

# MATERNAL SERUM DEHYDROEPIANDROSTERONE SULFATE LEVELS AND SUCCESSFUL LABOR INDUCTION

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**Abstract-** To evaluate the maternal serum dehydroepiandrosterone sulfate level as a factor associated with the outcome of labor induction. Venous blood was collected from 45 women at the initiation of labor induction. Pregnancies complicated by maternal corticosteroid use, antepartum chorioamnionitis, or cesarean delivery for indications other than arrest disorders, were excluded from analysis. In 42 women meeting inclusion criteria, induction followed established protocol. Serum dehydroepiandrosterone sulfate levels were measured by radioimmunoassay and correlated with the outcome of each induction attempt. A successful result was defined as progression to active labor. The Welch approximate t-test, Mann-Whitney test, Fisher exact test, simple regression, and multiple regression were used for statistical analysis, with  $p < 0.05$  considered to be significant. The mean ( $\pm$ standard error) dehydroepiandrosterone sulfate level was higher in women who progressed to active labor ( $n=25$ ) than in those with unsuccessful attempts ( $n=17$ ), ( $48.63 \pm 6.53 \mu\text{g/dl}$  versus  $26.86 \pm 5.17 \text{ mg/dl}$ , respectively;  $p=0.03$ ). Compared with women with dehydroepiandrosterone sulfate levels above  $60 \mu\text{g/dl}$ , women with lower levels had an unsuccessful induction odds ratio (OR) of 6.92 (95% confidence interval 1.74, 32.52,  $p=0.01$ ). The OR increased as dehydroepiandrosterone sulfate levels decreased. Dehydroepiandrosterone sulfate may be an important factor in successful labor induction.

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**Key Words:** Maternal serum dehydroepiandrosterone sulfate, labor induction

## INTRUDUCTION

Dehydroepiandrosterone (DHEA) sulfate is a weak androgenic steroid produced by the adrenal cortices of the pregnant woman and her fetus.

Binding sites for DHEA sulfate have been identified on the plasma membranes of human cervical fibroblasts (1), suggesting that the hormone may play a role in cervical connective tissue function.

Although DHEA sulfate administration has been reported to induce cervical ripening (2), and labor (3,4), the influence of endogenous maternal serum DHEA sulfate levels on the outcome of an induction attempt has not been defined. Among young nulliparas in labor at term, this level has been found to be significantly lower in women requiring oxytocin augmentation of labor than in those progressing spontaneously (5). We hypothesized that the endogenous maternal serum DHEA sulfate level is a factor that affects the outcome of labor induction.

More specifically, women with higher DHEA sulfate levels would be more likely to have successful labor inductions.

## MATERIALS AND METHODS

Fourty five women with singleton pregnancies undergoing labor induction were recruited prospectively over the course of 4 months. Use of corticosteroids, including those administered antenatally for fetal lung maturation, and antepartum chorioamnionitis, were criteria for exclusion due to their respective associations with potential adrenal suppression and myometrial dysfunction. All women had Bishop scores less than 5.

After obtaining informed consent and before initiation of induction, blood samples were collected and serum was stored at  $-20^{\circ}\text{C}$  until analyzed. Cesarean delivery for nonreassuring intrapartum fetal testing, vaginal bleeding, malpresentation, or fetal weight over 4000g further excluded 3 patients from analysis. For the 42 women fulfilling criteria, induction of labor was attempted following established protocols with intravenous oxytocin.

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## Maternal serum DHEA and labor induction

Dehydroepiandrosterone sulfate levels were measured by radioimmunoassay with commercial kits obtained from Kavoshyar co.

Each sample was assayed twice, with the reported dehydroepiandrosterone sulfate level was the average of the two determinations. Serum dehydroepiandrosterone sulfate levels were then correlated with the success or failure of an induction attempt. Using the definition of Watson et al (6), an induction attempt was termed "successful" if the patient reached the active phase of labor as demonstrated by a change in the slope of cervical dilation. Twenty five of the induction attempts were successful.

The preinduction dehydroepiandrosterone sulfate level and age of those women with successful induction attempts were compared with those with unsuccessful attempts using the Welch approximate t- test. Similar analysis were used for statistical comparison of birth weight, gestational age and parity. Bishop scores in the two groups were compared using the nonparametric Mann-Whitney test.  $P < 0.05$  was considered statistically significant.

## RESULTS

Compared the women with successful induction attempt the women with unsuccessful attempts had

**Table 2.** Relationship between maternal serum dehydroepiandrosterone sulfate levels and the incidence of unsuccessful induction of labor

| DHEA sulfate ( $\mu\text{g}/\text{dl}$ ) | Incidence of unsuccessful induction | Odds ratio   | 95% confidence interval |
|--|-------------------------------------|--------------|-------------------------|
| $\leq 80$                                | $\frac{17}{40}$ (42%)               | <b>2.95</b>  | 0.57, 15.27             |
| $> 80$                                   | $\frac{0}{2}$ (0%)                  |              |                         |
| $\leq 70$                                | $\frac{16}{34}$ (74%)               | <b>6.22</b>  | 0.84, 46.44             |
| $>70$                                    | $\frac{1}{8}$ (12%)                 |              |                         |
| $\leq 60$                                | $\frac{15}{28}$ (53%)               | <b>6.92</b>  | 1.47, 32.52             |
| $>60$                                    | $\frac{2}{14}$ (14%)                |              |                         |
| $\leq 50$                                | $\frac{14}{24}$ (58%)               | <b>7.00</b>  | 1.72, 28.41             |
| $>50$                                    | $\frac{3}{18}$ (16%)                |              |                         |
| $\leq 40$                                | $\frac{14}{23}$ (60%)               | <b>8.29</b>  | 2.05, 33.48             |
| $>40$                                    | $\frac{3}{19}$ (21%)                |              |                         |
| $\leq 30$                                | $\frac{14}{20}$ (70%)               | <b>14.77</b> | 4.05, 59.90             |
| <b><math>&gt;30</math></b>               | $\frac{3}{22}$ (27%)                |              |                         |

significantly lower preinduction Bishop scores ( $2.27 \pm 0.27$  versus  $3.05 \pm 0.23$ ;  $p = 0.03$ ) (Table 1).

**Table 1.** Characteristics of the study population

|                    | Successful Induction (n=25) | Unsuccessful Induction (n=17) | P    |
|--------------------|-----------------------------|-------------------------------|------|
| Maternal age(y)    | $24.73 \pm 1.01$            | $24.09 \pm 1.07$              | 0.66 |
| Gravidity          | $1.82 \pm 0.26$             | $1.63 \pm 0.24$               | 0.73 |
| Gestational age(d) | $288.41 \pm 1.08$           | $286.09 \pm 1.33$             | 0.14 |
| Birth weight(g)    | $3485.29 \pm 101.71$        | $3530.90 \pm 112.37$          | 0.85 |
| Bishop scores      | $3.05 \pm 0.23$             | $2.27 \pm 0.27$               | 0.03 |
| Parity             | $0.63 \pm 0.19$             | $0.45 \pm 0.20$               | 0.57 |
| Dilation           | $1.5294 \pm 0.17$           | $1.1818 \pm 0.18$             | 0.11 |

No other statistically significant demographic differences were identified between the two groups.

The mean ( $\pm$  standard error) dehydroepiandrosterone sulfate level was significantly higher in women with successful induction than in women with unsuccessful attempts ( $48.63 \pm 6.53$   $\mu\text{g}/\text{dl}$  versus  $26.86 \pm 5.17$   $\mu\text{g}/\text{dl}$ , respectively ( $P = 0.035$ )). The main cause of cesarean was failure of labor progress (77.8%).

When dehydroepiandrosterone sulfate levels were equal to or below 60 µg/dl, the OR for an unsuccessful induction increased progressively as the maternal serum dehydroepiandrosterone sulfate level decreased (Table 2). At levels above 60 µg/dl, the OR for an unsuccessful induction was not statistically significant.

## DISCUSSION

Parenteral administration of dehydroepiandrosterone sulfate has been used effectively for cervical ripening and labor induction. The proposed mechanism of action is an activation of total collagenolytic activity, resulting in uterine connective tissue remodeling. Recent animal studies (7) have suggested that dehydroepiandrosterone sulfate acts synergistically with interleukin-8 to increase collagenase, elastase, and gelatinase activity while decreasing the cervical collagen content. The cervical collagenolytic effect of dehydroepiandrosterone sulfate may also be mediated through prostaglandin E<sub>2</sub> because its synthesis is enhanced by dehydroepiandrosterone sulfate in human cervical tissue (8). Sufficient uterine connective tissue remodeling is important in allowing normal labor progression (9).

Our study provides clinical support for these animal and culture studies, suggesting a role for DHEA sulfate in successful induction of labor in humans. The endogenous preinduction dehydroepiandrosterone sulfate levels were significantly lower in patients with unsuccessful inductions than in those with successful inductions: additionally, the OR for an unsuccessful attempt increased progressively with decreasing dehydroepiandrosterone sulfate levels below a critical level (60 µg/dl). Above that, the OR did not meet statistical significance, perhaps due to a true threshold level.

As further evidence for a role of endogenous DHEA sulfate in successful labor induction, our study agrees with that of Liapis et al (10) in showing an association between higher Bishop scores and higher DHEA sulfate levels. The same investigators (10) found no such correlation with estradiol, estriol, progesterone, or cortisol, suggesting a direct role for DHEA sulfate (and not its metabolites) in uterine collagenase activation.

The levels of preinduction maternal serum DHEA sulfate appears to influence the ultimate outcome (success or failure) of an induction attempt. Although the mechanism of this action of dehydroepiandrosterone sulfate remains to be clarified, available

evidence implicates collagenase activation and a resultant remodeling of uterine connective tissue. Consequently, dehydroepiandrosterone sulfate may be an important factor in successful labor induction.

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