Original Article

Diurnal Variations in the Levels of Progesterone During Late Pregnancy

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ABSTRACT

Background: Progesterone is a C-21 steroid hormone, plays a major role in the occurrence, maintenance and termination of pregnancy.

Objective: To study the diurnal variations in the levels of progesterone at the start and end of the day during late pregnancy in women having different life set ups.

Study Design: Experimental and Observational Study.

Place of Study: This study was conducted at the Department of Gynae and Obs., Khyber Medical College, Peshawar.

Materials and Methods: Blood samples of 50 women between 26-40 weeks of gestation were collected at two different intervals with a gap of 12 hours. Progesterone level was estimated by Serozyme EIA method.

Results: The concentration of progesterone was found low in the early morning and high in the late evening in our population. Besides, the magnitude of fluctuations in the samples of two different intervals declined with progress of age and weeks of gestation.

Conclusion: Our findings support the recommendation of restricting progesterone measurements to morning hours at all ages particularly during late pregnancy which is important information for clinicians at the time of interpretation of results.

Key Words: Progesterone, diurnal variations, late pregnancy.

INTRODUCTION

Progesterone is the first biologically active compound in the steroid biosynthetic pathway, formed in the adrenal cortex, the testes in males and the ovaries and foeto-placental unit in females. The same hormone has also been called the female's reproductive hormone as it regulates the accessory organs during the menstrual cycle and prepares the uterus for implantation of blastocyst. Some research workers demonstrated that due to luteal phase deficiencies, 64% women had infertility[1]. Besides, the said hormone helps in maintaining pregnancy and prepares breasts for lactation.

The measurement of progesterone is important to confirm ovulation, luteal phase defect, to evaluate patients at risk from spontaneous abortion and to monitor replacement therapy[2]. Its therapy is advised for breast cancer, breast pain, child spacing, withdrawal bleeding, Pre-Menstrual Syndrome, poor endometrial receptivity, post menopausal complications and when the level is low during pregnancy[3].

Due to principle role of this hormone in pregnancy and substantial variations during reproductive life of women, it should be estimated in different racial groups. An experimental study on animals described circadian variations in plasma progesterone in the morning and night samples[4]. The diurnal variation of testosterone hormone also has been well documented[5]. A previous study showed diurnal variation in the level of cortisol hormone, maximum concentration was found early in the morning and then declined through out the whole day and reached to minimum level at the evening[6].

In our early study, we found peak level of the progesterone in the second trimester which again declined in the last trimester[7]. While Burtis and Ashwood got peak concentration of hormone in the last trimester of pregnancy[8]. These conflicting observations also created our interest to study the level of progesterone two times a day i.e. in the early morning and at late evening particularly during late pregnancy in women having different nutrition, life style and environment.

MATERIALS AND METHODS

A total of 50 women (30 multiparas and 20 primiparas) in between 26 and 40 weeks of gestation from three villages of District, Nowshera were selected for this study. All of them had moderate socio-economic background and age range from 18 and 42 years. The participants had regular menstrual cycles, normal obstetric history, and had never used any hormonal medications or contraceptives. A scrutiny was done to exclude women with poor general health, had HIV/AIDS, polycystic ovarian diseases, congenital

abnormalities and those who did not give birth to live, healthy, singleton infants at term.

All the women were also subjected to a questionnaire including family income, family members, status and occupation, living condition and personal history like age, height, weight, dietary history, history of ailment and medication, onset of puberty, menses frequency, age at marriage, age at first delivery, history of lactation, history of delivery, parity, history of twins, gestation procedure, gestation period and previous laboratory investigation. Then objective of the study was explained to the enrolled women in the mother language, Pashto and written consent was obtained.

Five milli litre fasting blood samples were collected between 08 and 09 a.m; and 08 and 09 p.m. for three consecutive days/ nights from each woman. The blood was allowed to clot at room temperature for 30-45 minutes. Then it was centrifuged at 3000 rpm for at least 10 minutes. The serum was kept at -20°C until used for analysis. Progesterone was determined by Serozyme EIA method using blood employing polyclonal antibodies against P-7 carboxy-ethyl-thioether-BSA as the antigen [9]. Statistical examination of the data was performed accordingly.

RESULTS

The results of our analysis as given in tables 1&2 highlighted a significant diurnal variation in the levels of progesterone during pregnancy. In almost all the cases, the mean level was found low in the early morning and high in the late evening.

Table No.1 describes that the overall mean concentration of progesterone during the start of the day was 110.1 ng/ml and start of the night 122.7 ng/ml ($P < 0.05$). Besides, the differences in concentrations in the two samples of different intervals declined with age of pregnant women.

Table No.2 describes that the overall mean levels of the hormone was 107.8 ng/ml in the early morning and 123.9 ng/ml during the late evening ($P < 0.05$). The maximum difference (20.8 ng/ml) in the levels of the two samples was observed during 26-30 weeks and minimum (12.1ng/ml) during 36-40 weeks of gestation in our population.

Table No.1: Progesterone level (Mean ± SD) during late pregnancy.

Age of women (In years)	Morning Level (ng/ml)	Evening Level (ng/ml)	P. Value
18-22	106.6 ± 4.8	124.5 ± 6.1	P < 0.01
23-27	108.2 ± 4.9	123.7 ± 6.1	P < 0.01
28-32	110.5 ± 4.9	122.4 ± 5.9	P < 0.05
33-37	111.9 ± 5.0	121.8 ± 6.0	P < 0.05
38-40	113.1 ± 5.1	120.9 ± 5.8	P < 0.05

Table No.2: Progesterone level (Mean ± SD) during gestation.

Weeks of Gestation	AM level (ng/ml)	PM level (ng/ml)	P. value
26-30	105.4 ± 5.1	126.2 ± 5.7	P < 0.01
31-35	108.2 ± 5.6	123.6 ± 5.4	P < 0.05
36-40	109.7 ± 5.9	121.8 ± 5.3	P < 0.05

DISCUSSION

The measurement of progesterone in maternal blood is essential for the maintenance / care of pregnancy. In our previous published article, we investigated the concentrations of the same hormone during three trimesters of pregnancy[7]. We observed quite different values in the third trimester from the already reported data[8]. Because of the conflict findings in the third trimester, this study was designed to determine the levels of progesterone twice a day at two different intervals during late/third trimester of pregnancy.

In the present work, we found same figures in our morning samples as observed in our previous study[7]. But we got significantly higher figures ($P < 0.05$) during the late evening. The cause of this conspicuous diurnal pattern is not known. Similar fluctuations in the concentrations of progesterone were reported in an early experimental study on animals[4]. A significant variation/rise in the level of testosterone from 08 am to 08 pm was also documented in men[5]. Other workers observed circadian variations in the levels of cortisol, and got maximum values early in the morning and minimum values at the late evening[6]. In contrast to our work, Dame et al found no consistent diurnal variations in the level of progesterone at any gestation[10]. Other researchers also demonstrated negative fluctuations in the same hormone during the luteal phase in heifers[11]. Hence, further work is needed to exploit more the pattern of variations of this important hormone through out the day during the reproductive age of women.

Besides, the values of the two tables showed that the differences in the samples of two intervals were high at the young age and 26-30 weeks of gestation but later presented progressive decline in both groups. The possible reason for the decline may be the body's homeostatic mechanism for the adjustment of precursors as needed to placenta for the production of this hormone. But still there is major difference even at 36-40 weeks of gestation and in the last age group. This warrants that if one has to advise/measure progesterone level for diagnostic or prognostic purposes, he should be aware of the idea of diurnal variations during late pregnancy and hence appropriate to extract the blood samples in the morning hours.

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