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Relation between dehydroepiandrosterone sulfate (DHEA-S) and success of labour induction in prolonged gestation

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ABSTRACT

Objective: To evaluate the relationship between maternal Dehydroepiandrosterone sulphate (DHEA-S) and success of labour induction in prolonged gestation. **Methods:** Fifty (50) women with a prolonged pregnancy > 41 weeks were included in the prospective study. After full history, examination, Bishop's score was recorded by two observers, followed by ultrasound scan and cardiotocography (CTG) to assess foetal condition. Ten (10) mL of venous blood was taken for measuring plasma DHEA-S level before induction of labour. Induction of labour was carried out by Misoprostol 25 µg vaginal suppository every 4 hours for 6 doses maximally. Patients in the first, second and third stages of labour were managed according to Ain Shams University Maternity Hospital protocol. The outcome measures, success of labour induction, relation between both DHEA-S and Bishop's score and the success of labour induction. **Results:** In this study, there was no significant difference between the group of failed induction and group of successful induction regarding the mean age, mean body mass index (BMI), mean parity, mean birth weight, and mean Apgar score at 5 minutes. The mean serum DHEA-S was significantly higher in successful induction group compared to failed induction group (106.2±10.3 versus 44.7±16.3 µg/dL) and the mean Bishop's score was also significantly higher in successful induction group compared to failed induction group (7.3±1.0 versus 4.5±0.5), ($P<0.001$). In this study, there was significant direct correlation between serum DHEA-S and Bishop's score, the higher DHEA-S is related to higher Bishop's score ($r=0.785$; $P<0.001$). Using ROC curve, the serum DHEA-S at cutoff level 90.6 µg/dL was a predictor of successful labour induction with 97.2% sensitivity and 92.3% specificity. **Conclusions:** Pre-induction serum DHEA-S assay can be used beside clinical assessment and Bishop's score to anticipate successful induction of labour in prolonged gestation.

1. Introduction

Approximately 5%–10% of pregnancies are post-term. Studies show a reduction in the rate of cesarean deliveries and in neonatal mortality with a policy of routine labour induction at 41 weeks gestation [1].

The American College of Obstetricians and Gynecologists recommended misoprostol use in induction of labour and

abortion because of proven safety and efficacy [2]. There is no consensus about the optimum dose and dosing interval of misoprostol, high or frequent doses of Misoprostol (50–100 µg 3 hourly) are associated with short insertion to delivery interval time and high incidence of uterine hyperstimulation [3–4]. On the other hand, low or less frequent doses of misoprostol (25 µg 6 hourly) cause fewer complications with longer insertion to delivery interval time [3, 4].

DHEA-S is a weak androgenic steroid produced by the adrenal cortex of both the pregnant woman and foetus and acts as intermediary hormone in the foeto-placental production of androstenedione, testosterone, estrone and estradiol [5]. Corticotrophin Releasing Hormone (CRH) is produced by the foetus and by placental

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syncytiotrophoblasts. CRH production increases near term and activation of the foetal Hypothalamic–Pituitary–Adrenal (HPA) axis induces CRH production and secretion of DHEA–S by increased activity of the foetal adrenals [6].

DHEA–S is a measurable biochemical marker of cervical maturation. It stimulates collagenase and gelatinase production and increases the synthesis of PGE2 by human cervical tissues which leads to cervix maturation. It exerts its effect on the cervix through specific binding sites (receptors) in the cellular plasma membrane of the cervical fibroblasts [7].

The animal studies have suggested that DHEA–S acts synergistically with interleukin–8 to increase collagenase, elastase and gelatinase activity and to decrease cervical collagen content [7].

Evidence has also been suggested that DHEA–S enhances hyaluronic acid (HA) production and also acts as a stimulator of HA synthesis in human cervical fibroblasts [8]. DHEA–S stimulates neutrophil responses to HA with subsequent increase in water content, collagenase, elastase and gelatinase activities and decrease in collagen concentration in the cervix of rabbits. ElMaradny *et al.*, suggested that the DHEA–S + HA–induced changes in cervical connective tissue may play important role in cervical maturation [7].

Collagenase activity in the uterine cervix increased significantly after repeated intravenous injections of DHEA–S into pregnant women at term with the proposed mechanism of estrogen induced activation of collagenolytic activity mediated through placental conversion of DHEA–S to 17 β –estradiol. Maternal serum levels of DHEA–S are significantly lower in those clinically requiring augmentation than in those progressing spontaneously through labour [7–8].

This study was designed to evaluate the relationship between maternal Dehydroepiandrosterone sulphate (DHEA–S) and success of labour induction in prolonged gestation.

2. Materials and methods

Women with a prolonged pregnancy >41 weeks were included in the prospective study which was conducted at Ain Shams University Maternity Hospital for induction of labour to detect the relationship between maternal Dehydroepiandrosterone sulphate (DHEA–S) and success of labour induction in prolonged gestation after informed consent and approval of the study protocol by the institute ethics committee.

Fifty (50) Women with prolonged pregnancy >41 weeks, sure of dates, with singleton pregnancies and vertex presentation were included in this study. The gestational age was calculated from 1st day of last menstrual period (LMP) and confirmed by first trimester ultrasound scan.

Women with non–vertex presentation, multiple pregnancies, foetal distress, macrosomic fetus, prelabour rupture of membranes, medical disorders with pregnancy

and contraindication for induction of labour or vaginal delivery were excluded from this study.

After full history, examination, Bishop's score [9] was recorded by two observers, followed by ultrasound scan and cardiotocography (CTG) to assess foetal condition. Ten (10) mL of venous blood was taken for measuring plasma DHEA–S level from each woman included in this study before induction of labour. The blood samples were taken in plain tubes, centrifuged immediately and plasma was stored at -7°C till time of analysis. Collected samples were analyzed for DHEA–S level by ELISA technique (Diagnostic Products Corporation [DPC], Los Angeles, CA, USA), the Coat–A–Count DHEA–S is designed for quantitative measurement of DHEA–S in plasma and serum. The test can detect as little as 1.1 $\mu\text{g/dL}$ of DHEA–S.

Induction of labour was carried out by Misoprostol 25 μg vaginal suppository every 4 hours for 6 doses maximally [3,4]. Induction attempt was considered successful when the patient reached the active phase of labour (4 cm or more cervical dilatation) and developed regular effective uterine contractions (3–5 per 10 minutes each lasting 40–60 seconds), (successful induction group = 37 women).

Induction attempt was considered failed if the patient did not reach the active phase of labour after 6 doses of Misoprostol 25 μg (failed induction group = 13 women).

Patients in the first, second and third stages of labour were managed according to Ain Shams University Maternity Hospital protocol.

The outcome measures, success of labour induction, relation between both DHEA–S and Bishop's score and the success of labour induction.

2.1. Sample size justification

Sample size was calculated using Epi Info[®] version 6.0, setting the type–1 error (α) at 0.05 and the power ($1-\beta$) at 0.8, data from a previous study [10]. According to these values and at 95% confidence interval, a minimal sample size of 47 women was accepted to reach statistically acceptable figure. Therefore, 50 women with prolonged gestation were recruited in this study.

Statistical analysis was performed using statistical package for social sciences (SPSS[®]) for Windows[®] version 15.0. Descriptive statistics for measured variables were expressed as mean and standard deviation (for metric data).

Differences between two groups were measured using student's *t*–test (for parametric variables), Association between variables was assessed using Spearman's rank correlation coefficient (for non–parametric variables). Associations between measured variables were estimated using ROC curve. Validity of study parameters was evaluated in terms of sensitivity and specificity. Significance level was set at 0.05.

3. Results

In this study, there was no significant difference between the group of failed induction and group of successful induction regarding; the mean age (24.1±2.6 versus 25.2±2.9 years), mean BMI (31.2±1.5 versus 31.4±1.4 kg/m²), mean parity (1.6±0.7 versus 1.9±1.1), mean birth weight (3.2±0.3 versus 3.1±0.4 kg), and mean Apgar score at 5 minutes (8.2±0.9 versus 8.1±1.1) ($P>0.05$).

The mean serum DHEA-S was significantly high in successful induction group compared to failed induction group (108.2±10.3 versus 44.7±18.3 µg/dL) and the mean Bishop's score was also significantly high in successful induction group compared to failed induction group (7.3±1.0 versus 4.5±0.5), ($P<0.001$).

In this study, there was significant direct correlation between serum DHEA-S and Bishop's score, the higher DHEA-S is related to higher Bishop's score ($r=0.785$; $P<0.001$; Figure 1).

Using ROC curve (Figure 2), the serum DHEA-S at cutoff level 90.6 µg/dL was a predictor of success of labour induction with 97.2% sensitivity and 92.3% specificity.

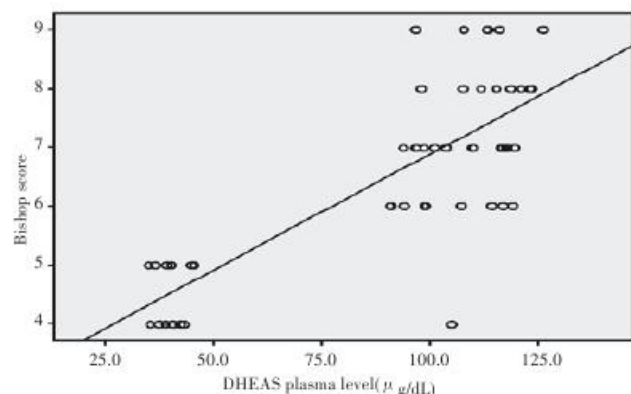


Figure 1. The correlation between serum DHEAS level and Bishop's scores.

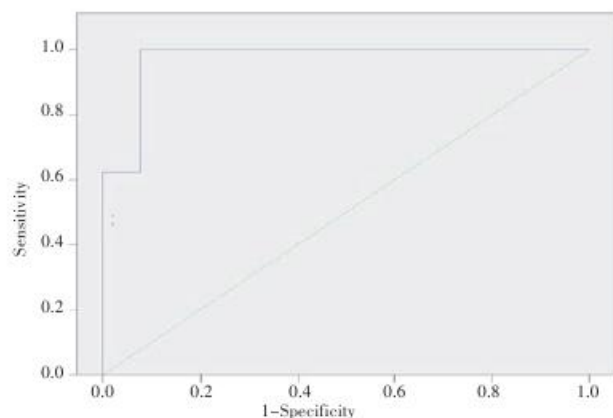


Figure 2. The ROC curve for serum DHEAS as a predictor of successful labour induction.

4. Discussion

Prolonged pregnancy is associated with significant risks to the pregnant woman, including labour dystocia (9%–12% versus 2%–7% at term), perineal injury due to foetal macrosomia (3.3% versus 2.6% at term) and high rate of cesarean delivery [11]. It is also associated with significant risks to the foetus such as increased perinatal mortality rate, low 5-minute Apgar scores [12], increased risk of umbilical cord compression from oligohydramnios and meconium aspiration [13]. Labour induction offers the alternative to such complications when continuation of pregnancy is no longer beneficial to the mother or her foetus [14].

Dehydroepiandrosterone sulphate (DHEA-S) is a weak androgenic steroid produced by the adrenal cortices of the pregnant women and foetus. Binding sites for DHEA-S have been identified on the plasma membranes of uterine cervix fibroblasts.

Previous studies suggested that maternal serum levels of DHEA-S were significantly lower in those clinically requiring augmentation than in those progressing spontaneously through labour [7,8,10], so this study was designed to evaluate the relationship between maternal Dehydroepiandrosterone sulphate (DHEA-S) and success of labour induction in prolonged gestation.

Fifty (50) Women with prolonged pregnancy 41 weeks, sure of dates, with singleton pregnancies and vertex presentation were included in this study. Induction of labour was carried out by Misoprostol 25 µg vaginal suppository every 4 hours for 6 doses maximally [3,4].

Induction attempt was considered successful when the patient reached the active phase of labour (4 cm or more cervical dilatation) and developed regular effective uterine contractions (3–5 per 10 minutes each lasting 40–60 seconds), (successful induction group = 37 women).

The outcome measures, success of labour induction, relation between both DHEA-S and Bishop's score and the success of labour induction.

In this study, there was no significant difference between the group of failed induction and group of successful induction regarding; mean age, BMI, parity, birth weight, and Apgar score at 5 minutes.

In this study; the mean serum DHEA-S was significantly high in successful induction group compared to failed induction group (108.2±10.3 versus 44.7±18.3 µg/dL) and mean Bishop's score was also significantly high in successful induction group compared to failed induction group (7.3±1.0 versus 4.5±0.5). Such results reflect the effect of serum DHEA-S on the ripening of the cervix and hence, the pre-induction level of DHEA-S might influence the outcome of an induction attempt.

In this study, there was significant direct correlation between serum DHEA-S and Bishop's score, the higher DHEA-S is related to higher Bishop's score ($r=0.785$;

$P < 0.001$), also, Dogany *et al.*, reported strong association between Bishop's scores and serum DHEA-S, the higher serum DHEA-S, the higher the Bishop's score [10].

Liapis and colleagues, found that the mean serum DHEA-S was significantly high in successful induction group compared to failed induction group ($1\ 335.0 \pm 885.0$ versus 558.2 ± 191.4 ng/mL; respectively) and they concluded that the high DHEA-S concentrations in maternal plasma may play an important role in pregnancy by producing favourable cervical conditions for delivery or by triggering the labour itself, also, they concluded that serum DHEA-S was an important predictor for the success of labour induction [15].

One hundred and sixty one women (161) more than 41 weeks were included for induction of labour in university of Arizona Health Center by Maciulla & colleagues, they found that the serum DHEA-S was significantly high (109.01 μ g/dL) in successful induction group compared to failed induction group (58.78 μ g/dL) [16].

Using ROC curve in this study to detect the best cutoff point of serum DHEA-S as predictor of successful labour induction, serum DHEA-S at cutoff level 90.6 μ g/dL was a predictor of successful labour induction with 97.2% sensitivity and 92.3% specificity.

Maciulla & colleagues, found that the natural logarithm of DHEA-S levels did not correlate with the Bishop's scores. This may be explained by the diversity in assessment of Bishop's scores between different observers being a subjective method [16].

Maciulla & colleagues, concluded that women with lower levels of DHEA-S had an unsuccessful induction and the number of unsuccessful inductions increased as DHEA-S decreased.

This study found that pre-induction serum DHEA-S assay can be used beside clinical assessment and Bishop's score to anticipate successful induction of labour in prolonged gestation.

Conflict of interest statement

We declare that we have no actual or potential conflict of interest in relation to this manuscript exists.

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