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KEYWORDS: Puberty;
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A STUDY OF SERUM ESTRADIOL LEVELS IN THE FEMALE POPULATION DURING VARIOUS PUBERTAL STAGES



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ABSTRACT:

Objective: This study was designed to determine the normal as well as pathologic levels of estradiol in among Pakistani female population in different pubertal stages as no study has been previously done on this topic.

Method: Serum estradiol levels of one hundred thirty one female subjects were evaluated at the Reproductive Physiology laboratory of the NIH, Islamabad, using Microparticle Enzyme Immuno Assay (MEIA) technology of M/s Abbott Laboratories. Subjects were divided in to into pre-pubertal, peri-pubertal and pubertal stages. Samples from the pubertal stage subjects were taken in the follicular phase.

Statistical Analysis: Data were compared using student 't'-test. Results: Mean estradiol levels (mIU/ml) were 65.02+10.46 in the follicular phase, 152.04+302.16 during ovulatory phase (mIU/ml), Luteal phase showed E2 7532.91+1684.40 in the luteal phase. (mIU/ml), which were highly significant ($P < 0.01$). The results revealed that age within the different age groups varied non-significantly, while significant differences were observed in case of pathological groups within the same pubertal stage.

Conclusion: The study showed that the level of estradiol gradually increased from prepubertal to peri pubertal stage and reached at peak value at puberty stage.

INTRODUCTION

Estradiol is basically a steroid hormone, secreted in major quantities only by the ovaries and in minute amount by placenta [1]. Estradiol is not only important for female sexual differentiation during gestation, but also for sexual development at the onset of puberty and regulation of menstrual cycle [2]. The primary source of this hormone is from the aromatization of testosterone [3]. With regard to pubertal development, the human population can be divided into three groups (our own ref), pre-pubertal (5-9 years), peri-pubertal (10-15 years) and pubertal (more than 15 years). The pubertal stage is subdivided into follicular phase, ovulatory phase and luteal phase, each of these phases has different concentration of E2. During pre-pubertal stage, the observed level of E2 is very low in quantity, because of no sexual differentiation. During the peri-pubertal stage, there is slight increase in E2 level due to sexual maturation. The third stage has great diversity in estradiol concentration due to the onset of the menstrual cycle. At ovulation the level of estradiol fall considerably until the luteal cells become active, resulting in a secondary gentle of estradiol concentration. During pregnancy the maternal serum estradiol level highly increased an sustained through out the pregnancy. During luteal phase estradiol along with progesterone is secreted by corpus luteum which stimulates further endometrium growth. If ovum not fertilized then there is further drop in estrogen and progesterone. Clinical studies suggest that estradiol acts as a protective factor in adult brain postmenopausal women suffer from as increased risk of brain injury associated with neurodegenerative disease such as Alzheimer's disease and estrogen replacement

therapy [4]. In Pakistan, no research work has been carried out at pre-pubertal, peri-pubertal and pubertal stages to determine the estradiol concentration. Therefore the present study was designed to fulfill the following objectives.

1. To assess the role played by elevated or depressed levels of estradiol during different stages.
2. To determine the relationship between age and elevated or depressed levels of estradiol among all the stages.
3. To examine the relation of similarity and difference of E2 concentration between three phases of pubertal stage.

Materials and methods:

Serum estradiol levels of one hundred thirty one female subjects were evaluated at the Reproductive Physiology laboratory of the NIH, Islamabad, using Microparticle Enzyme Immuno Assay (MEIA) technology of M/s Abbott Laboratories. Subjects were divided in to into pre-pubertal, peri-pubertal and pubertal stages. Informed consent was taken from all the patients. Samples from the pubertal stage subjects were taken in the follicular phase.

Statistical Analysis: Data were compared using student 't'-test.

RESULTS

This is retrospective study was conducted to evaluate the level of estradiol at pre pubertal , peri pubertal and pubertal stages in women. The data was consisted on 131 subjects.

At pre pubertal stage the range was (5-9) years and observed level of E2 lied between (47.6+1.453). there was no abnormality seen.

At peri pubertal stage the range of age was 11-15 years with E2 level (66.21+67.81). there was no elevated depressed level observed.

The pubertal stage was age range 16-20 years. there was great variation in level of E2. the observed elevated level was (190+42.025) which was non significant. the conc. of E2 at normal level was (107+23.84) which showed highly significant results. phase analysis was divided into 3 phases at pubertal stage. the follicular phase has no abnormality. the observed level of E2 was (65.02+10.46) and analysis was (22.38+3.70) as shown in Table 1 and 2

Table:1 pre-pubertal vs peri pubertal

Stages	Age	Level
Pre pubertal	7+1.418 d	47.6+1.453b
Peri pubertal	14.67+0.887 d	66.21+6.78 b
Pubertal (Follicular phase specimen)	22.38+3.70	65.02+10.46

a = non-sig
b = sig
c = more sig
d = H. sig

Table:2 LEVEL ANALYSIS OF PRE PUBERTAL STAGE

Stages	Age	Level
Normal	18.5+0.28 d	190.16+42.29 d
Elevated	17.6+0.33 a	19.63+0.25 a
Depressed	18.78+4.99 d	103.25+23.81 d

The ovulatory phase showed great diversity. Observed elevated level was (152.40+302.16) which was non sig and depressed level was (18.5+0.45), which was also non sig. Luteal phase showed age analysis (3.86+0.85) which was highly sig. E2 analysis showed (72.35+1684.40) which was highly sig. as shown in Table 3

TABLE :3: PHASIS ANALYSIS OF PUBERTAL STAGE

PHASIS	AGE	LEVEL
Follicular phase	22.38+3.70	65.02+10.46
Ovulatory phase	18.5+0.45 b	152.40+302.16 a
Luteal phase	18+0.85 b	72.35+1684.40 d

a = non-sig
 b = sig
 c = more sig
 d = H. sig

Comparison between pre pubertal and peri pubertal stage showed age wise highly sig and level wise significant. While comparison between peri pub and pub stages showed age highly sig and level non-significant. The pubertal and ore pubertal showed age most sig and level also most significant as shown in Table 4.

TABLE 4

STAGES	RANKS	AGES	LEVEL
PRE -PUBERTAL	A-B	Highly Sig	Sig
PERI-PUBERTAL	B-C	Highly Sig	Non sig
PUBERTAL	C-D	Most Sig	Most Sig

Normal – Normal comparison between different stages and age wise analysis showed in table 5 and Table 6.

Table:5 NORMAL Vs NORMAL

STAGES	AGE	NORMAL
PRE PUBERTAL	7+1.418 ^a	47+1.53 ^a
PERI PYBERTAL	13.88+0.44 ^c	35.99+4.05 ^c
	14.08+0.326 ^a	89.94+14.77 ^a
PUBERTAL	19.63+0.25 ^d	504.19+55.38 ^d
	18+0.204 ^a	37.90+61.34 ^a

Table:1.4 age wise analysis

stages	Age	Level
A-B	P<0.01 d	P<0.05 b
B-C	P<0.01 d	P<0.05 b
C-D	P<0.01 d	P<0.01 d
D-E	P<0.01 d	P<0.01 d
E-F	P<0.01 d	P<0.01 d
F-G	P<0.05 b	P<0.01 d
G-H	P<0.05 b	P<0.01 c
H-I	P<0.05 b	P<0.01 c
F-J	P<0.05 a	P<0.01 d
F-K	P<0.05 a	P<0.01 c
H-L	P<0.05 a	P<0.01 c

A-B	5-9	B-C	11-13	C-D	14-15
D-E	15-16	E-F	16-17	F-G	17-18
G-H	18-19	H-I	19-20	F-J	17n-17ab
F-K	18n-18ab	H-L	19n-19ab	I-M	20n-20ab

DISCUSSION

Estradiol is basically steroid hormone. Its basic function is to cause cellular proliferation and growth of tissues of sexual organs and other organs related to reproduction. It is important for female gestations, sexual development and at the onset of maturity. It is responsible for the regulation of menstrual cycle. The development of breast, vagina, urethra and fallopian tubes is under the control of this hormone. During childhood estradiol is secreted only in small quantity, but following puberty its secretion increased under the influence of pituitary. At this time the female sexual organs change from those of a child to adult, including the size of endometrium also increased [1,5]. The present study is divided into three stages on the basis of cyclic changes in female ovulatory period. The pre-pubertal stage, which starts from the age of 5 year and end at the age of 9 year, has low level of hormone due to immature development of sexual organs. But as age proceeds in per-pubertal stage with age range (10-15) year there is slight increase in level of estradiol observed. This increase in E2 level is due to development of ovary, which is under the control of pituitary. But no abnormality is observed in both above stages. The pubertal stage where the ovulation takes place at its peak level. But its maximum increase in estradiol level observed at that stage. However sudden decrease is also noted, which is due to abnormal development of ovary and other sex organs. Hyper secretion of estradiol is a significant cause of infertility and miscarriage. A study conducted at Vanderbilt University has shown that too much estrogen can negatively impact a woman's fertile window and may prevent an embryo from implanting. In female with polycystic ovary syndrome, hypothalamic dysfunction resulting increased plasticity of GnRH, altered pituitary sensitivity, which in turn cause negative feedback of estradiol, which causes hyperandrogenism and abnormalities of various types [6-8]. In present study the pubertal stage is analyzed according to phases. In follicular phase the development of ovary cells is at immature stage therefore no elevated level is observed. At voluntary phase slight diversity is observed. This is because of development of ovary increased from 10-20 folds more than follicular phase [9]. Both elevated and depressed levels are observed. At luteal phase, due to achievement of maximum growth of sexual organs a great diversity is observed in level of hormone [10]. The secretion of hormone observed at its maximum peak. But depressed levels also observed. This is due to improper or dysfunction in development of sex organ. The age wise analysis of pre pubertal, per pubertal and pubertal stages also done. It showed that level of estradiol increased as age increased. There is gradual increase in level of E2 from age groups of per pubertal to per pubertal. But there is sudden increase in E2 level from peri pubertal age groups.

CONCLUSION

The present study concluded that level of estradiol show gradual increase from pre-pubertal to peri-pubertal stages and become maximum at puberty where ovulation takes place. So Estradiol hormone plays an important role in ovulation.

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent: Informed consent was obtained from all individual participants included in the study. **Conflict of Interest:** The authors declare that they have no conflict of interest.

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