Lycopene Ameliorates Ovarian Follicular Maturation in Rat Model of Polycystic Ovarian Syndrome: A Histomorphological and Functional Study

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Original Article

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ABSTRACT

Background and Aims: The polycystic ovarian syndrome is a menacing metabolic condition with high prevalence rate in Asian countries involving women of reproductive age. This study was commenced to assess favorable effects of Lycopene---a dietary component in letrozole-induced PCOS rat model.

Materials and Methods: Fifty adult female Sprague Dawley rats were divided into five groups, ten rats each for a study of 5weeks. Control group A was given standard rat diet. Rats of experimental group B were given 1mg/kg of Letrozole to induce PCO model. Group C was given 1mg/kg of letrozole+15mg/kg/day of lycopene. Group D was given 1mg/kg of letrozole+ 500 mg/kg/day metformin. Group E was given 1mg/kg of letrozole +combination of Lycopene and metformin together. Relative body weight was taken on the day1, day21 and end of experiment. Antioxidant activity was tested using CAT, SOD and MDA. Ovaries were removed for H&E staining and studied under light microscopy. Statical analysis was carried out for result interpretations.

Results: The results showed, reduced rat weight by use of Lycopene. Histological architecture of ovary showed better count of secondary and graafian follicles towards normal values which was quite reduced in group B proved by significant *p-value*<0.001. While raised number of atretic follicles in group B 6±1.6 was reduced to 3±0.9, 4±0.6, 4±0.7 in group C, D &E respectively. Overall improvement in distorted/ cystic ovaries was noted by treatment therapy, evident by significant p-value. Group B showed mean count of cyst 7±1.0, which was brought to 2±0.5, 3±0.8, 2±0.7 in groups C, D &E. Elevated Oxidative markers (ROS) were also reduced.

Conclusion: Dietary intake Lycopene can ameliorate histological and oxidative damage in polycystic ovaries.

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Key Words: Lycopene, letrozole, oxidative stress, PCOS.

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BACKGROUND

The most frequent endocrine disorder, polycystic ovarian syndrome (PCOS) was first described in 1935 by Stein and Leventhal. The presence of at least two of the three criteria: persistent anovulation, hyperandrogenism (clinical or biological), and polycystic ovaries, is acknowledged mainly by specialized society recommendations for the diagnosis of PCOS[1]. Infertility, metabolic syndrome, obesity, impaired glucose tolerance, type II diabetes mellitus (DM-2), cardiovascular risk, depression, obstructive sleep apnea (OSA), endometrial cancer, and nonalcoholic fatty liver disease/nonalcoholic steatohepatitis (NAFLD/NASH) are among the many morbidities linked to PCOS[2]. PCOS patients usually have high oxidative profile which causes disturbance in antioxidant balance resulting in production of reactive oxygen species. According to the National Institute of health (NIH) and Rotterdam criteria, 6 –10% of women of the reproductive age group (15-49 years) are affected by PCOS[3]. The prevalence of this syndrome is higher among Pakistani women (52%) than among Western Caucasian women, 20%–25% in UK[4].

Letrozole is a nonsteroidal aromatase inhibitor. Aromatase is an enzyme that catalysis the conversion of androgen to estrogen in granulosa cells. Treatment with Letrozole, inhibits this conversion (testosterone to estradiol) and keeps body at hyperandrogenic state (a critical component for the formation of PCOS model)[5,6].

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Letrozole exposed adult female rats exhibit almost all the features of PCOS.

Insulin-sensitizing agents, such as biguanides, are used to treat PCOS. Metformin, an antidiabetic drug, helps ovaries to make hormones, either directly or indirectly[7]. In type 2 diabetes, biguanides help the insulin receptor's tyrosine kinase activity. Prolonged use of metformin can cause various side effects. Over the last few years, many trials of supportive management like lifestyle modification, acupuncture, yoga, meditation, aromatherapy, homeopathy, weight loss, and antioxidants have been given in PCOS[8].

Lycopene (C40H56) was first discovered in the tomato by Millardet in 1876 and was later named by Schunck[9]. Nowadays, it is ubiquitous in the diet of humans around the world due to its powerful antioxidant properties[10]. It is a member of the beta carotenoid group, vibrant red in color with a molecular weight of 536.89 g/mol, corresponding to 89.45% carbon and 10.51% hydrogen. It has pH ranging 3.5 – 4.5 and is insoluble in water[9].

The main source of Lycopene in the human diet is tomato, the lycopene content may vary significantly due to environmental factors, agricultural techniques as well as tomato types and ripening[11]. Other than tomatoes, it also appears in seeds and peel residues of other vegetables and fruits like watermelon, apricot, papaya, guava, red grapes, pink grapefruit, pumpkins, rosehip fruit, orange, mango, pomegranate and carrot[12,13].

It has a high scavenging ability for singlet oxygen free radicals because of high number of double bonds in its structure that can donate many electrons to free radicals[14]. Lycopene can improve the cellular antioxidant defense system through the regeneration of the non-enzymatic antioxidants, vitamins E and D. In fact, it is believed that Lycopene can protect vitamin E[15]. It also protects cellular apoptosis and necrosis by fighting against ROS.

In this study, the effects of Lycopene were assessed, and is anticipated to recover the complications caused due to PCOS.

MATERIALS AND METHODS

Fifty female Sprague Dawley rats , six to eight weeks old with no gross abnormality weighing 155–220 g[16]. were kept in the animal house of national institute of health sciences Islamabad for duration of 5 weeks (35 days). They were kept under standard temperature at 22 ± 0.5°C in air-ventilated room and were housed into clean stainless-steel cages under 12-hour light and dark cycle with 50% to 60% humidity[17]. Rats were given food and water ad libitum. Rat pellets and tap water was used as food during the whole experiment[18]. Animal handling, treatment and scarification was done as approved by Ethical committee of Department of animal NIH, Ref no. Riphah/IIMC/IRC/21/64.

PCOS model was achieved in 21 days by giving 1mg/kg/day of letrozole[19]. There were five groups in total. Each group comprised 10 female rats. Control group A was kept on standard routine pallet diet and water. Positive control group B was given 01 mg/ Kg letrozole mixed in standard diet. Group C was given 15mg / kg/day lycopene. Group D was given metformin 500mg/ kg/day. Group E was given 500mg / kg /day metformin and 15 mg/kg/day lycopene. Letrozole was given throughout the experiment, while metformin and Lycopene were given from day 22 till day 35 in treatment groups C, D, and E.

Before the completion of the experimental study, a pilot study was done at the end of the third week to confirm PCOS induction. Rats were sacrificed on day 36, 24 hours after the termination of experiment. Right ovaries were excised for histopathological study and the left ovaries for antioxidant assessment.

Anthropometrical parameters

Change in body weight was recorded at day 1 and day 21 and day 35 among all the experiment groups. Ovarian weight and gross appearance were evaluated among all the groups.

Ovarian histomorphology

The excised ovaries were fixed in 10 % formalin and processed further as a routine histological procedure; they were serially sectioned at 5um thickness using microtome. Three sections per ovary were done so not to miss any follicle. The slides were stained with hematoxylin and eosin using standard protocol. The mean count of secondary, graafian, atretic and cystic follicle were taken. Additionally, the diameter of cystic follicles were measured using, ImageJ software (1.53K Wayne Rasband and Contributors NIH, USA Java 1.8.0-172, 64-bit).

Estimation of oxidative stress

Ovarian tissue was homogenized in 2 ml of phosphate buffer (pH 7.4) and centrifuged at 12000 rpm for 30 min at 4 °C. Supernatant was collected to determine the antioxidant status of following assays: catalase (CAT), superoxide dismutase (SOD), malondialdehyde (MDA)[20].

Statistical analysis

All values were expressed as mean ± SEM. Data analysis was done using IBM SPSS statistics 21. Analysis of Variance (ANOVA) and Tukey's post hoc test for multiple comparisons. The value for $p < 0.05$ were considered significant.

RESULTS

Rat relative body weight

The maximum gain in body weight on day 35th was 325g, observed in the disease control group B (PCOS induced model) among all groups under study, showing significant p-value. Relative weights on day 35th in group C, D & E was 289, 290 & 279 respectively. Although there was a gradual increasing pattern of weight in all groups, from day 1st to day 21st and 35th. Weight gain in group B,

C, D & E on day21st was significant compared to control group A with p<0.001. It remained highly significant at day 35th as well. But it was non-significant when recorded on the first day among all groups (Figure:1).

Gross Appearance of Ovary

Normal control (group A) showed round to ellipsoid shape ovaries which were pale whitish in color and smooth in texture. In PCO, disease control (group B) ovaries became swollen, bulky, with irregular margins due to cystic appearance. These ovaries were found to be ovoid, deformed, crumpled, hard masses that possessed reddish to brownish shade (Figure:2). All three treated groups (C, D &E) showed improved appearance in terms of few cysts with slightly better regular margins.

Maximum rats showed whitish coloured ovaries, they comprise 36% of the total. Pale whitish ovaries were 26%. These two colours are indicative of normal ovaries with minimal changes noted. While 16% pink, 12% reddish and 10% brownish ovaries were seen among diseased and those rats which were in recovery phase (Figure:3).

On the basis of shape, most ovaries were round & ellipsoid with 24% each. Cysts were found in 20% of ovaries and 18% were edematous or swollen. Twelve % of ovaries were irregular in shape due to deformity. Shrunken ovaries were also noted, which were only 2% of the total (Figure:4).

Rat Ovarian weight

Disease control group B (PCOS) showed highest mean ovarian weight 0.22g (220mg). In other groups i.e., group C, D & E mean ovarian weights are decreased to 0.11g, 0.15g, 0.13g respectively which is close to control group A 0.09g (Figure:5).

Results were found to be significant (*p value* <0.001), using ANOVA. The inter group comparison using Post Hoc Tukey test shows, three treatment groups C, D, E and control group when compared with disease group B, results were highly significant statistically (*p-value* <0.001).

While when treatment groups C, D, E and control group A, were compared among themselves result was non-significant.

Control A, Diseased control B, Lycopene group C, Metformin group D and Combined group E

Ovarian Histology

In rat ovaries with PCOS, number of secondary and graafian follicle were decreased significantly, while more atretic and cystic follicles were noted mean of diameter was also higher.

In treatment groups C, D & E number of secondary and graafian follicles were improved. Atretic and cystic follicles were decreased with reduced diameter. Combination group showed best results among three groups and lycopene proved itself better than metformin.

Oxidative Stress Markers (MDA, CAT, SOD)

The mean level of MDA was very high 185.84±1.7 in diseased control group B, as compared to the normal Group A 143.98±0.9. While Lycopene, metformin and their combination reduced these levels by a highly significant amount 157.14, 165.34 & 151.94 respectively. The mean value of CAT was decreased in diseased control group B to 5.93, while normal control group showed mean of 33.62. In response to treatment by Lycopene, metformin and their combination helped in achieving CAT values near to normal i.e: 35.9, 29.5 & 39.6 respectively. Similarly, SOD mean levels were also lowered to 5.61 in diseased control group B, which was regained back to near normal in treatment groups C, D & E recorded as: 9.4, 6.4 & 10.0 Mean value of normal control that was recorded to be 8.48.

Since this is my own original controlled experimental research study, the table and figures presented are derived from my own research findings and data. As such, providing external citations for these tables and figures is not applicable or required. I have included descriptive titles and captions under (Table 1, Figures 6-11) respectively to properly cite and explicate these representations of my original results within the manuscript

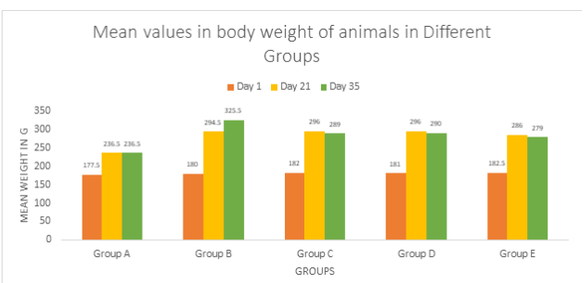

Fig. 1: Bar chart showing body weights of all the groups A, B, C, D & E at Day 1, Day 21 and Day 35th . n= 10, *p-value* ≤ 0.001

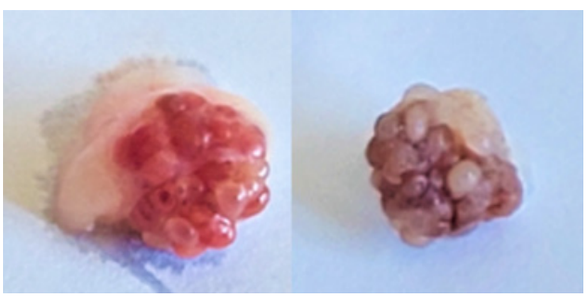

Fig. 2: Ovary of diseased group B; colour (red & brown) and shape (cystic & irregular)

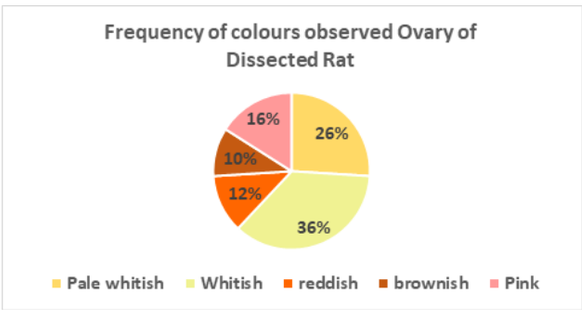

Fig. 3: Frequency of colours obtained in all groups under study are shown in pie chart

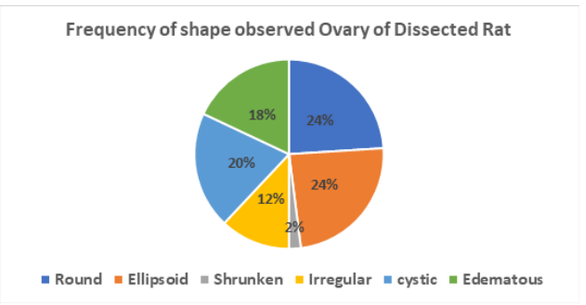

Fig. 4: Frequency of shapes obtained in all groups under study are shown in pie chart

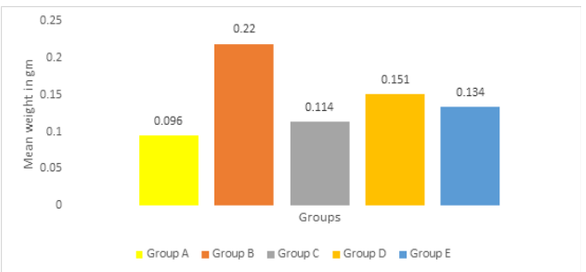

Fig. 5: Bar chart showing, rat mean ovary weight (g) in five study groups Control A, Diseased control B, Lycopene group C, Metformin group D and Combined group E

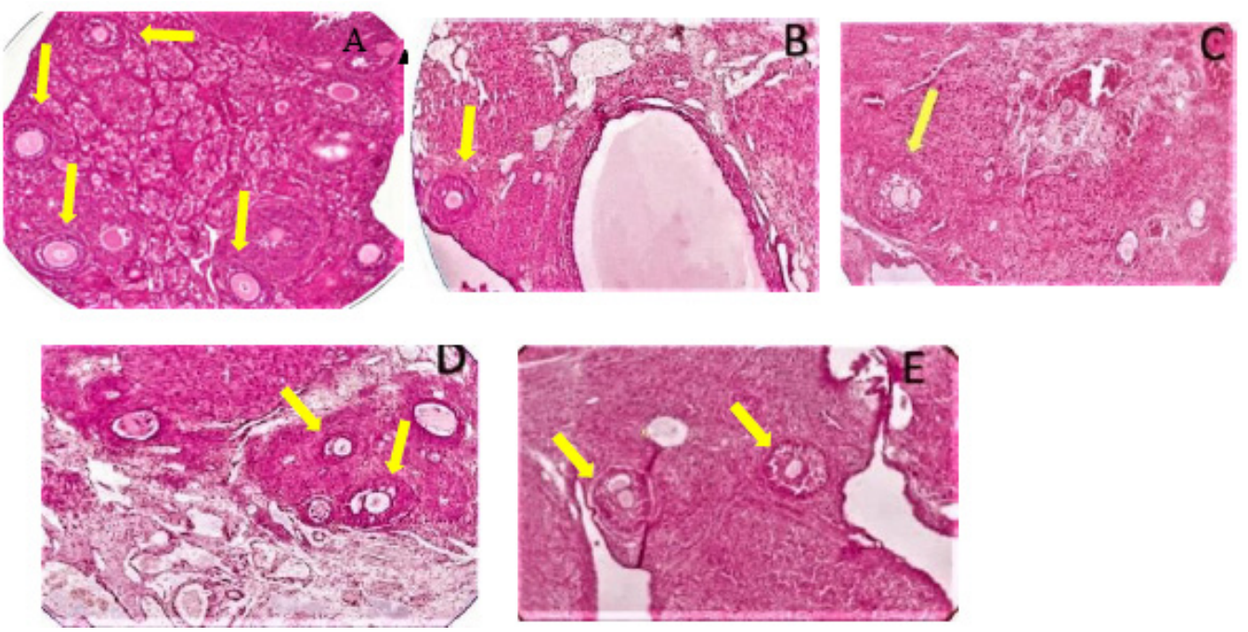

Fig. 6: Secondary Follicles: Photomicrograph of transverse sections of rat ovary showing secondary follicles pointed by yellow arrows in normal control A, diseased control B, Lycopene group C, Metformin group D & Combined group E (H&E stains at 10×10X).

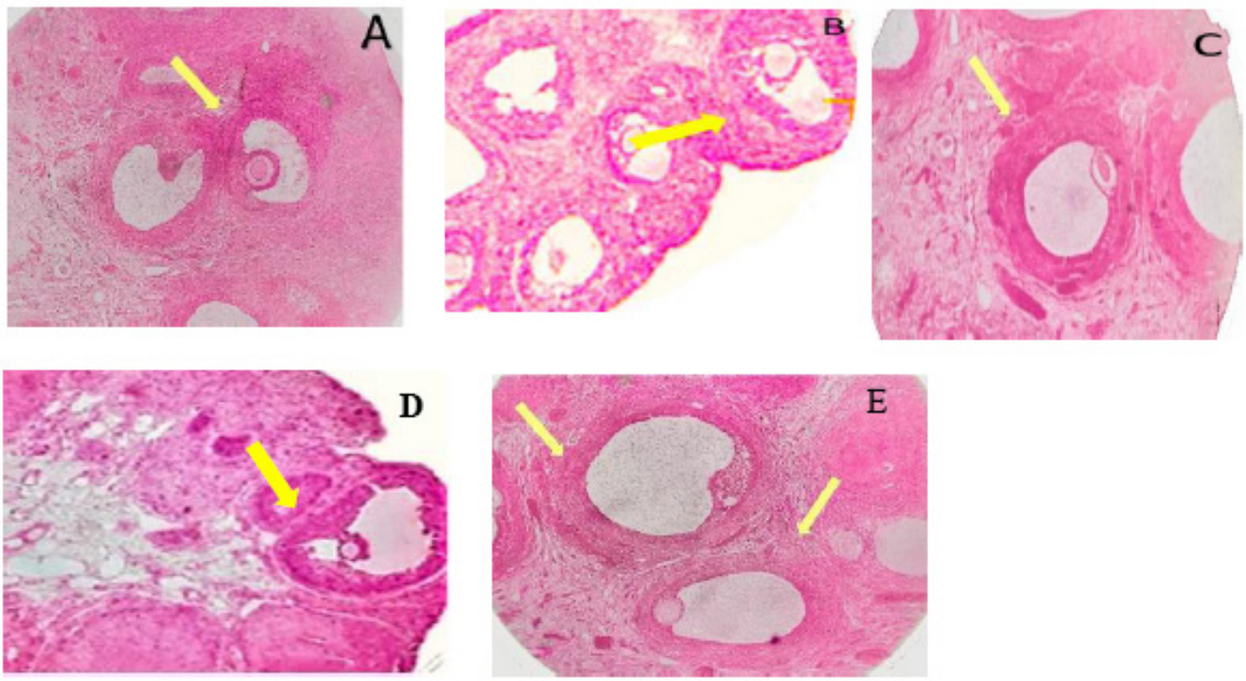

Fig. 7: Graafian Follicle: Photomicrograph of transverse sections of ovary, H & E-stained slides at 10 ×10X, showing graafian follicles pointed by yellow arrow. A: a normal graafian follicle. B: early graafian follicle distorted, C: healthy size graafian follicle. D & E: yellow arrow shows graafian follicles in metformin & combined group respectively.

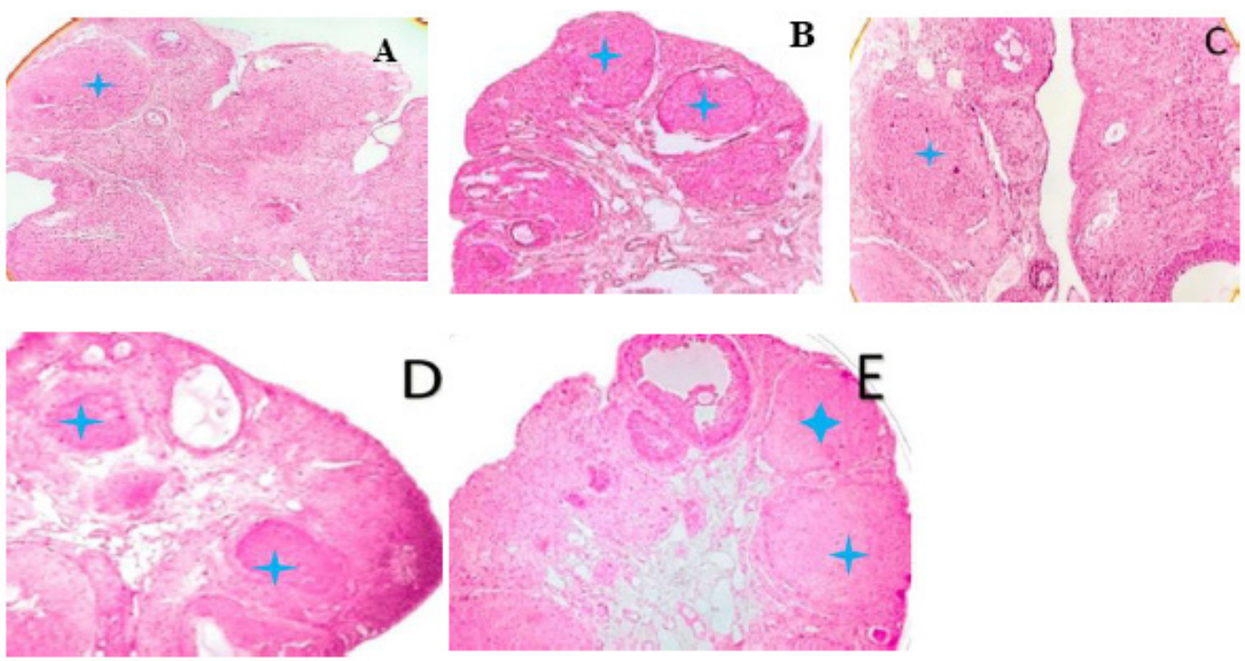

Fig. 8: Atretic Follicles: Photomicrograph of transverse sections of ovary, (H&E-stained slides at 10×10X) showing atretic follicles marked by blue stars. A: a normal presence of atretic follicles. B: PCO filled with AF,
C: lycopene group with fewer atretic follicles. D: metformin & E:combined group blue stars show less atretic follicles.

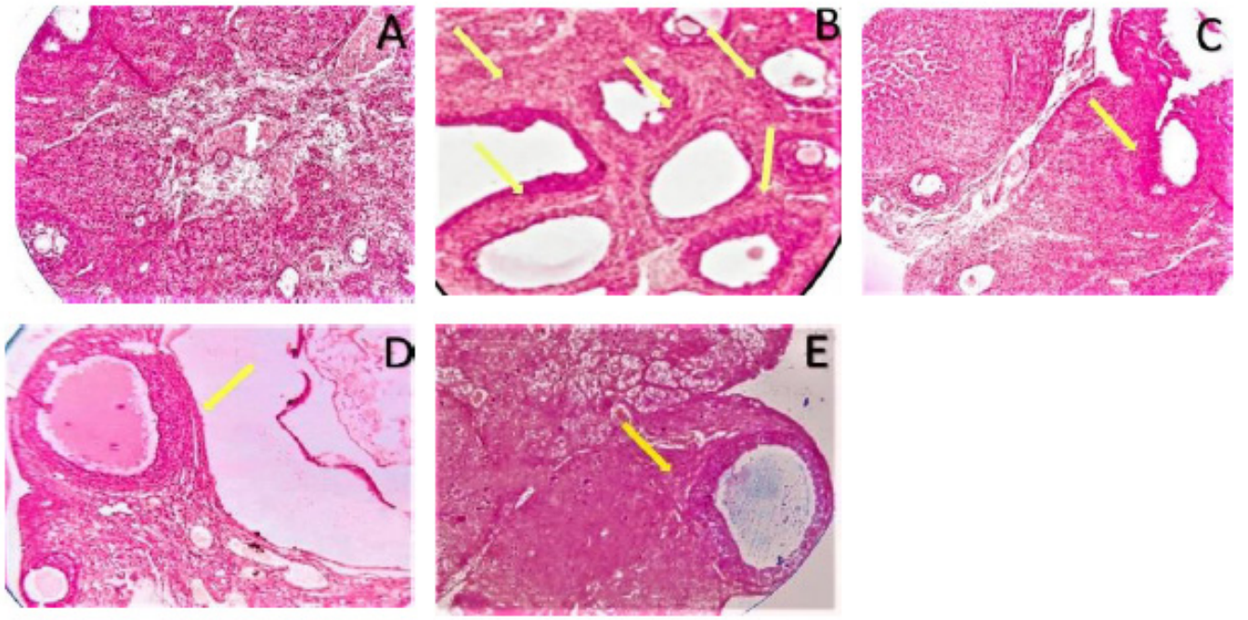

Fig. 9: Cystic follicles: Photomicrograph of transverse sections of ovary, (H&E-stained slides at 10×10X) showing Cystic follicles. A: presence no cystic follicle noted. B: PCO filled with CF, C: cystic follicles cleared off. D & E shows even improved ovary.

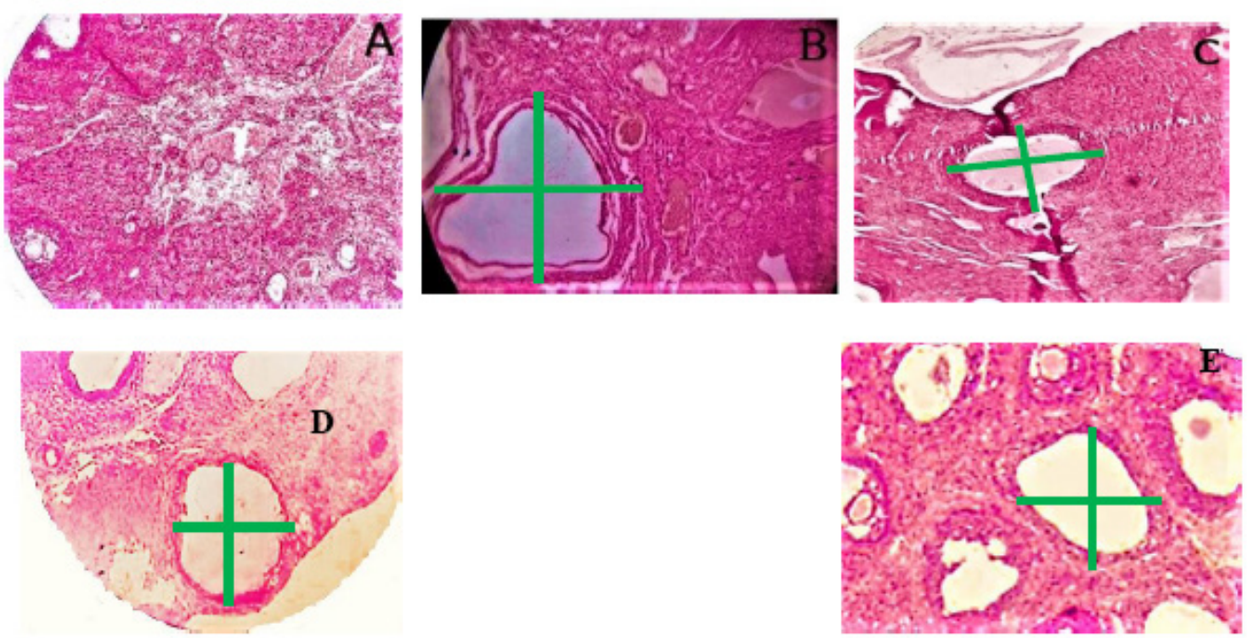

Fig. 10: Diameter of Cystic Follicles: Photomicrograph of transverse sections of ovary, (H&E-stained slides at 10×10X) showing diameter of Cystic follicles. B: a large cyst occupying almost whole field of vision, indicated by two dimensional lines. C: size of diameter of cystic follicle is much reduced. D & E shows regression in cystic diameter.

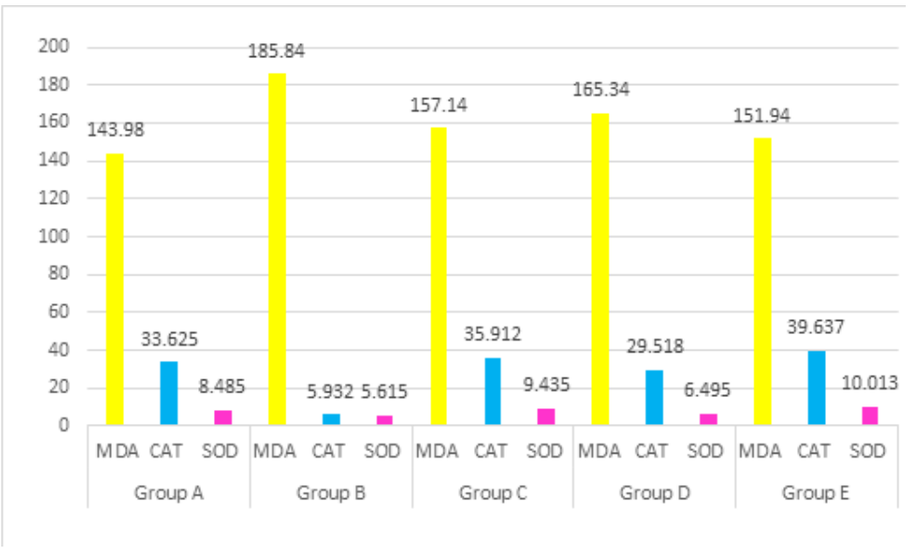

Fig. 11: Bar charts showing levels of MDA, CAT, SOD among groups normal A, disease B, lycopene C, metformin D, combination E.

Table 1: Mean ±SEM of count of Secondary, Graafian, Atretic, cystic and diameter of cystic follicles among all groups.

Parameters	Group A (Control)	Group B (PCOS)	Group C (Lycopene)	Group D (Metformin)	Group E Lycopene+Metformin
Mean number of secondary follicles	4±0.21	1±0.18	3±21	2±0.34	4±18
Mean number of Graafian follicles	3±0.15	0.1±0.1	3±0.31	2±0.33	4±0.16
Mean number of atretic follicles	2±0.13	6±0.52	3±0.3	4±0.22	4±0.22
Mean number of cystic follicles	0.00±0.00	7±0.34	2±0.16	3±0.26	2±0.23
Mean diameter of cystic follicles	0.00±0.00	912±40.09	465±26.98	597±22.93	475±21.93

DISCUSSION

Griffin *et al*.in 2002[21] documented the complex nature of PCOS due to broad spectrum of clinical presentations, including metabolic and reproductive disorders[22]. The effective management can be attained by combination of lifestyle modifications like weight loss, exercise, stress free life and healthy dietary intake with lower lipid content and use of fresh vegetables and fruits.

Decreased number of secondary follicles and graafian follicles in PCO group, was proved by a review study done in 2019, by Masoumeh Mohammadi, published in Tehran[23]. He described all changes on cellular level to strengthen his work, explaining role of ROS in ovarian steroidogenesis, testosterone production, luteolysis, oocyte maturation, ovulation and fertilization. The literature search showed no effect of steroidogenesis over primordial follicles in control and experimental groups[4]. In current study, the three treatment groups, confirmed improved number of secondary follicles indicative of absence of cytogenesis and retrieved normal folliculogenesis. Maximum secondary follicles were revived with combination of Lycopene and metformin. Saeed sherafatmanesh *et al*. in 2020[24] used thylakoid an antioxidant along with metformin showed beneficial effects on functional parameters and counteracted oxidative and glycated stress in ovarian microenvironment, demonstrate inconsistency with the present study.

Maryam Ekramzadeh *et al*. in 2019[24] proved that caraway extract counteracts metabolic and hormonal PCOS symptoms and positively affected folliculogenesis, ovulation and pregnancy rate. According to Nur. G. kulhan,[25] it can be hypothesized that Lycopene directly affects cumulus-oocyte complex (COC). Lycopene supports lipid metabolism facilitating beta oxidation. Thus, providing energy supply assuring correct spindle assembly and chromosome separation during meiosis.

The current study showed that the count of graafian follicle was inconsistent with the previous studies explaining logical grounds and justified mechanisms. The treatment groups showed better and healthy graafian follicles. Inter-group comparisons showed the number of graafian follicles were highest in combination group, while Lycopene was effective in recovery of graafian follicles than metformin alone. It is important to document that no contrary study was found in this regard[26]. Study by Giovaana Di Emidio *et al*. on PCO rat model by using L. Carnitine showed improvement, not only in count of graafian follicle but also it's good size diameter[27].

In the present study, the increased number of atretic follicles were found in the PCOS group. But an improved

ovarian environment is revealed by reduced follicular atresia and restored steroidogenesis by use of Lycopene. Although, count of the atretic follicles was also reduced in metformin and combination groups but still, count was not as few as, in normal group. This observation of current study is inconsistent with previous study done by Ghazal shaheen *et al*. in 2018, who showed the reduction in count of atretic follicles but many of them were still evident[28]. Another study by Ali Almajwal *et al*, 2019[29] revealed ROS's involvement in apoptotic cascade activation in atretic follicles along with the appearance of macrophages within granulosa cells.

In the present study, multiple fluid-filled sacs on the ovarian surface were noted "follicular cysts" in the PCOS group. On microscopy, they showed the absence of oocyte, granulosa cell layer attenuation and theca and cellular debris hyperplasia in antrum. The size of these cysts was of variable diameters, more significant than that of the other follicles correlating to increased intra-ovarian androgen levels. Kafali *et al*. observed similar cysts in PCOS rat model[24]. The Lycopene treated group possessed well-developed antral follicles showing improvement from a typical cyst seen in the PCOS group. A similar study by Rezvanfer *et al*.in 2012,[30] who used 'pioglitazone' and showed reduction in number of cystic follicles and a high number of secondary and Graafian follicles thus collaborating with findings noted in present study[31]. Sarwat Jahan *et al*. performed similar study using rutin (antioxidant) in Letrozole induced PCOS and observed reduced number of cysts. There was study by Olugbeni T,*et al*. in 2019, who used dehydroepiandrosterone along with vitamin C for 15 days to reduce the number of formed cysts[32].

Nur G. Kulhan *et al*. 2019 studied oxidative damage in rat ovaries induced by Cisplatin (anticancer) and concluded reversal of ovarian damage with improved histological architecture by use of lycopene. This conclusion provided basis, that damaged ovary (PCOS) can also treated by lycopene for ameliorative effects[32].

In current study, PCO group showed higher levels of oxidative stress, measured by presence of ROS. Demet Aydogan Kirmizi *et al* 2021[33], is of thought that regardless of cause of cellular damage (hypoxia, physical and chemical agent ,aging, apoptosis)free radical is the main factor, therefore the efficacy of anti-oxidant and anti-inflammatory should be considered[34]. Work done by Marc Schumacher *et al*. showed, ROS leading to ovarian dysfunction in PCOS along inflammatory cytokines that can implicate in folliculogenesis[35]. Minhee Jang *et al*. used red ginseng, to restrain inflammatory and oxidative response for maintaining folliculogenesis[36].

In results of present study, MDA was reduced by use of lycopene while its level was lowered down in metformin and combination group as well. Fereshteh Ghorat *et al*.in 2019, demonstrated highly raised MDA in PCO patients as comparison to the controls. Another study by Eleonora Okuskhanova *et al*. showed consistent results of MDA levels being raised in PCOS when compared with normal group[32]. Contrary to present study, MDA levels were found to be similar in patients with PCOS as in normal group was seen by Karadeniz et. al. This observation suggests that the presence of insulin resistance in PCOS patients has no effect on MDA level[37]. As per a previous meta-analysis report, by Girotti *et al*. 2017, the MDA level was 47% more in PCOS women than in contrast to the controls. It is suggestive of oxidative stress status and cellular damage being produced in ovary[38]. Habib ur Rehman *et al*. also showed similar results indicative of DNA strand breakage[4]. Present study results, are in accordance with the action of antioxidant therapy it may implement critical role in three different approaches: minimize/ prevent, repair, and remove oxidative damage[39].

Use of lycopene proved itself beneficial for preservation of normal levels of CAT and SOD as depicted by present results showing higher values as compared to diseased group. Metformin also had improved values of SOD and CAT. While when it was co-administrated with lycopene enhances super oxide scavenger ability and attained better levels of SOD and CAT. Muhammad Al Shariati *et al*. proved that CAT and SOD levels were improved by use of antioxidant in female reproductive system preventing infertility, in humans trials given in 2016.24 Luid Sheild *et al*. determined that vitamin C caused raised level of SOD and CAT even more than found in normal group[40]. His results are inconsistent with present study.

In 2013, the result of one meta-analysis by Brain L *et al*. also showed that SOD activity was 34% less in PCOS patients than in controls[41]. Saleem *et al*. examined the activity of SOD both in serum and follicular fluid from women with PCOS undergoing intracytoplasmic sperm injection they showed SOD activity was significantly less in serum and follicular fluid in PCOS as comparison to normals[42].

One meta-analysis (Loke *et al*,2018) reported, research on 30 PCOS women, all showed increased total antioxidant capacity (TAC) when treated with antioxidant[36]. It is inconsistent with present study that TAC (total antioxidant capacity) was increased by use of lycopene, as to compensate total oxidative stress.

CONCLUSION

Lycopene amplifies the aromatization of androgens into estrogen and improves the histo-morphological features by reducing oxidative stress in the ovarian tissue. It was found more effective than metformin in restoring normal ovarian parenchyma while it's combination with metformin was found hence more efficient.

CONFLICT OF INTERESTS

There are no conflicts of interest.

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الملخص العربى

الليكوبين يحسن من نضج الجريبات المبيضية في نموذج الجرذان لمتلازمة المبايض المتكيسة: دراسة نسيجية شكلية ووظيفية

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الخلفية والأهداف: تعتبر متلازمة المبايض المتكيسة حالة أيضية خطيرة ذات معدل انتشار مرتفع في البلدان الآسيوية تصيب النساء في سن الإنجاب. بدأت هذه الدراسة لتقييم التأثيرات المفيدة لليكوبين - وهو مكون غذائي في نموذج الجرذان المصابة بمتلازمة المبايض المتكيسة المستحثة بالليتروزول.

المواد والطرق: تم تقسيم خمسين من إناث جرذان سبراغ دولي البالغة إلى خمس مجموعات ، عشر جرذان لكل مجموعة لدراسة مدتها ٥ أسابيع. تلقت مجموعة التحكم أ نظامًا غذائيًا قياسيًا للجرذان. تلقت جرذان المجموعة التجريبية ب ١ ملغم / كغم من الليتروزول لإحداث نموذج المبايض المتكيسة. تلقت المجموعة ج ١ ملغم / كغم من الليتروزول + ١٥ ملغم / كغم / يوم من الليكوبين. تلقت المجموعة د ١ ملغم / كغم من الليتروزول + ٥٠٠ ملغم / كغم / يوم من الميتفورمين. تلقت المجموعة هـ ١ ملغم / كغم من الليتروزول + مزيج من الليكوبين والميتفورمين معًا. تم أخذ الوزن الجسدي النسبي في اليوم ١ واليوم ٢١ ونهاية التجربة. تم اختبار النشاط المضاد للأكسدة باستخدام الكاتالاز و السوبر أوكسيد ديسميوتاز والمالونديالديهايد. تم إزالة المبايض لصبغها بالهيماتوكسيلين والإيوسين ودراستها تحت المجهر الضوئي. تم إجراء التحليل الإحصائي لتفسير النتائج.

النتائج: أظهرت النتائج انخفاضًا في وزن الجرذان باستخدام الليكوبين. أظهرت البنية النسيجية للمبيض عددًا أفضل من الجريبات الثانوية والجريبات البوغية نحو القيم الطبيعية والتي كانت منخفضة جدًا في المجموعة ب كما ثبت من خلال قيمة p<٠,٠٠١ ذات الدلالة الإحصائية. في حين انخفض العدد المرتفع من الجريبات الضامرة في المجموعة ب ٦ ± ١,٦ إلى ٣ ± ٠,٩ ، ٤ ± ٠,٦ ، ٤ ± ٠,٧ في المجموعات ج ود وهـ على التوالي. لوحظ تحسن عام في المبايض المشوهة / المتكيسة بواسطة العلاج ، كما هو واضح من قيمة p ذات الدلالة الإحصائية. أظهرت المجموعة ب متوسط عدد الأكياس ٧ ± ١,٠ ، والتي انخفضت إلى ٢ ± ٠,٥ ، ٣ ± ٠,٨ ، ٢ ± ٠,٧ في المجموعات ج ود وهـ على التوالي. تم خفض مؤشرات الأكسدة المرتفعة (أنواع الأكسجين التفاعلية) أيضًا.

الاستنتاج: يمكن لتناول الليكوبين الغذائي أن يخفف الضرر النسيجي والتأكسدي في المبايض المتكيسة.