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Research Article

**A COMPARATIVE RESEARCH TO ASSESS THE
ACHIEVEMENT OF SCIENTIFIC PREGNANCY THROUGH
INTRACYTOPLASMIC SPERM INJECTION****¹Dr. Syeda Sajila, ² Dr Hafiz Muhammad Sultans, ³Dr Tayyaba Tariq**¹Mayo Hospital Lahore²Medical Officer Urology Department Jinnah Hospital Lahore³Allied Hospital Faisalabad, PMDC # 81953-P.**Abstract:**

Objective: The objective of this research is to liken top to middle estradiol share with probability of fruitful beginning afterward-intracytoplasmic sperm inoculation.

Methodology: This research was directed in Service Hospital, Lahore (February 2017 to August 2017) and contained pair exposed to intra-cytoplasmic semen inoculation. Down-regulation of ovaries was measured by envisioned spur, ovulation beginning, oocytes recovery, intra cytoplasmic semen inoculation, in vitro maturing of embryos and lastly blastocysts transmission. Serum estradiol was distinguished by enzyme-linked immunosorbent scrutiny on ovulation initiation routine embryo communication. Letdown process was noticed by beta human chorionic gonadotropin 5-25mIU/ml [Group I; non-pregnant]. Women having beta human chorionic gonadotropin >25mIU/ml and having no cardiac action afterward 4 weeks of transmission was put in Group II (pre-clinical abortion) and endorsement of foetal heart in last included Group III (clinical pregnancy). Facts were studied by means of SPSS.

Results: Total 323 pairs originally registered, embryo transmission was passed out in 282[87.3%] women. Scientific pregnancy was attained in 101[36%] pairs, whereas 61(21.63%) had pre-clinical abortion and 120[42%] pairs were non-pregnant. The highest/middle-luteal proportion stayed little [(2.3) in patients who have great oocyte ripeness [p=0.001] and insemination degree (p=0.003) related to non-pregnant women who had extraordinary crowning/middle-luteal estradiol proportion [2.56].

Conclusion: Extraordinary top estradiol done preservation of ideal stages in middle-luteal phase is compulsory for establishment of pollinated ovum and achievement of scientific pregnancy.

Keywords: Aided generative cure, measured ovarian spur, Embryo transmission, Gonado trophin discharging hormone agonists, Intra-cytoplasmic sperm vaccination, Peak estradiol, mid-luteal estradiol, proportion of top/middle luteal E2. [JPMA 64: 780; 2014].

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INTRODUCTION:

Aided imitation is technical aid provided to unproductive pairs. The actions signify a combination of development in composition, endocrinology, pharmacology, diagnostic technology and medical carefulness [1, 2]. The most important actions working in assisted reproductive clinics (ARC) include in vitro pollination and intra-cytoplasmic sperm injection (ICSI). ICSI includes particular action strategy in which pair is intricate for period of slightest 6 weeks [3, 4, 5]. The widespread, luxurious and rigorous cure of at slightest six weeks of pair's participation regrettably ends up through extreme achievement ratio of 25-30%. The adverse pregnancy check arises as hindrance for the pair as well as unproductiveness experts. There are many parental and foetal reasons that is liable for letdown of implantation throughout the thin gap of embedding. Finding of one of these aspects might help in assortment of pairs, development of cure strategies and guess of ICSI results [6].

ARCs doing well in creation all likely efforts to develop achievement rates. The top estradiol (E2) dignified on the day of human chorionic gonadotrophin (hCG) management is linked through expansion and development of cavities and improved result after in vitro pollination (IVF)-ICSI processes. The strict part of middle luteal E2 is subject to alterations on foundation of calculation on diverse days of luteal stage. Few researches highlighted character of proportion of peak-middle luteal E2 on pregnancy consequence, few researchers found that proportions superior as compared to five were linked with an opposing result. [7] The benefit of this research was to discover a link of E2 proportion in follicular and mid-luteal stage with pregnancy result.

METHODOLOGY:

The research was led in Service Hospital, Lahore (February 2017 to August 2017). Population was designed by means of Formula $n = Z^2 pq/e^2 = (1.96)^2 (0.3) (0.7) / (0.05)^2 = 323$ 'e' is border of mistake. Research shows that positive pregnancy proportion of ICSI is about 25-30%. After noting the possibility, we got population of 323 patients at 95% confidence interval (CI) with 5% brim of mistake. By means of suitability population, 323 agreeable pairs were registered meeting present standards of women age 18-41, length of sterility greater than 2 years, mutually ovaries having no morphological defects, regular menstrual order (25- 35 days), body mass index (BMI) of 18-27 kg/m², basal Follicle-stimulating hormone (FSH) (day 2) serum equal <10IU/mL, selected for extended procedure by Gonadotrophin releasing hormone agonist (GnRha),

stimulated by inoculation of recombinant sac inspiring hormone (rFSH; Puregon) and retained on progesterone provision with 400mg cyclogest pessaries. Women on GnRh rival, short-down instruction with GnRH agonist and ICSI with sperm recovery by testicular operation were omitted.

Population was down-regulated with regular injection DecaPeptyl (GnRha) from middle-luteal stage of previous cycle shadowed by controlled ovarian stimulation (COS) with rFSH (injection Puregon S/C) from second to third day of sequence for 13±2 days. Ripeness of sac was measured by Trans-vaginal scan (TVS) opening from fifth day of COS till result of Oocyte pick-up (OPU). Ovulation induction (OI) with intra-muscular inoculation of hCG (Pregnyl 10,000 IU) was done with majority of established sacs; magnitude >20mm. Venous models were occupied for approximation of top E2 on that day. Oocytes were saved 36 hours later on OI by vaginal ultrasound probe with 16G connector and double lumen oocyte aspiration pointer on 14th, 15th or 16th day of COS. Together oocytes were exposed and moved to the incubator for around 1-2 hours prior to ICSI measures. Semen examination was done by strict Kruger's standards. ICSI by microinjections of spermatozoa was done at correct approaches to the site of polar body underneath the microscope. Pollinated embryos (occurrence of two pro-nuclei; 2PN) was measured and embryos sorted on different days for their developing features in vitro; cleavage till disparity into separate cell kinds by creation of fluid-filled cavity (blastocysts). Embryo transfer (ET) of blastocysts was completed seven days after OI by Sims-Wallace Embryo Replacement Catheter under ultrasound supervision. Luteal care was kept by progesterone vaginal pessaries (Cyclogest 400mg) twice a day from day of OPU. Examples for mid-luteal estimation of E2 were taken on day of ET on day 19 or 20 of sequence.

Solitary serum beta hCG measurement was done on examples obtained by peripheral venipuncture fourteen days afterward egg gathering as result indicator. TVS was done at 5-week gestation to recognize scientific pregnancy from pre-clinical abortion. On foundation of beta CG and TVS, outcomes were classified into sets; I, non-pregnant by beta hCG 5-25mIU/ml; II, pre-clinical abortion beta hCG>25 mIU/ml having no foetal cardiac action on TVS; III scientific pregnancy having beta hCG>25 mIU/ml and cardiac action established by TVS.10 The Top/middle-luteal E2 was designed in all of three sets. Pregnancy results and related degrees were well-defined by means of normal meanings as shadows: Oocyte retrieval degree was figure of oocytes saved

in contrast to sum of cavities designed. The percentage of ripe oocytes was oocyte ripeness degree. Fertilization rate (FR) was share of micro-injected oocytes subsequent in 2PN creation. Implantation rate (IR) was quantity of gestational sacs visualized on TVS separated by quantity of embryos moved. [13] Pregnancy rate (PR) was designed by existence of an intrauterine gestational sac detected on TVS each number of patients in sequence. Information was entered into MS Excel and transferred to SPSS 15 for numerical investigation. Qualitative variables (age group) were abridged in terms of incidences and percentages and average standard deviation (SD) was used for continuous/quantitative variables. For inferential study, nonstop variables were seen whether they

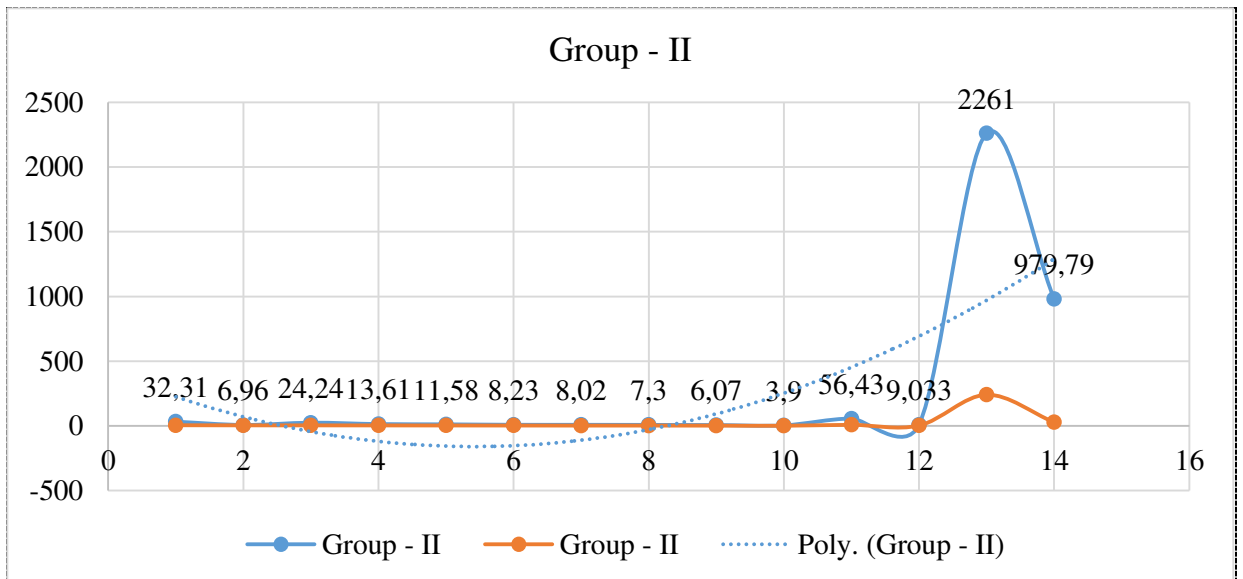
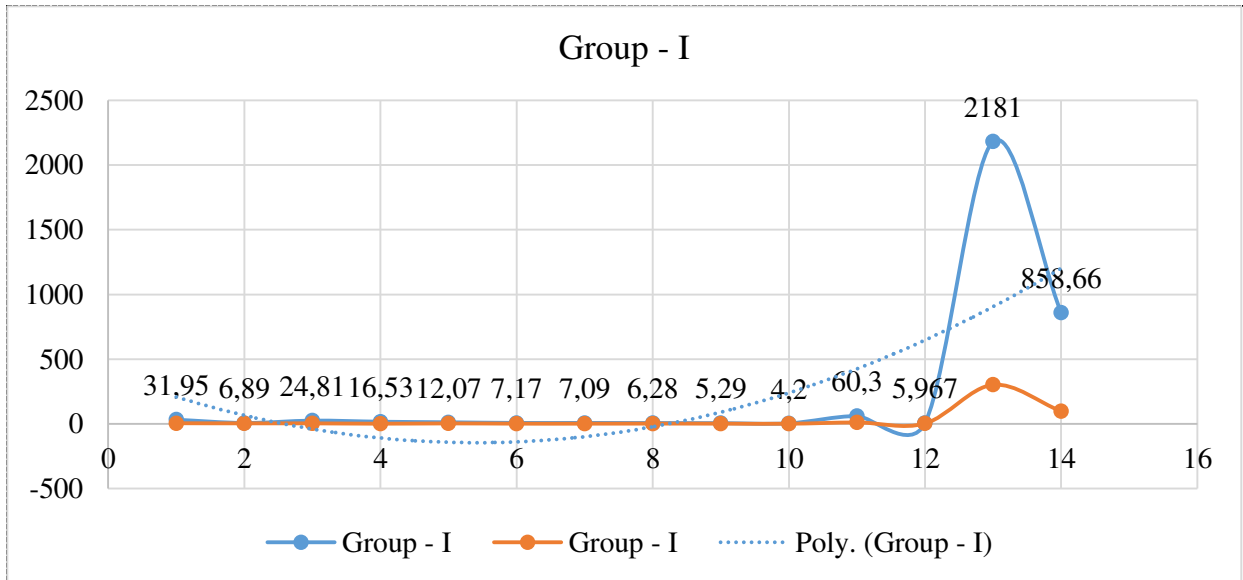
shadowed usual delivery. This inference was done by means of Kolmogorov-Smirnov's test and if P value found to be greater than 0.05, variables were measured to be normally dispersed. Outcomes of standard variables in result groups were likened by examination of variance, while Kruskals Wallis test was used for non-normal variables. In all numerical study, $p < 0.05$ was measured statistically important.

RESULTS:

In total of 323 pairs primarily registered, embryo transfer (ET) was carried out in 282(87.3%) women. Scientific pregnancy was attained in 101(36%) pairs, whereas 61(21.63%) pairs had pre-clinical abortion, and 120(42%) pairs were non-pregnant. The over-all average age of women was 31.55 ± 4.62 years with

Table – I: Demographic and cycle characteristics

Rates in percentages	Group - I		Group - II		Group - III		P value
	Mean	±SD	Mean	±SD	Mean	±SD	
Age (Years)	31.95	4.61	32.31	4.7	32.17	4.71	0.871
Duration of sterility (Years)	6.89	3.78	6.96	3.82	7.46	4	0.529
Body Mass Index (kg/m ²)	24.81	3.68	24.24	3.64	23.56	3.63	0.042
Antral follicular sum	16.53	1.15	13.61	3.27	13.07	2.55	0.001
Ovarian Volume by Ultrasound (cm ³)	12.07	3.33	11.58	2.82	10.9	2.78	0.004
Pre Ovulatory Follicle	7.17	1.4	8.23	2.47	8.31	1.7	0.000
No of oocytes/patient	7.09	1.32	8.02	2.11	8.21	1.52	0.000
No of oocytes Metaphase II	6.28	1.94	7.3	2.05	8.03	1.44	0.000
No of oocytes inseminated	5.29	1.59	6.07	1.64	6.65	1.07	0.000
Number of puregons in one day	4.2	0.76	3.9	0.64	3.83	0.48	0.000
Total quantity of puregons	60.3	10.96	56.43	7.88	53.99	5.72	0.000
Endometrial thickness	5.967	2.691	9.033	2.345	11.455	2.037	0.000
Highest Estradiol on the day of hCG pg/ml	2181	301.56	2261	240.23	2529.05	193.99	0.000
Estradiol in mid luteal phase pg/ml	858.66	97.21	979.79	27.36	1109.46	136.28	0.000



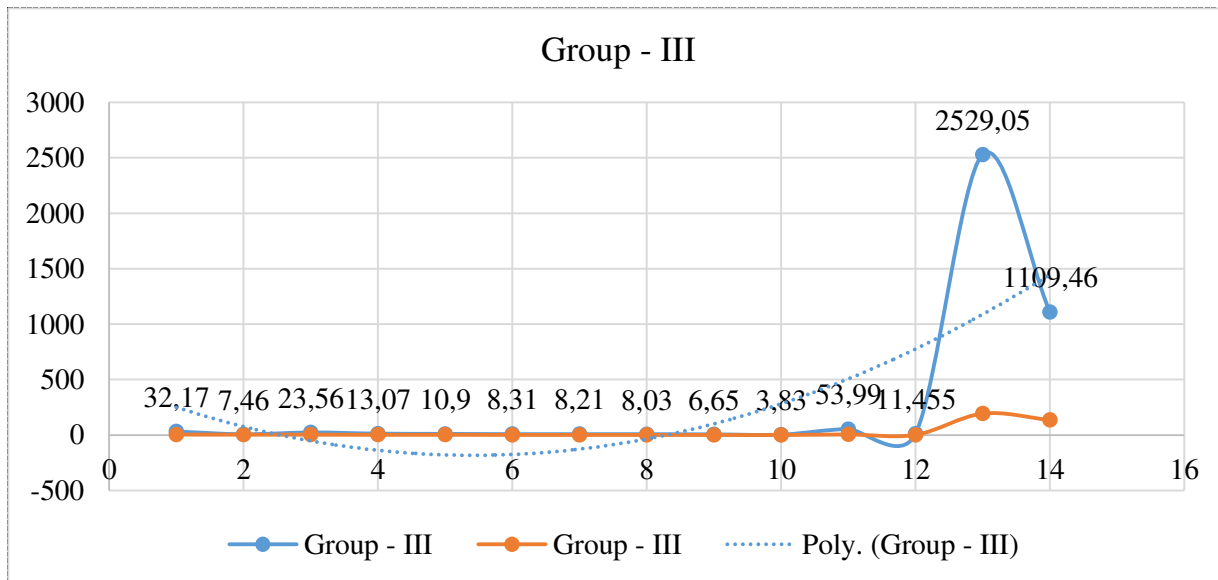
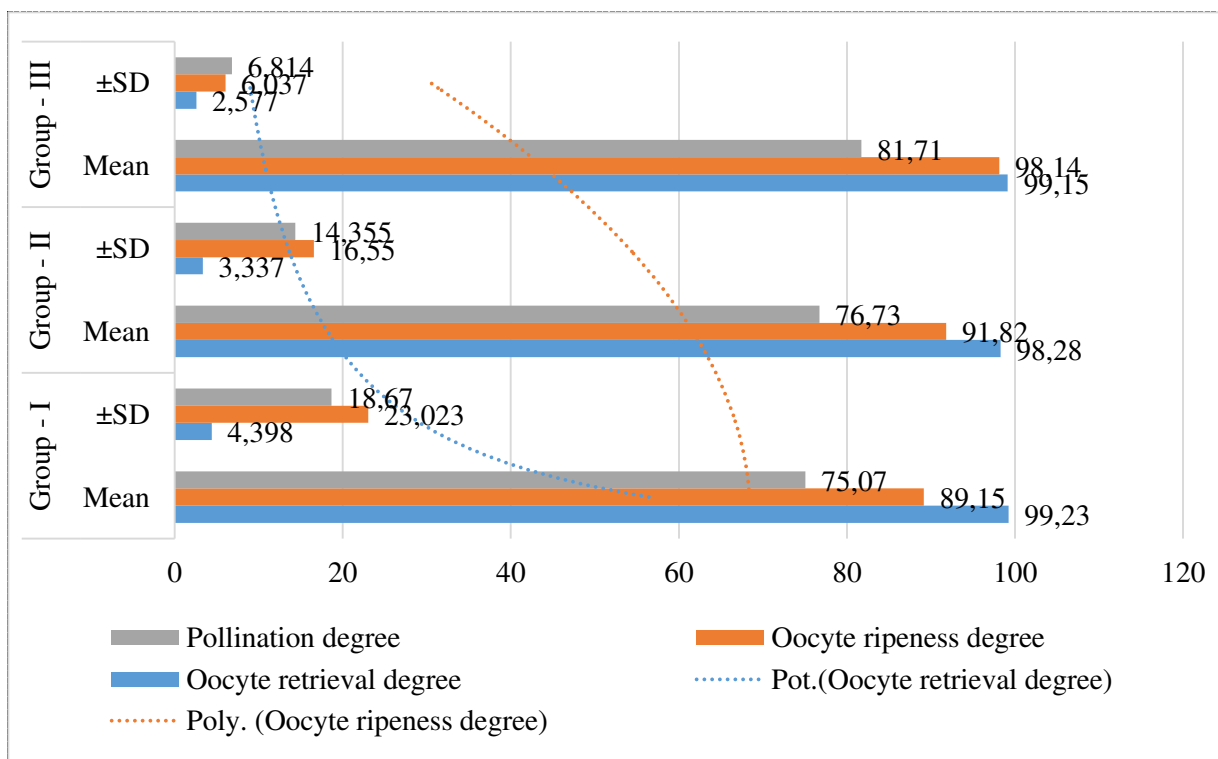


Table – II: Contrast of generative rates

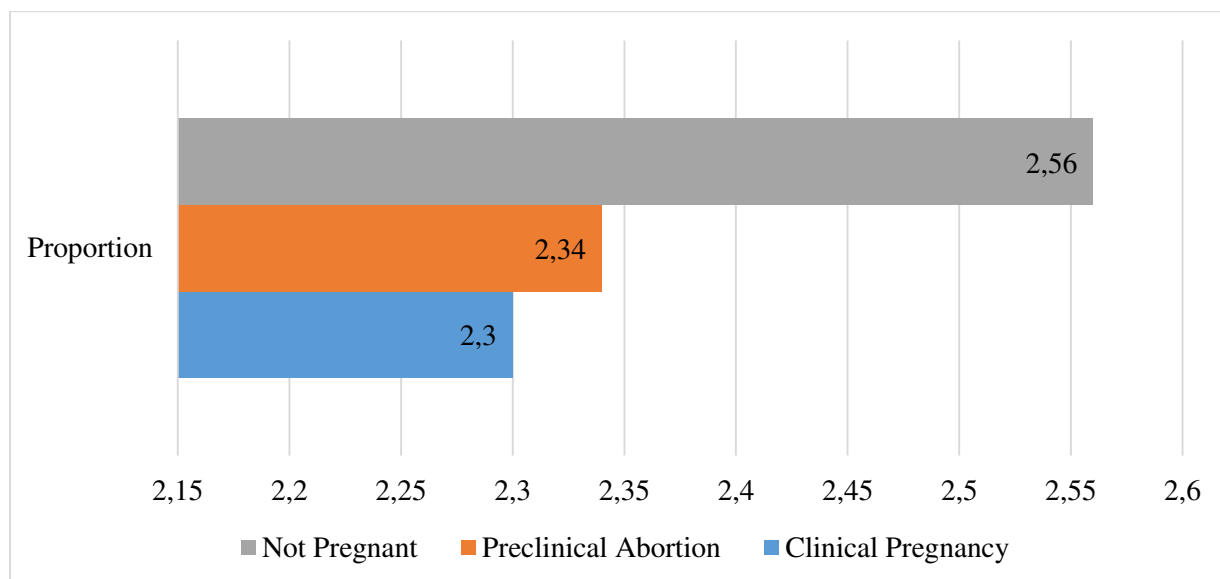
Rates in percentages	Group - I		Group - II		Group - III		P value
	Mean	±SD	Mean	±SD	Mean	±SD	
Oocyte retrieval degree	99.23	4.398	98.28	3.337	99.15	2.58	0.217
Oocyte ripeness degree	89.15	23.02	91.82	16.55	98.14	6.04	0.001
Pollination degree	75.07	18.67	76.73	14.36	81.71	6.81	0.003



Duration of sterility to be 7.48 ± 3.68 years. women reason of sterility was found in 70(25%) patients, 36 (13%) had mysterious sterility, man sterility was 113(40%) and together they were accountable in 63(22%) circumstances. Women had an average BMI of $23.55 \pm 3.86 \text{kg/m}^2$ by endometrial width of 8.58 ± 3.41 . Entire quantity of puregons used/patient were 60 ± 3.07 , whereas used/day were 4.00 ± 0.21 . Oocytes retrieved per patient were 19.35 ± 0.52 (oocyte recovery rate was 97.21 ± 6.8) out of which 15.07 ± 0.49 were inseminated (FR: 61.01 ± 1.71), 10.57 ± 0.42 sliced (cleavage rate: 53.05 ± 22.95) and 1.63 ± 0.03 blastocysts moved (31.20 ± 2.99). In comparison to highest/middle-luteal proportion in altogether sets were designed (Figure). In the non-pregnant set value was 2.5, it was 2.34 in set of pre-clinical abortions and it has 2.30 in set that had scientific pregnancies (Table-1). The last set with little peak/mid-luteal proportion demonstrated better oocyte quality parameters and endometrial thickness with less number of rFSH injections. Top E2 stages were the uppermost in similar set III related to other two (Table-2). IR of 83.66 ± 22.84 in set III was also superior than set II 4.92 ± 21.804 .

Table – III: Comparison of highest/middle-luteal Estradiol ratios

Pregnancy/Abortion	Proportion
Clinical Pregnancy	2.3
Preclinical Abortion	2.34
Not Pregnant	2.56



DISCUSSION:

The work of E2 unconfined in follicular stage is accountable for follicular growth as well as endometrial proliferation and hyperplasia of both glandular and stromal constituents. This is likely by gathering of precise proteins, developmental aspects, hormones in addition to up-regulation of hormone receptors. The approximation of differences in E2 covered throughout proliferative and secretory phase of endometrial order by its effect on follicular growth, endometrial expansion and uterine openness could therefore help in deliberation of E2 proportions for better consequence and progress in scientific pregnancy rates after ICSI. The part of E2 levels on

day of hCG management for progressive pregnancy result is not acknowledged by few researches. In this research, set III patients with highest/middle luteal E2 proportion of 2.3, patients had the uppermost peak E2 in which higher number of oocytes were recovered with little quantity of rFSH (puregon) which is similar to other studies [8]. Alike outcomes were stated by Kara et al. Development with oocyte and embryo superiority limitations with high peak E2 was detected by few others. Other researchers detected upper peak E2 levels with improved pregnancy proportions. On the other side, few researches recommended a destructive role of high E2 levels on day of hCG management for pregnancy

accomplishment. [20,21] In this research our patients with high peak E2 helped in improved oocyte ripeness, pollination and cleavage of embryos. In inspiration cycles of ICSI with GnRha therapy, 2-3 weeks needed for the reinstatement of pituitary function. [9] In these days, corpus luteum saves production of E2 and progesterone (P) in best amounts to uphold endometrial receptivity through decasualization. [10] Very few sets have witnessed that mid-luteal E2 levels do not upset IVF result. An increase was noticed in E2 in luteal segment of pregnant females that is in contract by rumors of numerous study sets. Fujimoto et al. witnessed lower pregnancy degree in females with reduced E2 stages in late mid-luteal stage in IVF cycles. [10] Reduction in luteal E2 of set I patients were related with reduced intercessory prayer (IP) and PR in our research, which is similar to researches completed by others. Establishment was unsuccessful in luteal phase of set I patients because of deterioration in purpose of corpus luteum having fall in middle-luteal E2 and announcement of Inhibin. The deterioration in middle-luteal E2 and P stages were noted to be related with letdown of beginning. The reduction in E2 stages through mid-luteal stage was extra in non-pregnant ladies compared to pregnant ladies ($p < 0.001$) having proportion of 2.3 related with scientific pregnancy and > 2.3 was found in non-conception sequence. Contradictory outcomes of highest and mid-luteal E2 points have been stated among beginning and non-conception sequences which might not spread numerical importance. In the end it was suggested that absence of numerical important difference by Ng et al. was little pregnancy proportions in those sets. The proportion of highest/mid-luteal E2 level greater than 2.5 expected reduced establishment degree and pregnancy result. Establishment of embryo depends on excellence of embryos and endometrial receptiveness.[3] Meanwhile blastocysts with extreme establishment potential were cast-off in this research, therefore improved establishment was credited to endometrial receptiveness delivered by protection of hormones in luteal stage. Increased E2 shaped by rising follicles upsurges endometrial receptiveness which reduces it vulnerable to apposition, attachment and apposition for intruding blastocyst [11]. This receptiveness is needed to be upheld in luteal stage for fruitful result. The outcomes of this research tinted that augmented endometrial thickness was perceived in females who had a peak/mid-luteal E2 proportion of 2.3. The P levels are not stated in our research due to prejudices with the usage of progesterone pessaries after OPU. Many researches completed on approximation of top to middle luteal E2 proportions deviate on foundation of time for approximation of luteal E2. In our

research, serum E2 level was projected on day of blastocyst transmission, which is seven days afterward OI. This approximation was completed in 11 days after OI by Ganesh et al. who got that luteal E2 stages were a gifted indicator for fruitful pregnancy [12]. As this is the primary research in Pakistan determined a cut-off worth for the E2 proportions, that will allow Assisted Generative Technology (ART) to visualize a conception by estimation of Peak/mid-luteal E2 proportion.

CONCLUSION:

The proportion greater than 1 in all result groups for examining impact of top/middle-luteal estradiol on pregnancy result afterward ICSI designated that worth of peak E2 was continuously noted to be greater than middle-luteal E2. The top and mid-luteal E2 was extreme in patients who required scientific pregnancy connected to pre-clinical abortions and non-pregnant set. Moreover, a proportion of 2.3 in scientific pregnancy set highlighted reputation of middle-luteal E2 in upkeep of pregnancy.

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