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Original Research Paper

# Correlation between miR-21 Expression and hormonal change in woman with polycystic ovary syndrome

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**Abstract:** And dysfunction of reproductive age, which is frequently accompanied by a metabolic disorder and hormonal imbalance. Recent evidence implicates microRNAs (miRNAs), particularly miR-21, as key regulators of metabolic and inflammatory pathways. The current study was designed to evaluate the expression level of miR-21 and its association with selected physiological markers in women with PCOS. **Methods:** Sixty women diagnosed as having PCOS, and 20 healthy women who served as controls were studied in a comparative cross-sectional study. The age of the participants varied between 20 to 41 years with a mean age of 28.18 ± 0.77 years. Serum was obtained from bloods and measured for hormonal biomarkers of luteinizing hormone (LH), follicle-stimulating hormone (FSH), anti-Müllerian hormone (AMH) and free testosterone. The expression of microRNA-21 was analyzed by qRT-PCR.
**Results:** The results reveal a significant increase ($p < 0.05$) of body mass index, AMH, LH, FSH and LH/FSH ratio in women with PCOS when compared to the control group. MiR-21 expression levels were also higher in the PCOS group. Important associations were also found: miR-21 expression was correlated with age and body mass index. **Conclusion**: Significant hormonal and metabolic changes associated with increased miR-21 expression occur in women with PCOS. These results indicate that miR-21 could be a potential biomarker for assessing the disease course and metabolic disorders in PCOS. More large-scale studies are needed to validate its diagnostic and prognostic value.

**Keywords:** PCOS, miR-21, physiological biomarkers, AMH, LH/FSH ratio

## 1. Introduction

Polycystic ovary syndrome (PCOS) is a complex, mysterious and public disease. It is a heterogeneous endocrine disorder that affects the reproductive age women worldwide [1,2]. This syndrome is characterized by the presence of enlarged, dysfunctional ovaries, hyperandrogenism and insulin resistance [3]. There is emerging evidence that polycystic ovary syndrome (PCOS) is the most prevalent reproductive endocrine disorder with a reported prevalence of 5%–26% in reproductive-age females [4,5]. The syndrome is treated primarily through exercise. Regular exercise can improve insulin sensitivity and decrease insulin resistance, a major problem with this syndrome[6,7]. Exercise also aids in maintaining an ideal weight range and shed excess body fat, further helping to enhance hormonal homeostasis and normalise the menstrual cycle[8,9].

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MicroRNA, a class of short non-coding RNAs 18-25 nucleotides long, serve as crucial post-transcriptional regulators of gene expression. Since miRNAs can directly target messenger RNAs (mRNAs), they can inhibit the translation of that protein or stimulate mRNA decay, and broad range of biological processes including lipid metabolism, inflammation, insulin signaling and adipogenesis could get trans-regulated by each miRNA. [10]. Among these regulatory molecules, miR-21 has been increasingly acknowledged for its roles in metabolic and inflammatory signaling potentiations[11].

MiR-21 in circulation has been found to be higher in obese individuals and patients with metabolic syndrome according to several reports[12]. MiR-21 expression is elevated in chronic low-grade inflammation, insulin resistance and disturbed lipid homeostasis, indicating a potential use of miR-21 as a biomarker in obesity associated metabolic dysfunction [13].

## 2. Methodology

This was a comparative cross-sectional study that included 80 women (60 PCOS and 20 normal weight control). The mean age of the patients was 28.18 ± 0.77 years-old; the ages ranged from 20 to 41 years-old. Study conducted July 1, 2025–March 1, 2026. In addition to the control group, blood samples were obtained from women with polycystic ovary syndrome who attended Al-Zahraa Teaching Hospital. For physiological biomarker analysis, five milliliters of venous blood from each participant was collected under aseptic conditions. These comprised LH, FSH, anti-müllerian hormone and free testosterone. Right after the Polyp-alt, transzoc-miRNA extraction kit was used to extract miRNA molecules from peripheral blood.

Table 1: qRT-PCR Primers for the expression level of miR-21 with their sequence:

| Primer | Sequence (5'-3') |
|---|---|
| miRNA Forward primer | F: TAGCTTATCAGACTGATGTTGA |
| miRNA Reverse primer | R: GTGCAGGGTCCGAGGT |

## 3. Results and discussion

*Distribution of samples according to age and number*

The result indicated significant increasing between group of samples as shown in figure 1.

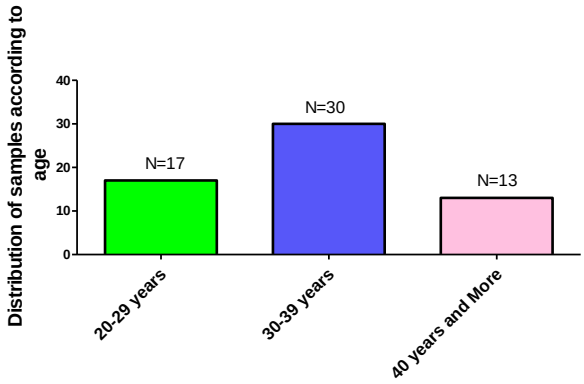


**Fig 1**:Distribution of samples according to age and number

*Distribution of samples according to body mass index*

The result indicated significant increasing between Sample and Control as shown in figure 2.

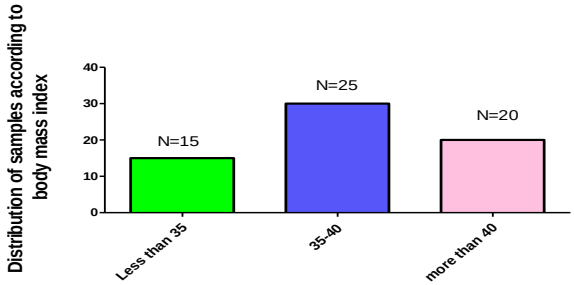


**Fig 2**: Distribution of samples according to body mass index

* Indicates significant increasing between sample and control

*Distribution of samples according to body mass index*

The result indicated different number between group of samples as shown in figure 3,4,5.

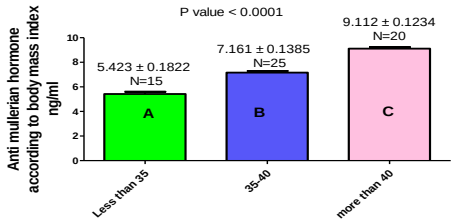

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**Fig 3**: Distribution of samples for anti mullarian-hormone level according to the body mass index

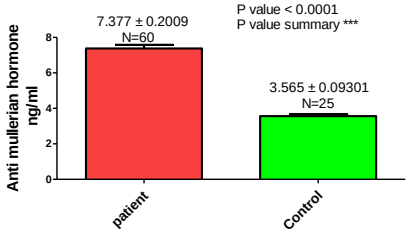


**Fig 4**: Distribution of samples for anti mullarian-hormone level

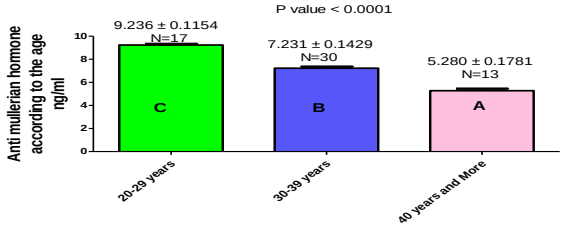


**Fig 5**: Distribution of samples for anti mullarian-hormone level according to the age

*Distribution of samples for Luteinizing Hormone level*

The result shows a significant increase in the sample when compared with the control group, as shown in Figure 6,7,8.

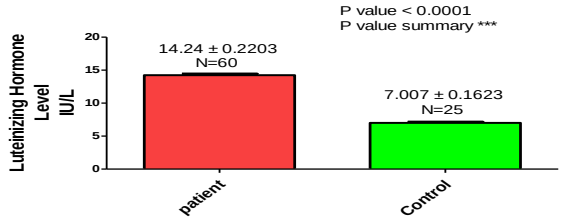


**Fig 6**: Distribution of samples for Luteinizing Hormone level

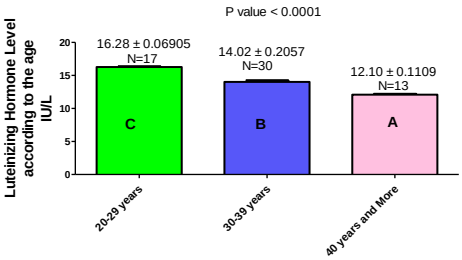


**Fig 7**: Distribution of samples for Luteinizing Hormone level according to the age

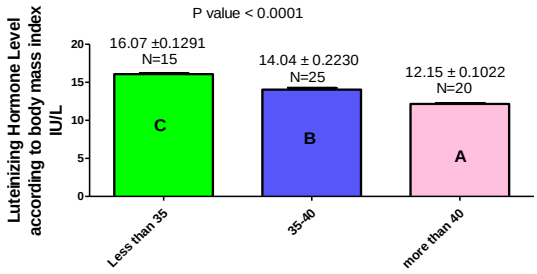


**Fig 8**: Distribution of samples for Luteinizing Hormone level according to body mass index

*Distribution of samples for Follicle-stimulating Hormone Level*

The result illustrate significant increasing between Sample and Control as shown in figure 9,10,11.

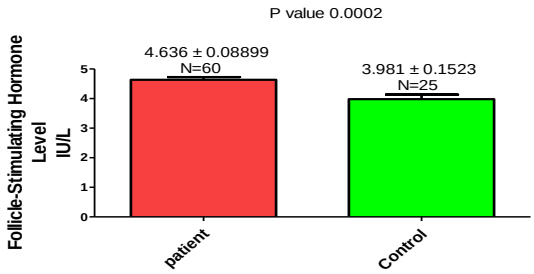


**Fig 9**: Distribution of samples for Follicle-stimulating Hormone Level

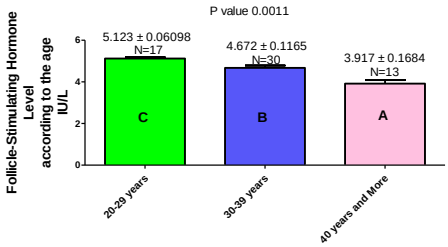


**Fig 10**: Distribution of samples for Follicle-stimulating Hormone Level according to the age

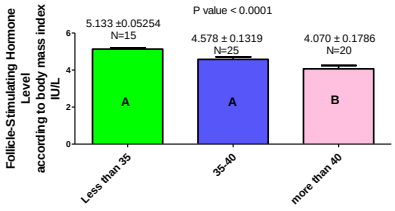

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**Fig 11**: Distribution of samples for Follicle-stimulating Hormone Level according to body mass index

## *Distribution of samples for LH/FSH Ratio*

The result illustrate significant increasing between Sample and Control as shown in figure 12,13,14.

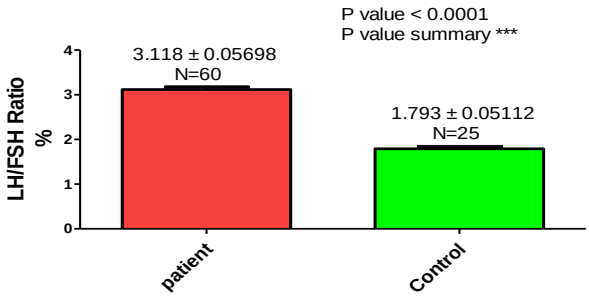


**Fig 12**: Distribution of samples for LH/FSH Ratio

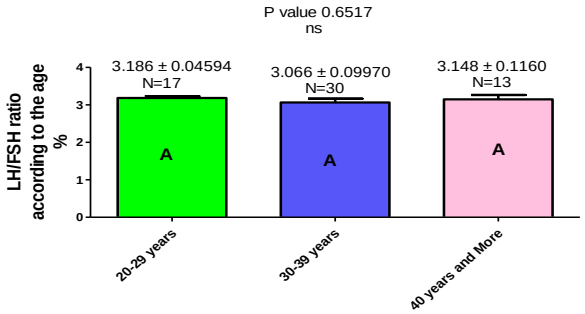


**Fig 13**: Distribution of samples for LH/FSH Ratio according to age

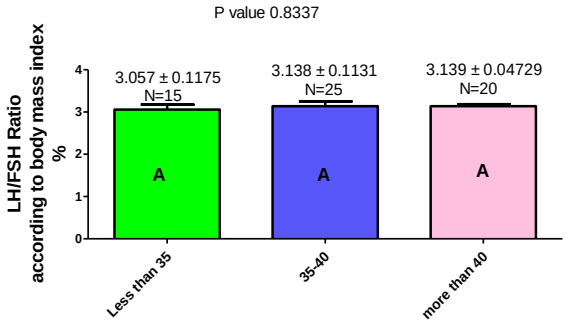


**Fig 14**: Distribution of samples for LH/FSH Ratio according to body mass index

## *Distribution of samples for MicroRNA-21 expression Level*

The result illustrate a significant increasing between Sample and Control as shown in figure 15,16,17.

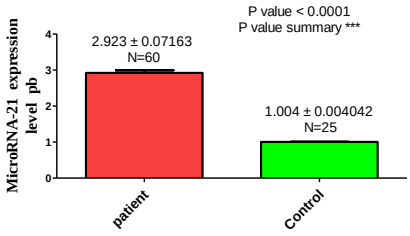


**Fig 15**: Distribution of samples for MicroRNA-21 expression Level

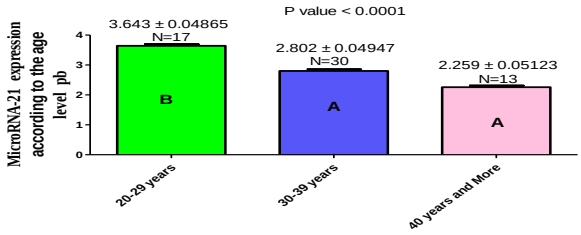


**Fig 16**: Distribution of samples for MicroRNA-21 expression Level pb according to age

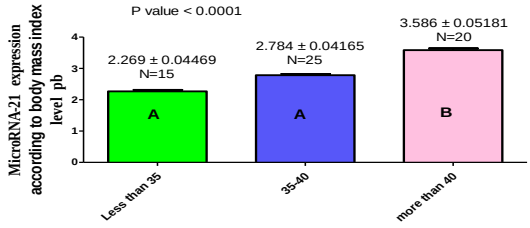


**Fig 17**: Distribution of samples for MicroRNA-21 expression Level pb according to body mass index

## *Distribution of samples for Free Testosterone Level*

The result illustrate a significant increasing between Sample and Control as shown in figure 18,19,20.

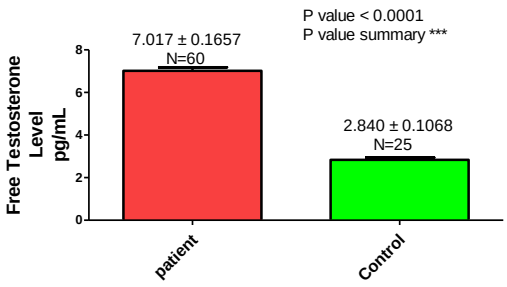


**Fig 18**: Distribution of samples for Free Testosterone Level

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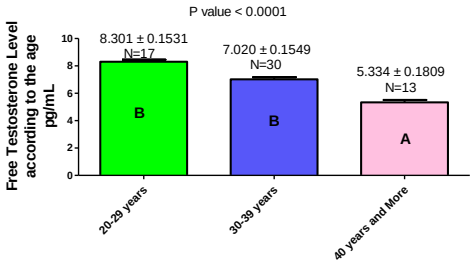


**Fig 19**: Distribution of samples for Free Testosterone Level according to age

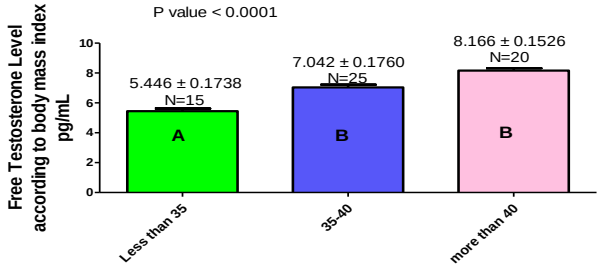


**Fig 20**: Distribution of samples for Free Testosterone Level according to body mass index

In PCOS women, the index is significantly higher ($p<0.05$) than the group without it, indicating a possible increase in insulin resistance that causes elevated levels of this hormone. This speeds fat storage, making it increasingly difficult to lose weight — even when calorie consumption is normal. Altered hormonal levels, including increased production of androgens that affect fat distribution and lead to greater central (visceral) rather than peripheral fat (14), also play a role.

Participants comprised healthy women aged 21–45 years recruited from their annual health check-up for hospital staffs and volunteers of the university community in Singapore; those with polycystic ovary syndrome (PCOS) and body mass index (BMI) were divided into four categories: non-PCOS (normal BMI), non-PCOS (high BMI), PCOS (normal BMI), and PCOS (high BMI). Generalized linear modeling analysis was conducted to compare clinical, ovarian, hormonal and metabolic parameters among these four groups. Among the 389 participants, 134 (34.4%) had PCOS and 255 (65.6%) were non-PCOS. Overall, 45.2% portion of the women had high BMI (≥ 23). PCOS women had a significantly higher body mass index than the non-PCOS group (mean (standard deviation): 25.14 ± 6.46 vs. 23.08 ± 4.36, $p <0.001$). Shallcross et al. (2017) showed that women with PCOS and above normal BMI had 2.96 times higher hair growth than those who have normal BMI (15).

Results: There was a significant increase ($p<0.05$) in the anti-Müllerian hormone level among women with polycystic ovary than the control group. The reason is An increase in the number of microfollicles occurs when several follicles all form within the same ovary. These follicles are the main source of AMH secretion; thus, more follicles correlate with higher AMH levels in blood. That is, in women with PCOS the number of follicles not only increases but the granulosa cells of each follicle also secrete higher than normal amounts of AMH. (16).

Results: The study found significantly ($p<0.05$) increased levels of Luteinizing Hormone and Follicle-stimulating Hormone in women with PCOS as compared to the control group. Nevertheless, in PCOS women according to their age there was Luteinizing Hormone and Follicle-stimulating Hormone significant difference ($p<0.05$). Additionally, PCOS women with different body mass index had significantly ($p<0.05$) different serum Luteinizing Hormone and Follicle-stimulating Hormone levels as well. the critical pathogenesis is that Increased GnRH pulse frequency preferentially induces LH rather than FSH secretion. Muscle tissue and fat-uptake during the post-ovulatory phase further derive feedback to LH, stimulating excessive NCOS-derived androgen generation, which is characteristic of polycystic ovary syndrome (PCOS) that manifests as chronic anovulation with elevated blood LH levels compared to average healthy women (17,18).

MicroRNA-21 expression was significantly higher ($p<0.05$) in women with PCOS as compared to control group. However, MicroRNA-21 expression significantly differed ($p<0.05$) by age. MicroRNA-21 expression differed significantly ($p<0.05$) according to body mass index (BMI) of patients with PCOS. Might also be because PCOS is associated with a state of chronic, low-grade inflammation. As inflammation rises, pro-inflammatory cytokines (IL-6 and TNF-α) elevate the expression of microRNA molecule (miR-21), which responds to inflammatory processes. Such inflammatory milieu leads to high levels of miR-21 in women with the disease. Suggests that insulin resistance is a feature of PCOS. High levels of insulin activate cellular signaling pathways, including the PI3K/AKT pathway which can

induce miR-21 expression. Increased miR-21 might aggravate metabolic disorder in PCOS. Excess androgens that are characteristic of PCOS can stimulate miR-21 expression in ovarian tissue, specifically granulosa cells. This disorder possibly interferes with normal follicle maturation along with ovulation(19,20).

## Conclusion

PCOS has been linked to significant hormonal and metabolic dysfunction, as indicated by the current study. Women with PCOS had greater body mass index, elevated anti-Müllerian hormone and luteinizing hormone levels, free testosterone and Beclin-1 as well as higher LH/FSH ratios in comparison to healthy controls. Moreover, microRNA-21 level was significantly higher in women with PCOS, and positively correlated with age and body mass index. These results indicate that miRNA-21 is a potential biomarker for worsening severity of the disease and metabolic risk in PCOS. Nonetheless, larger and longer-term studies are necessary to validate its potential diagnostic and prognostic value.

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## Author’s Contributions

Authors had equal contribution in this manuscript.

## Ethics

This study was conducted under approval by the medical ethics committee at the University of Kufa [2017]. Verbal and written consent was provided by parents and agreement for publication was obtained from both participants and researchers.

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