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# ROLE OF PROGESTERONE IN PREVENTING RECURRENT MISCARRIAGES IN PREGNANT WOMEN ATTENDING ANTENATAL UNIT OF SOUTH INDIAN HOSPITAL

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## ABSTRACT

**Background:** Progesterone plays an important role in regulating normal female reproductive functions. It is successful in preventing recurrent preterm delivery and unexplained miscarriages. Progesterone supplementation improves the pregnancy outcome in groups of recurrent miscarriages as progesterone is very important for embryonic survival, embryo development and implantation. Objective: To understand the role of progesterone in preventing recurrent miscarriages in pregnant women, to evaluate the outcome of Progesterone during pregnancy attending antenatal unit of south Indian hospital. **Aim and Objective:** To understand the role of progesterone in preventing recurrent miscarriages in pregnant women attending antenatal unit of south Indian hospital. **Setting:** Observational study was conducted over a period of 4 months from November 2013 to February 2014 in Antenatal Out Patient Department of Obstetrics and Gynaecology of Owaisi Hospital and Research Centre to evaluate the outcome of Progesterone during pregnancy and to study its role of preventing recurrent miscarriages. **Method:** Observational study was conducted over a period of 4 months from November 2013 to February 2014 in Antenatal Out Patient Department of Obstetrics and Gynaecology. **Results:**Out of 153 patients who agreed to give a written informed consent for the study, 11 patients preferred delivery outside our hospital. Average age of pregnant women was 30.6 ± 4.35 years (Range 15-40 years). Of 153 women 32 (20.9%) were of age group 15-20, 70(45.7%) women were between 21-25 being the highest, 39 (25.4%) women were between 26-30, 11(7.1%) women of age 31-35 and only 1(0.6%) woman between age 36-40 years. The women grouped under Gravida (the number of pregnancies), 54(35.2%) of them in Primi gravida being the largest number, other pregnant women were found in Gravida I - 42(27.4%), Gravida II- 42(27.4%), Gravida III- 26(16.9%) Gravida IV-21(13.7%) Gravida V- 05(3.2%) and 1(0.65%) pregnant woman in Gravida VI,VIII and X were given progesterone as a supportive treatment in order to give birth to a healthy and safe full term offspring . **Conclusion:** Progesterone treatment reduces the number of uterine contractions and significantly decreases pre term delivery rates. Progesterone supplementation was found to improve the pregnancy outcome in groups of recurrent miscarriages.

**KEYWORDS:** Progesterone, Pregnancy, Recurrent miscarriages, Ante natal, OPD.

## INTRODUCTION

Progesterone plays an important role in regulating normal female reproductive functions. After ovulation ovaries produce progesterone, a hormone that prepares the endometrium (the uterine lining) for the fertilized egg as it arrives from the fallopian tube. If the ovary fails to produce enough progesterone, infertility or early pregnancy loss may occur. This condition is known as luteal phase defect. There are two possible treatments for luteal phase defect - clomiphene citrate (or gonadotropins) and progesterone.[1] The causes of infertility can be divided into four major categories: i) the female factor; ii) the male factor; iii) combined factors; iv) unexplained infertility.[2] The important physiological actions of progesterone are: a) in the uterus and ovary: induction of ovulation, facilitation of implantation, and maintenance of early pregnancy; b) in the mammary gland: lobular-alveolar development in preparation for milk secretion[3,4] and c) in the brain: neurobehavioral expression associated with sexual responsiveness[5] and d) in the bone: prevention of bone loss.[6] It is a 21-carbon steroid and it is a precursor molecule for steroids biosynthesis. It is transported in the blood by transcortin. The half-life of progesterone is

approximately 5 minutes in the blood. During the luteal phase, the plasma level rises to a peak value of approximately 40-50 nmol/l (12-16 ng/ml).[7] Progesterone effects on ovulation, on cellular differentiation, on cellular proliferation in the uterus during the menstrual cycle and on the stromal decidualization. It also helps in regeneration, implantation, myometrial contractility.[8]

Preterm birth is the leading cause of neonatal mortality, responsible for over 1 million deaths annually. In 2010 approximately 12% of births in the United Stated were preterm. Progesterone is successful in preventing recurrent preterm delivery.[9] Preterm labour was defined as the simultaneous presence of contractions (> six contractions in 30 min) and cervical changes, either shortening and/or softening or dilation, by manual examination. Recurrence of preterm labour was defined as recurrence of contractions within 48 h after discontinuation of intravenous treatment and arrest of contractions. Arrested preterm labour was defined as a 12-h contraction-free period after intravenous therapy had been discontinued.[10] In women with a short cervix, treatment with progesterone minimizes spontaneous early preterm delivery.[11]

Supportive care in early pregnancy has a beneficial effect on the outcome of pregnancy.Drug treatment or other intervention is often requested even in absence of any aetiological factor in order to improve the outcome of future pregnancies.[3] Progesterone may be administered by daily injection, vaginal suppositories, or in pill form.Treatment is begun 3-4 days after ovulation. A clear rise in the basal body temperature graph or change in the ovulation predictor kit will help pinpoint the time of ovulation.[1] Progesterone can be administered vaginally in an 8% gel, compounded suppositories, or in tablets containing micronized P.[12] The actions of progesterone on the pregnant myometrium include relaxation of myometrial smooth muscle, blocking of the action of oxytocin, and inhibition of the formation of gap junctions.[13] Progesterone is effective for absence of menstrual period, hormone replacement therapy , infertility, abnormal thickening of the endometrium, breast pain, menopausal symptoms, premature labour, miscarriage, premenstrual syndrome, vaginal irritation and withdrawal symptoms due to drugs such as diazepam, alprazolam etc.[1]

## AIM OF THE STUDY

To study the role of progesterone in preventing recurrent miscarriages in pregnant women attending antenatal unit of south indian hospital.

## ETHICAL APPROVAL

Ethical approval was not required because there was no direct contact with the study population just a verbal consent was obtained from all the pregnant women before their prescriptions were analysed for prescription of Progesterone.

## METHOD

**Study Period:** The study was conducted over a period of 4 months from November 2013 to February 2014 and outcome of pregnancy was recorded later depending on the Delivery dates of the patient.

**Study Design:** Pharmacoepidemological studies can help in minimizing the inherent risk of drug use in pregnancy by establishing a profile of drug consumption, by evaluating the existing health services and by investigating the interventional measures.[14] The present observational study was conducted in Antenatal Out Patient Department of Obstetrics and Gynaecology of Owaisi Hospital and Research Centre to evaluate the outcome of Progesterone during pregnancy and to study its role in preventing recurrent miscarriages. All the pregnant women were encouraged to attend a dedicated early pregnancy clinic until 12 weeks gestation and outcome of the pregnancy was recorded after the delivery.

**Hospital Background:** Owaisi Hospital and Research Centre, Hyderabad, India is a tertiary care multispecialty teaching hospital with a massive seven storied structure and 1150 beds competently managed by senior professionals, highly experienced in their respective speciality which receives referrals from other private clinics, hospitals and general physicians.

**Patient Enrolment:** Pregnant women were enrolled only after obtaining a verbal consent.

**Patient Data Collection Form:** The demographic profiles of pregnant women along with parity, present and past history of associated medical, surgical, gynaecological and obstetrical illness, number of drugs prescribed per prescription, generic/brand names, drug dose, dosage form, frequency, duration of treatment were collected, sorted and classified in accordance with US FDA risk classification for pregnancy and the detailed information on the prescription records given in the past and at the time of enrolment documented in OPD case paper were recorded on the case record form.

**Inclusion criteria:** All women attending Owaisi Hospital and Research Centre with a history of consecutive first trimester miscarriages were enrolled via convenience sampling, in any trimester with or without a history of three or more consecutive first trimester miscarriages attending antenatal outpatient department greater than or equal to 15yrs of age, with or without co-morbidities, presented with the prescription on the OPD case paper with Progesterone written on it were included in the study. Women in whom no abnormality was detected and who subsequently became pregnant formed the study population.

**Exclusion criteria:** Pregnant women diagnosed with acute and chronic medical conditions requiring hospitalization were excluded from the study.

**Statistical Analysis:** Statistical analysis was doneby using descriptive statistics. Data was collected, tabulated and graphs were designed in Excel-2007. Continuous variables were presented as mean values ± Standard Deviation (SD) and categorical variables were presented as percentages.

## RESULTS

**Table 1 showing No. of Patients enrolled in the study grouped in age**

| Age | No. of Patients |
|---|---|
| 15-20 | 32 |
| 21-25 | 70 |
| 26-30 | 39 |
| 31-35 | 11 |
| 36-40 | 01 |

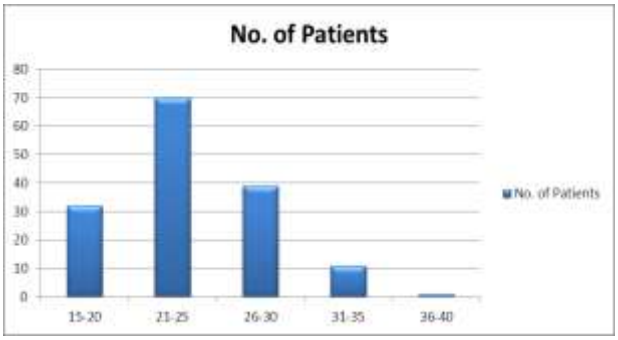


**Figure 1 showing No. of Patients enrolled in the study grouped in age.**

**Table 2 showing No. of Patients enrolled in the study grouped in Gravida's**

| Gravida | No. of Patients |
|---|---|
| Primi | 54 |
| II | 42 |
| III | 26 |
| IV | 21 |
| V | 05 |
| VI | 01 |
| VII | 00 |
| VIII | 01 |
| IX | 00 |
| X | 01 |

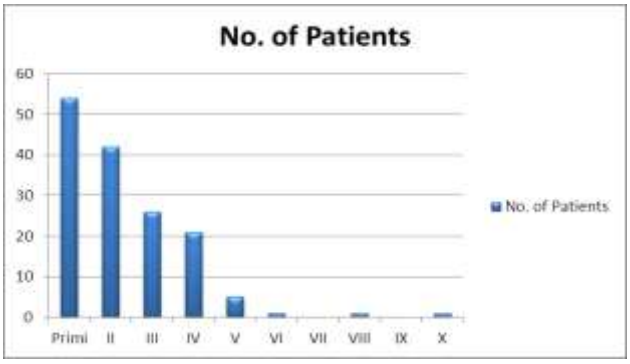


**Figure 2 showing No. of Patients enrolled in the study grouped in Gravida's.**

**Table 3 showing No. of Patients with previous history of Abortions:**

| Total Abortions | No. of Patients |
|---|---|
| 1 | 21 |
| 2 | 14 |
| 3 | 1 |
| 4 | 1 |
| 5 | 1 |

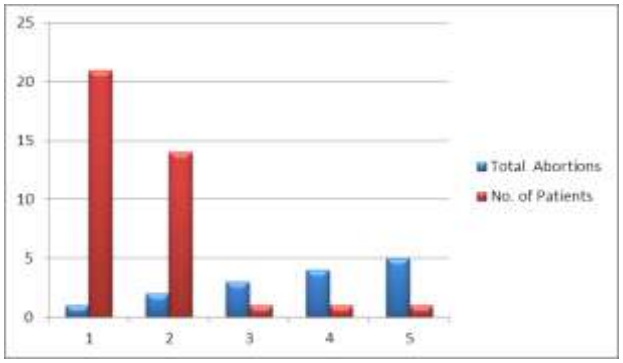


**Figure 3 showing No. of Patients with previous history of Abortions.**

**Table 4 showing No. of Patients enrolled in the study grouped according to Gestational age and Term of delivery (Pre –term Deliveries)**

| Gestational Age | No. of Patients |
|---|---|
| 25 weeks | 03 |
| 28 weeks | 01 |
| 32 weeks | 01 |
| 34 weeks | 01 |
| 35 weeks | 03 |

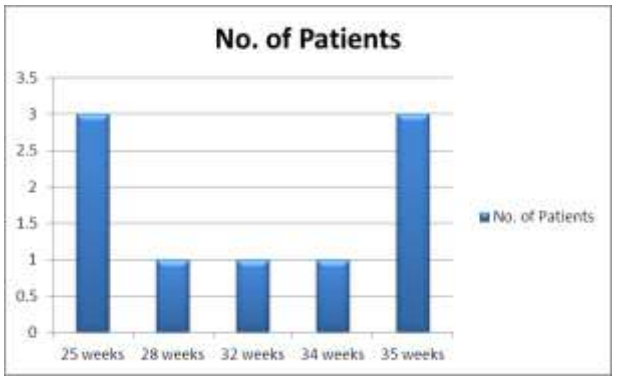


**Figure 4 showing No. of Patients enrolled in the study grouped according to Gestational age and Term of delivery (Pre –term Deliveries).**

**Table 5 showing No. of Patients enrolled in the study grouped according to Gestational age and Term of delivery (Full - term Deliveries)**

| Gestational Age | No. of Patients |
|---|---|
| 36 weeks | 24 |
| 37 weeks | 22 |

| | |
|---|---|
| 38 weeks | 51 |
| 39 weeks | 13 |
| 40 weeks | 06 |

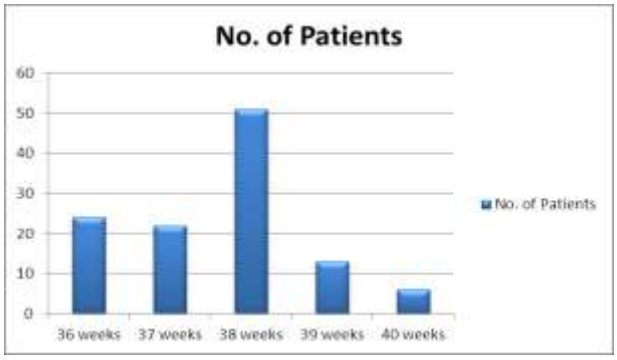


**Figure 5 showing No. of Patients enrolled in the study grouped according to Gestational age and Term of delivery (Full - term Deliveries)**

**Table 6 showing No. of Patients enrolled in the study showing Mode of Delivery**

| Mode of Delivery | No. of Patients |
|---|---|
| Normal Vaginal Delivery | 56 |
| Normal Vaginal Delivery (Episiotomy) | 02 |
| LsCs | 63 |
| ELsCs | 11 |

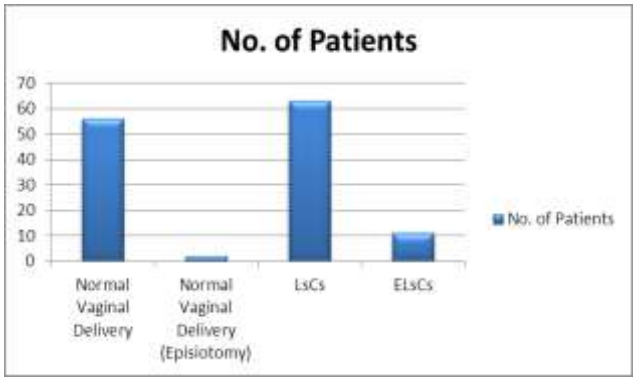


**Figure 6 showing No. of Patients enrolled in the study showing Mode of Delivery.**

**Table 7 showing No. of Male and Female babies delivered**

| Total Births (Sex) | No. of Babies |
|---|---|
| Males | 65 |
| Females | 72 |

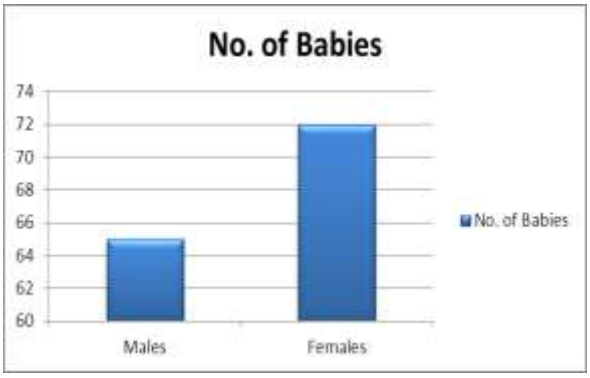


**Figure 7 showing No. of Male and Female babies delivered.**

**Table 8 showing Outcome of the drug, Progesterone in Patients**

| Outcome of the Drug | No. of Patients |
|---|---|
| Total Deliveries (NVD, NVDE, LsCs, ELsCs ) | 132 |
| Total Abortions (Missed / Spontaneous) | 4 |
| Still Birth | 1 |
| Intra Uterine Death | 1 |

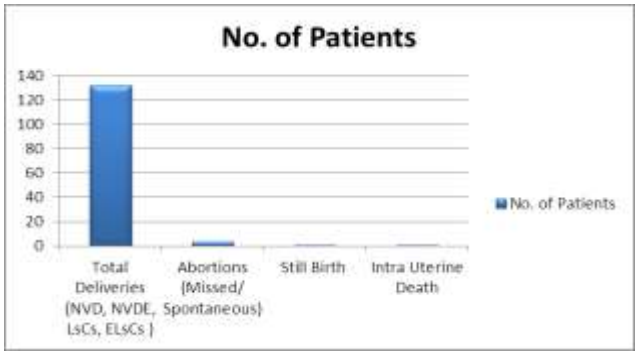


**Figure 8: showing Outcome of the drug, Progesterone in Patients.**

## DISCUSSION

A total of 200 pregnant women with previous history of Abortions and those in Primi gravida were interviewed, out of which 153 patients who agreed to give a verbal informed consent were enrolled for the study among them 11 patients preferred delivery outside our hospital. The demographic data of the study participants was collected such as Age (in years), Gravida [Number (%)]. Average age of pregnant women was 30.6 ± 4.35 years (Range 15-40 years). Of 153 women 32 (20.9%) were of age group 15-20, 70(45.7%) women were between 21-25 being the highest, 39 (25.4%) women were between 26-30, 11(7.1%) women of age 31-35 and only 1(0.6%) woman between age 36-40 years as depicted in Table and Figure 1.

The women were grouped under Gravida (the number of pregnancies), 54(35.2%) of them in Primi gravida being the largest number, other pregnant women were found in Gravida I - 42(27.4%), Gravida II- 42(27.4%), Gravida III- 26(16.9%), Gravida IV- 21(13.7%), Gravida V- 05(3.2%) and 1(0.65%) pregnant woman in Gravida

VI,VIII and X were given progesterone as a supportive treatment in order to give birth to a healthy and safe full term offspring as depicted in Table and Figure 2.

The women enrolled were with Primi gravida and with previous history of abortions and it was found that 21, 14,4,1,1 patients with I, II, III, IV, V history of abortions respectively as shown in Table and Figure 3.

The pregnant women were analysed till they delivered in order to conclude the aim of the study and to monitor the effect of Progesterone in delivering a full term offspring hence the Term of delivery [pre term (20 <=37 weeks), Full term(>37-40 weeks)] and the mode of delivery [Normal Vaginal Delivery (NVD), Normal Vaginal Delivery with Episiotomy (NVDE), Lower Segment Caesarean Section (LsCs), Emergency Lower Segment Caesarean Section (E-LsCs)],IUDs and Abortions(missed/spontaneous), total number of off springs (males/females) delivered were also taken into consideration.

On evaluating effect of Progesterone on all the above mentioned parameters it was found that there were 9 pre-term births 3 (1.9%) in weeks 25 and 35 and 1(0.6%) in weeks 28,32,34 respectively . The numbers of full term births recorded were 24 (15.6%) in 36 weeks, 22(14.3%)in 37 weeks, 51 (33.3 %) in 38 weeks being the highest number, 13 (8.4%) in 39 weeks, 6 (3.9%) in 40 weeks which was a good finding for the studyas depicted in Tables and Figures 4 and 5 correspondingly.
The total number of NVD's were found to be 56 (36%) same with Episiotomy was 2 (1.3%), LsCs were 63 (41.1%) being the highest value and ELsCs were 11 (7.1%). The total numbers of descendants born were 137 out of which 65 (42.4%) were Males and 72 (47%) were Females as illustrated in Tables 6and 7 respectively.
In total there were 4 (2.61 %) abortions noticed contributing 2(1.31%) each for Missed and Spontaneous, 1 (0.65) IUD and one Still Birth as shown in Table and Figure 8.

## CONCLUSION

Recurrent miscarriage, the loss of three or more consecutive pregnancies, affects approximately 1 % of women. Despite the possibility to identify etiological factors in up to 50% of cases, unexplained recurrent miscarriage remains to thwart the clinician and creates a perturbed condition for effected couple. In the past many unreliable treatments were prescribed to improve outcome of pregnancy. Now a days progesterone supplementation, helps to prevent recurrent miscarriages and has proved to be effective as a supportive care in pregnancy, it confers a notably favorable effect on the outcome of present and future pregnancies.

The present study justifies the use of progesterone as intensive management therapy (a) To prevent recurrent miscarriages (b) To prevent pre term delivery (c) To reduce number of uterine contractions (d) To prevent spontaneous early pre term delivery (e) To manage recurrent miscarriages. Our study provides information that can be used to counsel effected couple about their chance of success in the future and also prevents unwarranted intervention.

## ACKNOWLEDGEMENT

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**Disclosure of interests:** The authors have no Conflicts of Interest to declare.

**Contribution to authorship:** This work was carried out in collaboration between all authors. All authors read and approved the final manuscript.

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