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Emerging and Re-emerging Animal Health Challenges in Low and Middle-Income Countries

The Effect of Polycystic Ovary Syndrome on Physiological and Biochemical Indicators in *Albino rabbits*

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Abstract | Polycystic ovary syndrome (PCOS) is a multifaceted endocrine ailment which affects large number of women during their reproductive years and results in heterogeneous metabolic and hormonal derangements. The current study aimed to evaluate the effect of PCOS on blood glucose levels and liver enzyme. A total of 100 grown up, reproductive adult female Albino rabbits was divided into two groups (n = 50). In the control group PCOS wasn't motivated, while in the residual other group (n = 50) PCOS was motivated with a alone i.m. testosterone injection every day. Biomarkers assessed include: Glutamic-Oxaloacetic Transaminase (GOT), Alanine Aminotransferase (ALT), Alkaline Phosphatases (ALP), Blood glucose, Luteinizing hormone (LH) and Insulin hormone. The research identifies a gap in the current understanding of the specific biochemical effects of PCOS on liver enzyme activity, glucose metabolism and LH disorder. The study aims to fill this gap in providing an exhaustive explanation of relation between PCOS and these biochemical markers. However, further results indicate female PCOS rabbits to exhibit pronounced alterations in liver enzyme levels together with blood glucose concentration, LH and insulin indicative of a metabolic and hormonal link for this syndrome. These findings indicate the significance of obligatory metabolic control in female rabbits with PCOS and suggest an attuned clinical intervention program to either clear out management strategy properly, further experiments are urgently warranted. Within this study, we have identified distinct patterns of ovarian gene expression underlying PCOS which could open new avenues for refined clinical diagnostics and treatment strategies in the future.

Keywords | Polycystic ovary syndrome (PCOS), Liver enzymes, Blood glucose, Luteinizing hormone, Insulin hormone

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INTRODUCTION

The review, focusing on the multifaceted treatment seems to be open-minded in the state and clinical prognoses of PCOS statements a 360° view over this

complicated syndrome (Kataoka *et al.*, 2022; Trummer *et al.*, 2019). It reinforces that PCOS is a complex not simple problem, but well configured one following an array of bodily effects.

Deregulated hormonal imbalances that were emphasized in the review, consisting of elevated androgen levels abnormal LH/FSH ratios an altered TEST-E2 ratio are crucial to PCSOS pathophysiology (Pereira-Eshraghi *et al.*, 2019; Jungari *et al.*, 2023). This leads to the multitudes of symptoms noted in patients.

The metabolic disturbances implicated in PCOS, including central obesity as determined by waist-to-hip ratios, increased lipid levels and impaired insulin sensitivity further reflect the syndrome's systemic scope (Li *et al.*, 2020; Romualdi *et al.*, 2010), both of which are complex traits. Not only do these metabolic disturbances add complexity to the presentation of PCOS, but it also can have a bearing on future health risks.

The dermatological symptoms, including hirsutism, acne, alopecia, and acanthosis nigricans, represent some of the dermatological symptoms associated with PCOS which also represent its major physical aspect as well psychosocial consequences (Fruzzetti *et al.*, 2002; Romero-Ruiz *et al.*, 2019). One major factor is such skin conditions force the patients to see a doctor as well this will really affect his quality of life.

This review underscores this wide range of clinical variability by identifying the heterogeneity in terms and descriptions, raising caution that exercise programs directed toward treated groups with specific sub-diagnostic features might not uniformly address general therapeutic strategies to reduce risk for non-communicable disease (Thathapudi *et al.*, 2014; Dravecká *et al.*, 2016).

Obesity has multiple molecular and physiological mechanisms that negatively affect female reproductive health. Of note is the perturbation of hypothalamic-pituitary-ovary (HPO) axis as one major pathway. In obese, increased levels of leptin results in a loss of the pulsing secrets pattern of Gonadotropin-releasing hormone (GnRH) inhibiting normal secretions patterns luteinizing and follicle stimulation hormones (Garcia and Peyrou, 2024). These hormonal misbalances can cause anomalies in menstruation and ovulation.

Adipose tissue was initial consider as a passive functioning fat depot, but is currently understood to be an important secretory endocrine member. As well as, altered secrets pattern of adipokines, particularly leptin and adiponectin in obesity (Luo *et al.*, 2021). These changes impact ovarian steroidogenesis and they are just a few of the many contributors which can disrupt hormonal milieu needed for reproduction as shown in research (Broughton and Moley, 2017).

Insulin resistance and hyperinsulinemia, common in

obesity, also play a crucial role. Elevated insulin levels stimulate ovarian theca cells to overproduce androgens, leads to a hyperandrogenic state reminiscent of PCOS (Ashraf *et al.*, 2019). Additionally, insulin inhibits the liver's productive of sexual hormones-binding globulin (SHBG), resulting in increased levels of freely circulating androgens (Garcia and Peyrou, 2024).

Chronic inflammation and oxidative stress, hallmarks of obesity, make hostile environments of oocytes and can negatively impact the endometrial lining (Manna and Jain, 2015). This inflammatory state can affect oocyte quality, viability, and the overall success of conception.

The spread of PCOS is highlighted in this article, where the researchers reported, the fund happening of PCOS was 7%, while fund PCOS happpeneing rate and androgen rised (AE)-PCOS was 12%". Adipose tissue dysfunction is presented as a key contributor to the chronic low-grade inflammations observed in PCOS (Johnson and Laloraya, 2022).

Johnson and Laloraya (2022) explained that obesity can lead to adipocyte hypertrophy, which results in hypoxia and subsequent activation of inflammatory pathways. Hypertrophies of adipocyte lead to hypoperfusion because contractile of blood vessels culminates in hypoxia and related activities of NFκB. Many studies suggesting that fast may enhance insulin sensitive and glucose tolerance through metabolic reprogramming and reduced calorie intake (Li *et al.*, 2021; Feyzioglu *et al.*, 2023). These mechanisms could be particularly relevant for PCOS patients, who often struggle with insulin resistance.

Interestingly, those studies on healthy individuals have shown minimal impact of fast on gluco-metabolic markers (Faris *et al.*, 2020). This contrast between the effects on PCOS patients and healthy individuals underscores the complexity of the relationship between fast and glucose homeostasis, while some studies indicate promising effects of fast on glycemic control in PCOS patients (Sari and Abdelrahim, 2024). In addition to reproductive health problems, the syndrome has a broader and more comprehensive clinical impact on many body systems. This has a particularly relevant connotation with metabolic syndrome as the association is well established highlighting those problems in reproductive health and metabolism may be interlinked especially among PCOS patients (Lim *et al.*, 2019). For very women, yet PCOS can also cause major concerns with reproduction and infertility. Symptoms, most notably menstrual irregularities (including amenorrhea), anovulation and subfertility can cause significant emotional distress (Inhorn and Patrizio, 2015).

Exploring these clinical features reveals a variety of

presentations for PCOS and highlights the fact that it is not just a reproductive condition, but an interconnected syndrome with significant health implications (Dar *et al.*, 2024).

Liver enzymes have long been known to be sensitive markers for liver health and functionality (Ozer *et al.*, 2008). This has often been seen as an indicator of liver stress or even hepatocellular damage (Kowalska *et al.*, 2018). Garcia-Beltran *et al.* (2024) found that oral contraceptive-treated adolescent girls with PCOS had higher ALT and GGT levels. These findings are particularly relevant within the realm of PCOS treats.

It's necessary to note this where elevations in liver enzymes are concerning, their interpretation requires careful consideration. Mild elevations may not always indicate clinically significant liver damage, and the threshold for what constitutes a clinically relevant increase can vary (Giannini *et al.*, 2005). The findings of Garcia-Beltran *et al.*, (2024) align with indicator grows body was suggested that metabolic health in PCOS patients may be differentially affected by various treatment options (Zegher *et al.*, 2021).

MATERIALS AND METHODS

Overall of 100 grown up, reproductive adult female rabbits (*Oryctolagus cuniculus*) align in age from 10-12 months were purchased from a district shop in Baghdad, Iraq. They was acclimatization to their casing and feeds diet for 2 weeks earlier to the start of trial in the animal house of General Company for Pharmaceutical Industry, Baghdad, Iraq.

An appropriate food consists of green mash given three times a daily; vegetable, fruit, and dry mash, two time weekly; and loose arrive to water is keep up. After acclimate, each of the rabbits were random divided into two groups (n= 50/group).

Control group of PCOS wasn't induced. The residual rabbits (n = 50) were given alone i.m. testosterone injection every day for four weeks at the dose rate of 4 mg/kg of the PCOS inducement.

The experiment was carried out for aggregate of five weeks through the week monitoring was conserved for the body weight evaluation and endocrinology indicators.

LABORATORY ANALYSIS

Blood specimens (5 mL) were collected sterilize from the marginal ear vein of every one rabbits, on a weekly base, beneath a suitable restrain protocol. They were conveyed into vacationers was contained thixotropic gel separator for serum separates, body weight was measured earlier to every one specimens/ blood collected.

The collected blood samples were analyzed in a certified clinical laboratory using standardized biochemical assays; GOT, ALT, and ALP. Enzyme activities were measured using spectrophotometric methods. While Blood glucose level is determine by use the glucose oxidase-peroxidase way. Serum is harvest and analysis of (LH) by commercial available enzymes linked immune-sorbent assay (ELISA) kits

STATISTICAL ANALYSIS

Data were entered into a statistical software package (e.g., SPSS or R) for analysis. Description statistical (mean, standard deviation, median, and range) were calculated of all measured parameters.

The statistical tests were applied included T-tests to compare mean values of liver enzymes and blood glucose levels between PCOS patients and reference ranges for healthy individuals. While the correlation analysis to examine the rapport among blood glucose and liver enzyme activities. Statistical significance level was taken at (P ≤ 0.05).

RESULT AND DISCUSSION

The current study was conducted on a total of (100) mature female rabbits, including (50) healthy rabbits who constitute the control group and the remaining (50) with PCOS.

Table 1, displays the (mean ± SD) of blood glucose level were measured in the control group and the group affected by PCOS, software package (t- test one way) analysis way was used in conjunction with SPSS Statistical Software for data analysis.

Table 1: The relationship between age and blood glucose level in adult rabbit together PCOS compare to monitoring group.

Variables	Body weight (kg)	GLU	P-value
Control (n=50)	4.75 ± 0.15	100.96±11.761	P≤0.05
Rabbits with PCOS (n=50)	5.56 ± 0.18	128.82±11.363	P≤0.05

Figure 1 displays the (mean±SD) of blood glucose level were measured in control group and the group affected by PCOS, software package (t- test one way) analysis way was used in conjunction with SPSS Statistical Software of data analysis.

The current study was conducted on a total of (100) mature female rabbits, including (50) healthy rabbits who constitute the control group and the remaining (50) rabbits with PCOS.

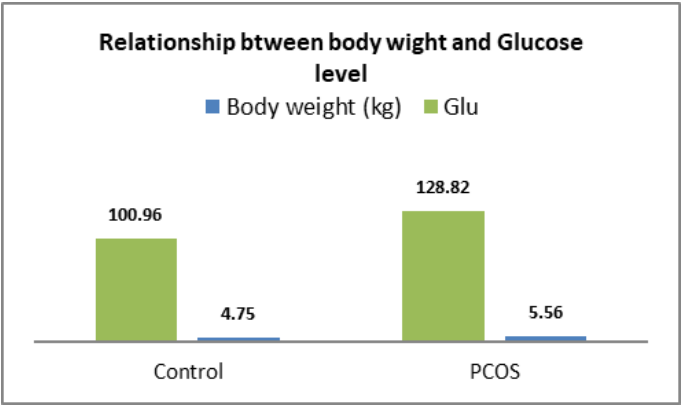


Figure 1: The relationship between body weight and blood glucose level in rabbits with PCOS compared to control group.

Table 2, displays the (mean $\pm$ SD) of GOT level were measured in the control group and the group affected by PCOS, software package (T- test one way) analysis way was used in conjunction with SPSS Statistical Software of data analysis.

Table 2: The relationship between bodies weight (kg) and GOT in adult rabbit together PCOS compare to monitoring group.

Variables	Body weight (kg)	GOT	P-value
Control (50)	4.75 $\pm$ 0.15	22.52 $\pm$ 6.144	P $\leq$ 0.05
Rabbits with PCOS(n=50)	5.56 $\pm$ 0.18	24.28 $\pm$ 11.761	P $\leq$ 0.05

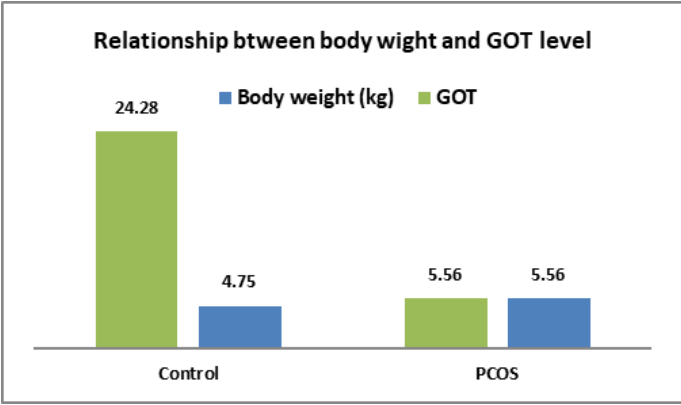


Figure 2: The relationship between Body weight (kg) and GOT level in Rabbits with PCOS compared to control group.

Figure 2 displays the (mean $\pm$ SD) of GOT level were measured in the control group and the group affected by PCOS, software package (T- test one way) analysis way was used in synchronism with SPSS program.

The current study was conducted on a total of (100) mature female rabbits, including (50) healthy rabbits who constitute the control group and the remaining (50) rabbits with PCOS.

Table 3, displays the (mean $\pm$ SD) of GPT level were measured in the control group and the group affected by PCOS, software package (t- test one way) analysis method was utilized in conjunction with SPSS Statistical Software for data analysis.

Table 3: Relationship between body weight (kg) and GPT level in adult rabbit together PCOS compare to monitoring group.

Variables	Body weight (kg)	GPT	P-value
Control (n=50)	4.75 $\pm$ 0.15	25.12 $\pm$ 39.284	P $\leq$ 0.05
Rabbits with PCOS (n=50)	5.56 $\pm$ 0.18	18.92 $\pm$ 56.802	P $\leq$ 0.05

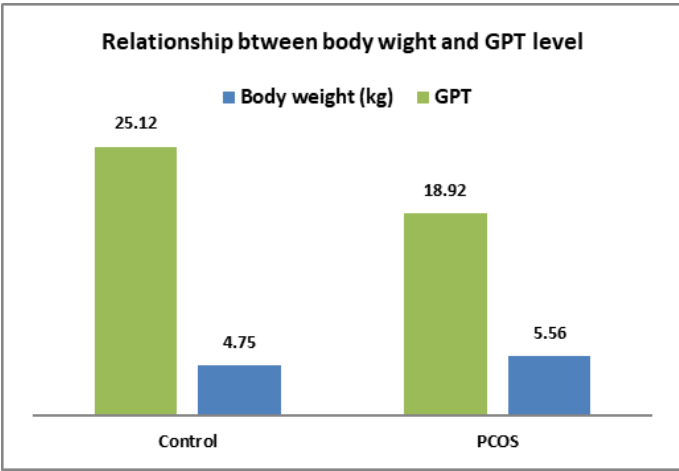


Figure 3: Relationship between Body weight (kg) and GPT level in Rabbits with PCOS compared to control group.

Figure 3 displays the (mean $\pm$ SD) of GPT level were measured in the control group and the rabbits with PCOS, software package (T- test one way) analysis way was used in synchronism with SPSS program.

The current study was conducted on a total of (100) Rabbits, including (50) healthy rabbits who constitute the control group and the remaining (50) Rabbits with PCOS.

Table 4: Relationship between body weight (kg) and ALP level in adult rabbit together PCOS compare to monitoring group.

Variables	Body weight (kg)	ALP	P-value
Control (n=50)	4.75 $\pm$ 0.15	82.12 $\pm$ 6.144	P $\leq$ 0.05
Rabbits with PCOS (n=5)	5.56 $\pm$ 0.18	197.96 $\pm$ 50.903	P $\leq$ 0.05

Table 4, displays the (mean $\pm$ SD) of ALP level were measured in the control group and the group affected by PCOS, software package (T- test one way) analysis way was used in synchronism with SPSS program.

Figure 4 displays the (mean ± SD) of ALP level were measured in the control group and the group affected by PCOS, software package (T- test one way) analysis way was used in synchronism with SPSS program.

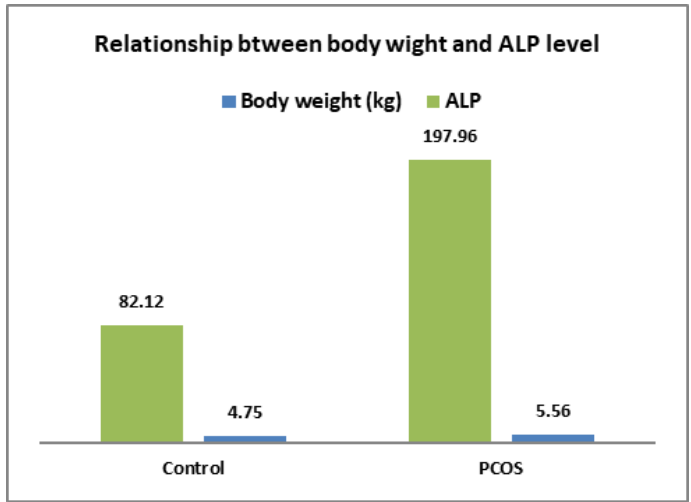


Figure 4: Relationship between body weight (kg) and ALP level in Rabbits with PCOS compared to control group.

Table 5: Relationship between body weight (kg) and Luteinizing hormone (IU/L) in adult rabbit together PCOS compare to monitoring group.

Variables	Body weight (kg)	LH hormone	P-value
Control (n=50)	4.75 ± 0.15	2.35 ± 0.05	P≤0.05
Rabbits with PCOS (n=50)	5.56 ± 0.18	6.64 ± 0.17	P≤0.05

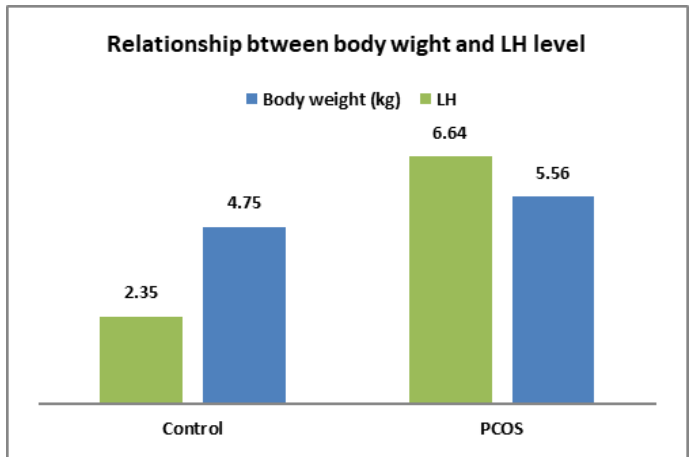


Figure 5: Relationship between body weight (kg) and LH level in Rabbits with PCOS compared to control group.

Figure 5 displays the (mean ± SD) of Luteinizing hormone (IU/L) were measured in the control group and the group affected by PCOS, software package (T- test one way) analysis way was used in synchronism with SPSS program.

Figure 6 displays the (mean ± SD) of Insulin hormone (IU/L) were measured in the control group and the group affected by PCOS, software package (T- test one way)

analysis way was used in synchronism with SPSS program.

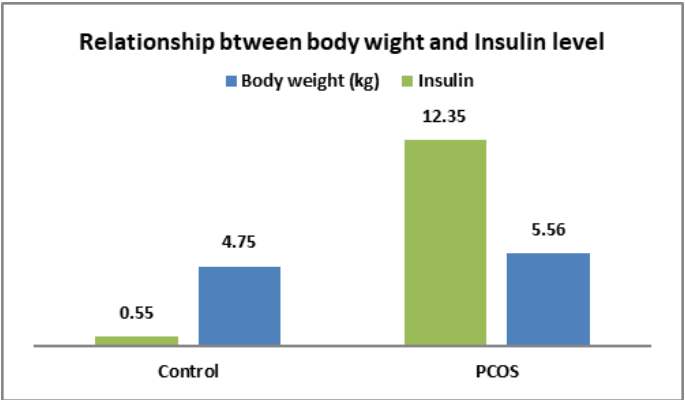


Figure 6: Relationship between body weight (kg) and Insulin level in Rabbits with PCOS compared to control group.

Table 6: Relationship between body weight (kg) and Insulin hormone (IU/L) in adult rabbit together PCOS compare to monitoring group.

Variables	Body weight (kg)	Insulin hormone	P-value
Control (n=50)	4.75 ± 0.15	0.55 ± 0.11	P≤0.05
Rabbits with PCOS (n=50)	5.56 ± 0.18	12.35 ± 2.03	P≤0.05

The elevated blood glucose in several participants underscore the associated among PCOS and insulin resistance. Insulin resistance was a well-documented feature of PCOS, contributing to hyperglycemia and an raised dangers of development type 2 diabetic (Purwar and Nagpure, 2022). The data indicate that regular monitoring of blood glucose is essential of patient with PCOS to manage and mitigate the risk of diabetes and related metabolic disorders (Liao et al., 2022).

Long-term studies are crucial to identify which PCOS phenotypes may lead to increased health risks in later life and to determine if there are variations in morbidity rates among patients (Purwar and Nagpure, 2022). PCOS is increasingly prevalent between adult female of reproduction age, often causing lifelong health issues. Interestingly, the condition's diagnostic criteria remain unclear, and its characteristics are complex. Further research into the genetics and pathophysiology of PCOS is essential to establish preventive measures and develop effective treatments (Purwar and Nagpure, 2022). PCOS is both a multifaceted and global condition, with its differential diagnosis still not fully understood. Recently, clinical practice has shifted towards a more proactive approach, focusing on prevention and conventional treatments for related disorders. Current therapeutic options include hormonal contraceptives, anti-androgen medications, metformin, and inositols (Purwar and Nagpure, 2022). Blood glucose levels alone seem inadequate for screening

or diagnosing the connection between hyperglycemia and Polycystic Ovary Syndrome (PCOS). Research suggests that PCOS may involve impaired insulin secretion. This could explain why postprandial (after-meal) glucose levels, rather than fasting glucose concentrations, more accurately indicate disrupted glucose metabolism and T2D risk in individuals with PCOS (Belsti *et al.*, 2024).

The analysis of liver enzymes, GOT and GPT, revealed that most participants had enzyme levels within normal ranges. This finding suggests that while PCOS is associated with various metabolic disturbances, it does not universally lead to significant hepatic inflammation or damage in the studied cohort. However, the wide range of ALP levels observed indicates potential variability in hepatic and biliary function, which could be influenced by factors such as diet, physical activity, and genetic predispositions (Garcia and Peyrou, 2024).

Recent studies on women with Polycystic Ovary Syndrome (PCOS) have shown elevated levels of alanine aminotransferase (ALT), suggesting liver stress (Ozer *et al.*, 2008; Koenig and Seneff, 2015). These findings align with previous research demonstrating PCOS's impact on liver enzymes (Kowalska *et al.*, 2018) and metformin's effect on ALT levels; though not on aspartate aminotransferase (AST) levels (Preiss *et al.*, 2008). ALT is recognized as a highly sensitive indicator of liver damage, typically showing changes before AST. While ALT is the primary marker, AST serves as a complementary biomarker, providing additional insights into liver function (Ozer *et al.*, 2008).

Our research found that PCOS status did not increase the risk of elevated ALT, GOT, or GPT. However, elevated liver enzymes are commonly observed in women with PCOS (Minato *et al.*, 2018), as is dyslipidaemia (Liu *et al.*, 2019). Liu *et al.* (2023) identified fasting insulin as a potential mediator between PCOS and liver diseases. Interestingly, a study of Korean adult female with PCOS found no significant association between normal-range insulin levels through a 75g glucose tolerance test (GTT), BMI >25 kg/m², and subsequent liver diseases (Won *et al.*, 2021). Our findings revealed a strong association between Type 2 Diabetes Mellitus (T2DM) and rised dangerous of elevated ALT levels. This supports recent evidence linking insulin resistance (IR) to liver dysfunction. Previous researches have shown that IR in adult women with PCOS can negatively impacts on liver functions (Falzarano *et al.*, 2022).

Liu *et al.* (2021) explained a connection between IR, obesity, and rised liver enzymes. A study of Chinese individuals found that IR significant rised the risk of high ALT, AST, and γ -glutamyl transferase (GGT) level. Other study identified serum ALT concentrations as an

independent predictor of diabetes (Ahn *et al.*, 2014).

The conflicts results of studies may be due to differences in participants characteristics, variables definitions, and measurement methods (Saei *et al.*, 2024). Several plausible techniques had been proposed to explain the associated between IR and impaired liver function, including inflammations, modifications in lipid metabolism, lipotoxicity, oxidative stress, and cytokine- induced liver injuries (Sakurai and Kubota, 2021).

An incresing way was noted in each parameters (body weight, LH, and insulin) of PCOS-inducemented group during the study weeks. It had been noted that PCOS is characterized by overweight as compared to non-PCOS adult female, elevated LH, and insulin hormones. In the current research, PCOS was stimulated of the rabbits by injection testosterone (4 mg/kg) for four successive weekly.

This leads to rise circulator androgens (testosterone) levels, which that are then converts into estrogens by aromatase activities (Sajjad *et al.*, 2016). Nevertheless, in PCOS rabbits, rised magnitude and recurrence of LH may be attributed to quick GnRH induce by the positive feedback mechanisms of the circulator estrogens on adenohipophysis (Chaudhari *et al.*, 2018). This rised LH more producing androstenedione of ovary stromal and thecal cells and eventaully it is once more time converts to estrone, exerted a stimulate effects on LH produce, as regards the increased insulin concentrations in the group with PCOS, it may be ascribed to short term testosterone treatment which causes change in the expressof lipolytic signals proteins of body adipose tissue in relationship to lipolytic activities and insulin resistance (Zang *et al.*, 2006) in the PCOS group. Moreover, insulin resistance and hyperinsulinemic conditions by their single or combined effects contribution toward rised body weight in the PCOS group (Baptiste *et al.*, 2010). It has been indicated that the sympathetic nervous systems interaction and causes dysregulation in PCOS (Yu *et al.*, 2024).

Hyperinsulinemia, hyperandrogenism, insulin resistance, cardiovascular disorders, and obesity have been attributed to hyperactivity of the sympathetic nervous system (Lansdown and Rees, 2012).

CONCLUSIONS AND RECOMMENDATIONS

Over recent decades, researchers have made significant strides in understanding the pathogenesis of Polycystic Ovary Syndrome (PCOS). Our current study, which examines the clinical features associated with PCOS, provides a comprehensive view of this complex condition.

Our findings highlight the metabolic implications of PCOS, with half of the studies reporting an increased waist-to-hip ratio and elevated lipid levels in affected individuals. Notably, rabbits with PCOS showed significantly higher blood glucose levels. Regarding liver enzymes, plasma alkaline phosphatase (ALP), LH and Insulin levels were frequently elevated, while no significant differences were observed in glutamic pyruvic transaminase (GPT) and glutamic oxaloacetic transaminase (GOT) levels. These results underscore the varied clinical manifestations of PCOS. They emphasize the need for personalized management strategies to effectively address the multifaceted nature of this condition. Overall, this study contributes to a deeper understanding of PCOS and its diverse impacts on women's health.

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NOVELTY STATEMENT

This study reveals novel biochemical indicators into PCOS by identifying significant alterations in liver enzymes, blood glucose and hormonal levels. Additionally, distinct ovarian gene expression patterns associated with PCOS could lead to improved diagnostics and treatments.

AUTHORS CONTRIBUTION

All authors contributed significantly and equally to their respective tasks and approved the final manuscript.

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CONFLICT OF INTEREST

The authors have declared no conflict of interest.

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