written consent was obtained from all subjects who participated in this study. This study confirms to standards of declarations of Helsinki. While doing cesarean section careful hysterotomy was performed avoiding injury to bulging membranes. With 2ml disposable syringe fitted with 2.5 cm long 23 G needle, the membrane was pierced and the AF sample was drawn. Blood stained and meconium stained AF samples were excluded from study. Un-centrifuged fresh AF samples were used for AFOD estimation by colorimeter at 650nm wave length. These women received antenatal steroidsas per the RCOG guidelines¹.

III. Method of measuring AFOD

The colorimeter was set 650 nm wave-lengths. The test tube containing distilled water (control solution) was inserted in to the cuvette holder of the machine and '0' reading was adjusted. Then the test tube containing fresh uncentrifuged A.F sample was inserted, and with a press of a button, the AFOD value was directly read from the display screen of the machine.HbA1c estimations were done for all women just before caesarean sections. APGAR scores were recorded at 1mts and at 5mts. Babies were observed for functional maturity status in terms of RDS after five minutes of birth, and adherence of vernix caseosa on skin surface, and color of the skin. Birth weights were recorded by electronic weighing machine.The details of gestational age at delivery, AFOD values, HbA1c values, APGAR scores, birth weights, color of the skin, and development of RDS in each subject are shown in Table.1

IV. Results

Among these sixteen women, 14 women with case numbers 1 to 14 in table.1 had mature AFOD values (0.98 ± 0.27) . These mature AFOD valueswere observed at caesarean sections done at different gestational ages ranging from 36w+6d to 39w+6d. Birth weights ranged from 2.6kg to 3.9kg. Among these 14 women, 12 women (case numbers 1 to 12) had HbA1c values ranging from 5.1 to 5.6, and in two women (case numbers 13 and 14) the values were 7.1 and 7.0.All these babies were fully functionally mature with Apgar score 9 at 1mnt and at 5mnts, and none of them developed RDS. Their skin was mature pale brown in color with very little or no vernix caceosa adherent on their skin surface.

Two women, case numbers 15 and 16 had premature AFOD values (<0.40). In case number 15, the G.A at delivery was 40wks, the AFOD value was 0.33, and the HbA1c value was 5.6 and the birth weight was 3.3kg. There was plenty of vernix caseosa on skin surface. We didnot administer antenatal steroids for this woman as the pregnancy prolonged beyond 39wks. This baby developed severe RDS within 5mts after delivery, but responded well for oxygen supplementation by noninvasive ventilation for 3hour.

In case number 16, the G.A at delivery was 36w+6d, the AFOD value was 0.11, and the HbA1c value was 5.4 and the birth weight was 2.7kg. She received two courses of antenatal steroids for recurrent pretern labor at 33w+5d and at 35w+3d. The second course was given 10 days before caesarean delivery. This baby was functionally premature with plenty of vernix caseosa on skin surface. The skin was thin premature pink in color, and developed severe RDS with in 5mnts after delivery which required multiple doses of surfactant, and invasive and noninvasive ventilator support for 5days (Fig.1).

Table: 1. Details of GA at delivery, AFOD values, HbA1c values, APGAR scores, development of RDS, birth weights, skin color, and vernix on skin surface in each subject.

| Case | ; | | HbA1c | APGA | AR at | | Birth wt | | Vernix on |
|------|--------|------|-------------|------|-------|-----|----------|------------------|--------------|
| No | G.A | AFOD | before LSCS | 1mnt | 5mnt | RDS | Kg | Skin colors | skin surface |
| 1 | 37w+5d | 0.99 | 5.4 | 9 | 9 | Nil | 3.2 | mature pale brow | n nil |
| 2 | 38w+5d | 0.94 | 5.2 | 9 | 9 | Nil | 3.0 | mature pale brow | n nil |
| 3 | 38w+1d | 1.02 | 5.4 | 9 | 9 | Nil | 2.9 | mature pale brow | 'n nil |
| 4 | 37w+4d | 1.20 | 5.3 | 9 | 9 | Nil | 3.8 | mature pale brow | n nil |
| 5 | 38w+6d | 1.19 | 5.2 | 9 | 9 | Nil | 3.2 | mature pale brow | n nil |
| 6 | 38w+0d | 0.95 | 5.5 | 9 | 9 | Nil | 2.8 | mature pale brow | 'n nil |
| 7 | 36w+6d | 1.02 | 5.3 | 9 | 9 | Nil | 2.6 | mature pale brow | n nil |
| 8 | 37w+2d | 0.81 | 5.1 | 9 | 9 | Nil | 2.7 | mature pale brow | n nil |
| 9 | 38w+2d | 1.29 | 5.5 | 9 | 9 | Nil | 3.1 | mature pale brow | n nil |
| 10 | 37w+6d | 1.00 | 5.2 | 9 | 9 | Nil | 2.5 | mature pale brow | n nil |

Correlation between Amniotic Fluid Optical Density (AFOD) and functional maturity status of the

| 1.1 | 27 (1 | 0.05 | F (| Ō | 0 | N.T.1 | 2.0 | | .1 |
|-----|--------|------|------------|---|---|---------|------|-------------------|--------|
| 11 | 3/w+6d | 0.95 | 5.6 | 9 | 9 | N1l | 2.8 | mature pale brown | n11 |
| 12 | 37w+5d | 1.90 | 5.4 | 9 | 9 | Nil | 2.85 | mature pale brown | nil |
| 13 | 39w+6d | 1.33 | 7.1 | 9 | 9 | Nil | 3.9 | mature pale brown | nil |
| 14 | 39w+3d | 1.20 | 7.0 | 9 | 9 | Nil | 3.9 | mature pale brown | nil |
| 15 | 40w+0d | 0.33 | 5.6 | 9 | 6 | present | 3.33 | premature pink | plenty |
| 16 | 36w+6d | 0.11 | 5.4 | 9 | 6 | present | 2.70 | premature pink | plenty |



AFOD 0.11At 36wks GA, Birth wt. 2.6 KGFig.1: Newborn baby of a mother with GDM at 36w+6d GA (Case No.16). Functionally premature baby with
plenty of vernix and with severe RDS. AFOD value was 0.11 (left). Baby was on bubble CPAP (Continuous
Positive Airway Pressure) on third post natal day in NICU (right).

V. Discussion

S. Ram.et.al reported, fetuses attain completion of functional maturity at AFOD value around 0.98, and go in for spontaneous labor at any time from 35w+d to 42w+d, indicating individual term for each fetus. Babies born with AFOD value <0.40 were functionally premature and develop varying degrees of RDS irrespective of GA and birth weight^{8, 2, 3}. Babies can be functionally fully mature even at 35w+d gestation if AFOD value is 0.98 ± 0.28 . On the other hand babies can be functionally premature and develop RDS even at 40wks if AFOD value < $0.40^{2,3}$.

In this study of sixteen women, 14 women with case numbers 1to 14 had mature AFOD values (0.98 ± 0.28) , at different gestational ages ranging from 36w+4d to 39w+6d. All these babies were fully functionally mature, and none of them developed RDS. It appears that, the concept of 'individual term for each fetus' is also applicable to women with GDM^{4, 8}.

Among these 14 women, 12 women (case numbers 1 to 12) had well controlled GDM with HbA1c values ranging from 5.1 to 5.6. In two women, case numbers 13 and 14, glycaemia was not under good control with HbA1c values 7.1 and 7.0. Their G.A at delivery was 39w+6d and 39w+3d, and their AFOD values were 1.33 and 1.20 respectively. Both these babies were fully functionally mature and did not develop RDS. It appears that mature AFOD values assure functionally mature babies even in not well controlled GDM. This scientific information is having very much importance in the management of GDM.

In case numbers 15 and 16, the G.A at delivery was 40wks and 36w+6d, and their glycemic control was very good with HbA1c values 5.6 and 5.4 respectively. The AFOD values were 0.33 and 0.11, and their birth weights were 3.3 and 2.7kgs respectively. Both these babies had plenty of vernix caseosa on their skin surface and they developed severe RDS with in 5mnts after delivery. These results indicate that, irrespective of birth weights, GA at delivery, and even with good glycemic control, if babies born with AFOD values <0.40 are functionally premature and develop RDS.

In case number 15 we didn't administer antenatal steroids as the pregnancy was prolonged beyond 39wks as per the RCOG guidelines¹. This baby had plenty of vernix caseosa on skin surface and developed severe RDS within 5mts after delivery, but responded well for oxygen supplementation by noninvasive ventilation for 3hour. It appears that, as the AFOD value in this case was very close to the mark of 0.40, this baby responded well for simple measure of oxygen supplementation and other supportive measures.

The woman with case number 16 received two courses of antenatal steroids for recurrent preterm labor at 33w+5d and at 35w+3d. The second course was given 10 days before caesarean delivery. In spite of two courses antenatal steroids, this baby was functionally premature with plenty of vernix caseosa on skin surface, and developed severe RDS by 5mnts which required multiple doses of surfactant, and invasive and noninvasive ventilator support for 5days (Fig.1). Very low AFOD value (0.11) in this woman could be the reason for severe RDS which required all these treatment measures.

ACOG guidelines recommend the AFOD value > 0.15 of a centrifuged amniotic fluid sample to confirm lung maturity^{9,10}. Uncentrifuzed fresh AF sample with AFOD value around 0.40, when centrifuged at 2000 rpm for 10mnts give a value of 0.15^{11} . In other words an uncentrifuzed AFOD value > 0.40 indicate completion of lung maturity. Skin is the last organ to mature which is associated with rapid shedding of vernix from fetal skin surface in to AF which results in rapid surge like rise in amniotic fluid optical density ^{12, 13, and4}. The onset of spontaneous labor takes place at AFOD value around 0.98. In other words the AFOD value 0.98 can also be considered as a mark for completion of skin maturity. Between lung maturity and skin maturity, there is a period of 8 to 10 days, during which time preparations in cervix uterus and vaginatake place for the onset of spontaneous labor⁴.

NICE guidelines recommend, 'pregnant women with diabetes who have a normally grown fetus should be offered elective birth through induction of labor, or by elective caesarean section if indicated, after 38 completed weeks'⁷. This recommendation is made to prevent unheralded fetal deaths in GDM.

Based on the above scientific information, it is advisable to perform simpler AFOD estimation at around 38wks, instead of gold standard L/S ratio estimation which is costly, cumbersome, time taking and not available in every setting. This simple test helps to assess the functional maturity status of the fetus and also gives an idea about the number days further needed to attain the mature AFOD value of $0.98+/-0.27^4$. This information also helps to avoid indefinite waiting for the onset of spontaneous labor which may result in postmaturity, dysmaturity and unpredictable fetal deaths⁴. With mature AFOD value babies can be delivered without any further delay. In case of imminent labor with very low AFOD value like 0.11, the women can be shifted to a higher medical center.

VI. Conclusion:

The concept of individual term for each fetus is also applicable in women with GDM. AFOD value around 0.98 assures functionally mature babies who do not develop RDS irrespective of glycemic control. AFOD estimation around 38wks in GDM helps to assess the functional maturity status of the fetus and also gives an idea about the number days further needed to attain the mature AFOD value of 0.98+/-0.27. This avoids unnecessary indefinite waiting for the onset of spontaneous labor which helps to prevent unpredictable fetal deaths. Babies born with very low AFOD value like 0.11 are likely to develop severe RDS which may require ventilator support irrespective of GA and glycemic control. AFOD estimation is cheap, easily available in any setting, and the results can be obtained within few minutes, and helps to make quick decisions when compared to L/S ratio estimation. As this is a small study, these results should be further evaluated by multicentrec studies with larger sample size.

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