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# Study the correlation between *Helicobacter pylori* and insulin resistance in a group of women with polycystic ovarian syndrome in Baghdad city

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SUMMARY

**AUTHORS' CONTRIBUTION: (A)** Study Design · **(B)** Data Collection . **(C)** Statistical Analysis · **(D)** Data Interpretation · **(E)** Manuscript Preparation · **(F)** Literature Search · **(G)** No Fund Collection

**Background:** Polycystic Ovary Syndrome (PCOS) is a widespread problem among women lived in Baghdad city in terms of its thorny relationship with insulin resistance, which is a relational element with the case of infection with the *Helicobacter pylori* bacteria in the same women. The phenomenon of insulin resistance and the health problems that follow it has become a matter of concern for Iraqi women who suffer from polycystic ovary syndrome and who have been diagnosed with *H. pylori.*

**Objective:** This study determined the effect of *H. pylori* infection on insulin resistance in a group of women with polycystic ovary syndrome (PCOS).

**Methods:** Cases were collected at Kamal Al-Samarrai hospital for infertility. The total number of Cases was 130 divided into 90 PCOS and 40 control from the staff of the hospital. Biochemical and immunological parameters of Fasting Blood Sugar (mg/dL), Insulin (mIU/L), HOMA-IR and Cytotoxin-binding antibodies (CagA_IgG) were used to find the effects of *H. pylori* infection on insulin resistance in PCOS patients.

**Results:** The results of this study observed the number of PCOs female groups who treated with metformin gave positive CagA-IgG (≥ 0.4) results were 26/40 (47.3%) *vs.* 29/50 (52.7%) of those who not treated with metformin in comparing with control groups with no cases had positive results, Statistically these differences were highly significant (P-value ≤ 0.0001). The data reveals that both the untreated and treated groups exhibit significantly elevated levels of fasting blood sugar (F.B.S), insulin, and insulin resistance (IR) when compared to the control group. However, the untreated group displays the highest levels for all these parameters.

**Conclusion:** The most cases of PCOs were obese and overweight BMI (Kg/m$^2$) among the untreated (not taken metformin treatment) groups, observed the number of PCOs female groups who treated with metformin had positive cagA-IgG. Both insulin levels and insulin resistance are markedly elevated in female with positive CagA-IgG status in both treated and untreated groups; this indicates a possible association between CagA-IgG positivity and metabolic disturbances, especially concerning insulin regulation and resistance.

**Keywords:** *H. pylori;* Polycystic ovary syndrome; Insulin resistance; CagA-IgG; Metformin

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## INTRODUCTION

Polycystic Ovary Syndrome (PCOS), an endocrine-metabolic illness that typically manifests in adolescence in women who are fertile, is actually a chronic type of anovulation with wide range of clinical symptoms and indicators. The main clinical features include polycystic Ovary Morphology (PCOM) on ultrasonography, irregular menstrual cycles, and the presentation of androgen excess (hirsutism, acne, and laboratory hyperandrogenism), the etiology is multifactorial, involving factors such as insulin resistance, excess androgen exposure, ovarian and hypothalamic dysfunction, genetic and epigenetic vulnerability, and processes associated with obesity [1,2].

Obesity is analyzed in around one-half of patients with PCOs, and they play a basic part within the improvement of IR and conceivably androgen hypersecretion in these ladies. Delays in diagnosis can cause comorbidities to worsen, which makes it more challenging to adopt lifestyle changes that are essential for improving PCOS symptoms and quality of life [3].

Obstructive sleep apnea (OSA), endometrial cancer, metabolic syndrome, obesity, impaired glucose tolerance, type 2 diabetes mellitus, cardiovascular risk, depression, and nonalcoholic fatty liver disease/nonalcoholic steatohepatitis (NAFLD/NASH) are just a few of the many morbidities associated with PCOS. While there are different screening guidelines for each of these conditions, the doctor must have a low threshold for workup in the event that PCOS patients exhibit any indication, with PCOS, many, if not most, women have insulin resistance. Insulin resistance (IR) is defined by a reduction in the tissue's sensitivity to insulin, which acts as the fundamental cause of diabetes [4,5].

It encompasses a critical part within the advancement of several metabolic diseases. The exact cause of insulin resistance in PCOS is still unknown; it is believed that the underlying problem is in the post-receptor phosphatidylinositol 3-kinase (PI3-K) insulin pathway, which mediates the effects of insulin on metabolism. In women with PCOS, other factor might also play a role in the development of insulin resistance. Such as elevated plasma testosterone level [6,7].

Weight gain, which may be mediated through inflammatory pathways, increases the severity of insulin resistance in women with PCOS. Only the PI3-Kpost-receptor insulin pathway becomes resistant to the effects of insulin after gaining weight and becoming obese, which is comparable to the insulin resistance that defines T2D and PCOS. Perhaps the more descriptive phrase "metabolic insulin resistance" should be used instead of the general word "insulin resistance" [8].

*H. pylori* (*H. pylori*) are gram-negative, spiral-shaped bacteria that mostly inhabit the stomach's lining cells., its one of the most prevalent infections that affect people [9]. About half of the world's population suffers from this bacterial infection, which is among the most prevalent in the globe [10]. The stomach germ is more common in underdeveloped nations and affects about 50% of the world's population. While some experts think the infection mechanism is unclear, others think that the patient's instruments, contact with him, or tainted food are some of the past sources of infection. The pathogenic pathways and virulence of *H. pylori* infection are divided into three phases: the development of sickness, the immunological response that follows, and the colonization of the stomach mucosa [11,12].

Studies demonstrate that *H. pylori* infection can result in inflammation and the generation of inflammatory cytokines which can trigger the development of diabetes [13,14] also response proinflammatory leads to infection causes in host cells results in a feed-forward stimulation loop that increases the effects of CagA and inflammation in the gastric mucosa that has been injected with CagA [15,16]. Cytotoxin-associated gene A (CagA) is a translocated oncoprotein that causes morphofunctional changes in gastric epithelial cells and a chronic inflammatory response that raises the likelihood of developing precancerous lesions. It is the most significant virulence factor in *H. pylori*. After tyrosine phosphorylation and translocation.

According to other research in this filed, *H. pylori* infection has been linked to the development of resistance to insulin (IR), and its infection is positively correlated with tumor necrosis factor α (TNF-α), which frequently causes insulin resistance (IR) and the onset of metabolic syndrome, and negatively correlated with serum leptin levels [17-19]. Tumor necrosis factor alpha (TNF-α) is a cytokine with pleiotropic effects on different kinds of cells. Numerous inflammatory responses have been found to be significantly regulated by it [20].

## METHODS

This study included 130 female aged 19 to 38 years, categorized into three cohorts: 40 treated (metformin) with PCOs and 50 untreated with PCOs. Additionally, 40 control. Female data encompassed various factors, including age, length, weight, and other clinical signs, including: Hair loss, alopecia, acne, hirsutism, stomach pain, and bloating.

Sample collection :Collected 5 ml blood from each outpatient from Kamal Al-Samarrai Hospital for Infertility and Baghdad Medical City with PCOs, and same volume from control which was then transferred into gel tubes, all samples were appropriately labeled, then sent to the laboratory using dry-ice packs to maintain low temperatures. The fasting blood sugar (FBS) serum values (mg/dl) were determined using the Mindray BA-88A machine, Insulin (mIU\L) was evaluated by COBAS INTEGRA 400 PLUS and Human Anti Cytotoxin-Associated Protein Antibody (CagA_IgG) was evaluated by ELISA.

**Inclusion criteria:** Based on the gynecologist's diagnosis, a serum sample from polycystic ovary syndrome patients was collected.

**Exclusion criteria:** Pregnant women.

**Determination of Fasting Blood Sugar (FBS) (mg/dL):** The blood sample was prepared after the centrifugation process, and only the serum was taken. An amount of 0.5 ml from serum was placed in the cuvette to read the absorption rate. The absorbance was measured at 505 nm. Serum fasting blood sugar (FBS) ≥120 mg/dl was determined by using the Mindray BA-88A machine, a semi-automated a variety of biochemical tests can be carried out using this biochemistry analyzer. FBS = 75-126 mg/dl (4.1- 6.1 mmol/l).

**Determination of fasting insulin (μU/mL):** Using the Roche Kit of the Cobas equipment 0.5 ml of serum was taken and placed in the device. COBAS INTEGRA 400 plus analyzer, a fully automated device that uses more than 140 applications for all types of sample matrices, was used to measure serum fasting insulin.

**Determination of HOMA-IR:** The level of blood sugar is measured. The patient's degree of insulin resistance is then determined using the equation in conjunction with the insulin ratio test.

### The following is an application of the HOMA-IR equation:

[(fasting glucose mg/dL) x (blood insulin μU/mL)]/405 or [(fasting glucose mmol/L) x (blood insulin μU/mL)]/22.5 (20) is the formula for insulin resistance. The ideal HOMA-IR insulin sensitivity is less than 1, levels above 1.9 indicate early insulin resistance, and a score of 2.5 or higher is considered a patient's IR [21].

**Determination of *H. pylori* (HP) IgG:** Blood samples (3ml) kept in a gel tube and left to clot at room temperature (about 25˚C), centrifugation at 3000 rpm for 10 minutes, the serum was used to assess Cytotoxin-binding antibodies (CagA_IgG) by indirect ELISA, depending on guidelines provided by manufacturer and read result by semi-automated Human Reader Hs (Human, Germany). The presence of CagA-IgG is determined by comparing with the CUT-OFF value (0.4).

The statistical analysis performed using IBM SPSS statistics software (version 26.0). Results analyzed using

Variation-ANOVA and expressed as mean ± standard error. The p-value was used to determine level of statistical significance, with p≤ 0.05 or p≤ 0.0001 being statistically significant.

## RESULTS

**Demographic results:** The results shown highly significant (P-value ≤ 0.0001) by observed the most cases of PCOs were obese and overweight BMI (Kg/m$^2$) among the untreated (not taken metformin treatment) groups than (taken metformin treatment) with 18/50 (51.4%), 21/50 (34.4%), 16/40 (26.2%), 16/40 (45.7%) respectively.

The results of the current study recorded the number of untreated (not taken metformin treatment) cases which diagnosed with PCOs were 35 out of 50 (41.7%) at the age groups (19-28) years, while the number of treated (taken metformin treatment) cases which diagnosed with PCOs were 25 out of 40 (29.8%) at the age groups (19-28) years. The results also documented the number of untreated (not taken metformin treatment) cases which diagnosed with PCOs were 12 out of 50 (30%) *vs.* 13 out of 40 cases of treated (taken metformin treatment) were at the age groups (29-38) years, While the less cases of PCOs of both untreated and treated cases were recorded at the age groups 38< were 2 (33.3%),3 (50%) respectively, Statistically these differences were non-significant (P-value=0.66) as arranged in **Tab. 1.**

**Symptom of PCOs among cases:** Alopecia and hirsutism both showed significant differences, with higher prevalence in treated and untreated groups compared to the control group, suggesting a strong association with the conditions being studied. The results of the study showed that there is a case of hirsutism in succession 20 (55.6%), 15 (41.7% and 1 (2.8%) in treated, untreated and control.

The results of the study showed that there is a case of alopecia in succession 31 (50.8%), 28 (45.9%), 2 (3.3%) in treated, untreated and control. Hair loss and acne: no significant differences were found among the groups. The data presented summarizes the prevalence of various symptoms (hair loss, alopecia, acne, and hirsutism) among three groups: treated, untreated, and control (**Tab. 2.**).

**Symptom of *H. pylori* among cases:** The results of this study showed the number of PCOs cases for those females who untreated (not taken metformin treatment) were suffered from stomach pain more than those females who treated cases were 28/50 (47.5%), 22/40 (37.3%),while the PCOs cases of both treated and untreated groups whose showed no stomach pain were 18/40 (25.4%),22/50 (31%) respectively, According to statistics, these disparities were very significant (P-value 0.002).

In regarding the bloating symptoms these symptom were founded mostly among females groups whose treated than untreated groups with 34/40 (40%), 27/50 (31.8%) respectively, while the untreated groups female whose not suffered from bloating were more than female groups whose treated 23/50 (51.%), 6/40 (13.3%) respectively, These variations were statistically significant. (P-value= 0.006) as arranged in **Tab. 3.**

The data reveals that although FBS levels do not show significant differences related to CagA-IgG status in either group, both insulin levels and insulin resistance are markedly elevated in individuals with positive CagA-IgG status in both treated and untreated groups. This indicates

**Tab. 1.** Characterization of Age range (years) and BMI (Kg/m2) between cases (treated, untreated) and control group.

| Variable | Category | Treated (n=40) | Untreated (n=50) | Control (n=40) | Total | P-value | Sig. |
|---|---|---|---|---|---|---|---|
| Age range (Years) | (19-28) | 25 (29.8%) | 35 (41.7%) | 24 (28.6%) | 84 (100.0%) | 0.66 | N.S |
| | (29-38) | 13 (32.5%) | 12 (30.0%) | 15 (37.5%) | 40 (100.0%) | | |
| | 38< | 2 (33.3%) | 3 (50.0%) | 1 (16.7%) | 6 (100.0%) | | |
| Total | | 40 (30.8%) | 50 (38.5%) | 40 (30.8%) | 130(100.0%) | | |
| BMI (Kg/m$^2$) | Normal weight | 8 (23.5%) | 11 (32.4%) | 15 (44.1%) | 34 (100.0%) | 0.001 | H.S |
| | Overweight | 16 (26.2%) | 21 (34.4%) | 24 (39.3%) | 61 (100.0%) | | |
| | Obese | 16 (45.7%) | 18 (51.4%) | 1 (2.9%) | 35 (100.0%) | | |
| **Total** | | 40 (30.8%) | 50 (38.5%) | 40 (30.8%) | 130(100.0%) | | |

**Tab. 2.** Symptom of PCOs among cases (treated and untreated) and control groups.

| Symptoms | | Studied groups | | | Total | P-value |
|---|---|---|---|---|---|---|
| | | Treated (n=40) | Untreated (n=50) | Control (n=40) | | |
| Hair loss | Yes | 40 (32.5%) | 46 (37.4%) | 37 (30.1%) | 123 (100.0%) | 0.19 N.S |
| | No | 0 (0.0%) | 4 (57.1%) | 3 (42.9%) | 7 (100.0%) | |
| Total | | 40 (30.8%) | 50 (38.5%) | 40 (30.8%) | 130(100.0%) | |
| Alopecia | Yes | 31 (50.8%) | 28 (45.9%) | 2 (3.3%) | 61 (100.0%) | ≤0.0001 H.S |
| | No | 9 (13.0%) | 22 (31.9%) | 38 (55.1%) | 69(100.0%) | |
| Total | | 40 (30.8%) | 50 (38.5%) | 40 (30.8%) | 130(100.0%) | |
| Acne | Yes | 14 (31.1%) | 17 (37.8%) | 14 (31.1%) | 45 (100.0%) | 0.99 N.S |
| | No | 26 (30.6%) | 33 (38.8%) | 26 (30.6%) | 85 (100.0%) | |
| Total | | 40 (30.8%) | 50 (38.5%) | 40 (30.8%) | 130(100.0%) | |
| Hirsutism | Yes | 20 (55.6%) | 15 (41.7%) | 1 (2.8%) | 36 (100.0%) | ≤0.0001 H.S |
| | No | 20 (21.3%) | 35 (37.2%) | 39 (41.5%) | 94 (100.0%) | |
| **Total** | | 40 (30.8%) | 50 (38.5%) | 40 (30.8%) | 130(100.0%) | |

a possible association between CagA-IgG positivity and metabolic disturbances, especially concerning insulin regulation and resistance.

**Tab. 4.** showed a comparative analysis of the average levels of fasting blood sugar (F.B.S), insulin, and insulin resistance (IR) across three groups: treated (G1), untreated (G2), and control (G3). The p-values for comparisons between groups (G1&G3, G2&G3, G1&G2) are all ≤ 0.0001, indicating highly significant differences (H.S) in F.B.S levels among the groups. The ANOVA p-value is also ≤ 0.0001, confirming that at least one group differs significantly from the others. Similar to F.B.S, the p-values for comparisons between groups are all ≤ 0.0001, indicating significant differences in insulin levels. The ANOVA p-value is also ≤ 0.0001. As well as, the p-values for comparisons are ≤ 0.0001, indicating significant differences in IR levels among the groups. The ANOVA p-value is ≤ 0.0001. The data reveals that both the untreated and treated groups' exhibit significantly elevated levels of fasting blood sugar (F.B.S), insulin, and insulin resistance (IR) when compared to the control group. However, the untreated group displays the highest levels for all these parameters.

**Tab. 5.** observed the number of PCOs female groups who treated with metformin positive cagA-IgG (≥0.4) results were 26/40 (47.3%) *vs.* 29/50 (52.7%) of those who not treated with metformin in comparing with control groups with no cases had positive results, These differences were statistically significant. (P-value ≤ 0.0001) as arranged in **Tab. 5.**

**Tab. 6.** data reveals that although FBS levels do not show significant differences related to CagA-IgG status in either group, both insulin levels and insulin resistance are markedly elevated in female with positive CagA-IgG status in both treated and untreated groups, this indicates a possible association between CagA-IgG positivity and metabolic disturbances, especially concerning insulin regulation and resistance.

## DISCUSSION

The results shown highly significant (P-value ≤ 0.0001) by observed the most cases of PCOs were obese and overweight BMI (Kg/m$^2$) among the untreated (not taken metformin treatment) groups than (taken metformin treatment) with 18/50 (51.4%), 21/50 (34.4%), 16/40 (26.2%), 16/40 (45.7%) respectively. Thus agreed with (Jensterle, et al., 2020 ) who metformin made strides the metabolic profile of women with PCOs throughout a harsh 36.1-month follow-up, particularly in terms of BMI, diastolic blood weight, and HDL cholesterol. Furthermore, women with PCOs who also had the metabolic abnormality at baseline seemed to gain more with metformin in terms of metabolism.

Findings imply that a contributing factor to polycystic ovarian syndrome (PCOS) is insulin resistance, which may raise the risk of cardiovascular disease. Compared to normal women, women with PCOS are more likely to have metabolic syndrome due to insulin resistance. According

**Tab. 3.** Symptoms of *H. pylori* among cases (treated and untreated) and control groups.

| Symptoms | | Studied groups | | | Total | P-value |
|---|---|---|---|---|---|---|
| | | Treated (n=40) | Untreated (n=50) | Control (n=40) | | |
| Stomach pain | Yes | 22 (37.3%) | 28 (47.5%) | 9 (15.3%) | 59 (100.0%) | 0.002 H.S |
| | No | 18 (25.4%) | 22 (31.0%) | 31 (43.7%) | 71 (100.0%) | |
| Total | | 40 (30.8%) | 50 (38.5%) | 40 (30.8%) | 130(100.0%) | |
| Bloating | Yes | 34 (40.0%) | 27 (31.8%) | 24 (28.2%) | 85 (100.0%) | 0.006 H.S |
| | No | 6 (13.3%) | 23 (51.1%) | 16 (35.6%) | 45 (100.0%) | |
| **Total** | | 40 (30.8%) | 50 (38.5%) | 40 (30.8%) | 130(100.0%) | |

**Tab. 4.** Comparative the mean levels of F.B.S (mg\dl) Insulin (mIU/L) and IR between cases treated, untreated and control.

| Test | Groups | M ± SD | G1&G3 | | G2&G3 | | G1&G2 | |
|---|---|---|---|---|---|---|---|---|
| | | | P-value | Sig. | P-value | Sig. | P-value | Sig. |
| FBS (70-120) | G1-Treated (n=40) | 96.32 ± 9.35 | ≤ 0.0001 | H.S | ≤ 0.0001 | H.S | ≤ 0.0001 | H.S |
| | G2-Untreated (n=50) | 109.20 ± 6.61 | | | | | | |
| | G3- Control (n=40) | 79.72 ± 6 | | | | | | |
| **Anova P-value** | | **≤ 0.0001 (H.S)** | | | | | | |
| Insulin (2-25) | G1-Treated (n=40) | 7.20 ± 3.35 | P-value | Sig. | P-value | Sig. | P-value | Sig. |
| | G2-Untreated (n=50) | 9.95 ± 3.87 | ≤ 0.0001 | H.S | ≤ 0.0001 | H.S | ≤ 0.0001 | H.S |
| | G3- Control (n=40) | 3.17 ± 0.97 | | | | | | |
| **Anova P-value** | | **≤ 0.0001 (H.S)** | | | | | | |
| IR (0-1.2) | G1-Treated (n=40) | 1.71 ± 0.83 | ≤ 0.0001 | H.S | ≤ 0.0001 | H.S | ≤ 0.0001 | H.S |
| | G2-Untreated (n=50) | 2.70 ± 1.10 | | | | | | |
| | G3- Control (n=40) | 0.6279 ± 0.20 | | | | | | |
| **Anova P-value** | | **≤ 0.0001 (H.S)** | | | | | | |

**Tab. 5.** Characterization of studied groups according to cutoff value to cagA-IgG (0.4) levels.

| CagA-IgG categories | Study Groups | | | Total | P-value | Sig. |
|---|---|---|---|---|---|---|
| | Treated (n=40) | Untreated (n=50) | Control | | | |
| Positive (≥0.4) | 26 (47.3%) | 29 (52.7%) | 0 (0.0%) | 55 (100.0%) | ≤0.0001 | H.S |
| Negative (>0.4) | 14 (18.7%) | 21 (28.0%) | 40 (53.3%) | 75 (100.0%) | | |
| **Total** | 40 (30.8%) | 50 (38.5%) | 40 (30.8%) | 130(100.0%) | | |

**Tab. 6.** Levels of diabetic screening among PCOs groups (treated and untreated) according to CagA-IgG categories.

| Test | CagA-IgG categories | Treated (n=40) | Untreated (n=50) |
|---|---|---|---|
| | | Mean ± SD | Mean ± SD |
| FBS (mg/dl) | Positve | 96.38 ± 10.87 | 109.03 ± 5.94 |
| | Negative | 96.21 ± 5.92 | 109.42 ± 7.58 |
| P-value | | 0.94 (N.S) | 0.84 |
| Insulin | Positve | 8.78 ± 3.00 | 11.26 ± 3.62 |
| | Negative | 4.25 ± 1.43 | 8.14 ± 3.53 |
| P-value | | ≤ 0.0001 (H.S) | 0.004 (H.S) |
| IR | Positve | 2.09 ± 0.77 | 3.05 ± 1.04 |
| | Negative | 1.01 ± 0.34 | 2.22 ± 1.03 |
| P-value | | ≤ 0.0001 (H.S) | 0.008 (H.S) |

to brief research, metformin improves the metabolic profile in PCOS. The long-term impact of metformin on metabolic markers in PCOS-afflicted women receiving normal care without a strict diet was assessed in the Indian study. Risk variables for metabolism were examined before and after using metformin [22]. Improvements in body mass index were observed. After starting at 34.3%, the prevalence of metabolic syndrome dropped to 21.4% (p = 0.0495). Women with PCOS who had metabolic syndrome at baseline experienced a substantially greater BMI reduction trajectory following metformin treatment than women without metabolic syndrome (p = 0.0369 for interaction). In summary, over a period of 36.1 months, metformin improved the metabolic profile of women with PCOS, particularly in terms of BMI [23]. Other Studies found that taking metformin and changing one's lifestyle decreased one's BMI. In PCOS, the majority of research reported comparable outcomes, although a small number also discovered that metformin decreased insulin resistance without lowering BMI [21].

The results were similar to those of the two Iraqi researchers [24]. The difference was statistically significant. (P<0.05) in body mass index between women with polycystic ovary syndrome and control ladies. The predominance of overweight and corpulence was also much greater in females with polycystic ovary syndrome. than in matched control women.

Comparison between treated and untreated PCOS groups showed a slight, but not statistically significant, increase in mean age in women participating in the study, respectively (84 (100.0%), 40 (100.0%), 6 (100.0%). This marginal difference, as indicated by the p-value of 0.66, suggests that while there may be a trend towards higher levels of age (19–28) in PCOS female, it is not large enough to draw definitive conclusions. This finding is consistent with some studies suggesting that environmental factors such as endocrine disruptors may be associated with PCOS, but more robust and larger studies are needed to confirm any significant associations [25]. This result agreed with [26], polycystic ovary disorder (PCOS) is the foremost common heterogeneous endocrine clutter among ladies of regenerative age. The pathogenesis of PCOS remains tricky; in any case, there's proved proposing the potential commitment of hereditary intelligent or inclinations combined with natural components [26].

Correlation Symptom of PCOs among cases (treated and untreated) and control groups: The results of the study showed that there is a case of hirsutism in succession 20 (55.6%), 15 (41.7% and 1 (2.8%) in treated, untreated and control. Its can explain by with a 60–80% incidence, androgen excess is a primary pathophysiological feature of PCOS. Our results agreed with Fauser who explain the hirsutism as a commonplace clinical appearance of hyperandrogenism detailed in up to 70% of ladies with PCOS [27]. In ordinary ladies, androgens are emitted in roughly break even with amounts by the ovaries and the adrenal glands. Conversely, hand, androgen emission from multiple sources is recognizable about 35% of female PCOS patients. The primary source of androgen in PCOS is the ovary, whereas adrenal hyperandrogenism in PCOS is conceivably the result of a few variables counting hyperinsulinemia, changed cortisol digestion system, and expanded ovarian steroid generation. In grown-up ladies with PCOS and in hyperandrogenemic youths [28].

The results of our study showed that there is a case of Alopecia in succession 31 (50.8%) 28 (45.9%) 2 (3.3%) in treated, untreated and control. androgenic alopecia (AGA) is predominant in 22% of subjects assembly demonstrative standards for PCOS. (AGA) is related with clinical hyperandrogenism in other ways, but not with more prominent hazard of metabolic or biochemical hyperandrogenism brokenness compared to PCOS alone [29]. According to a retrospective investigation, the most accurate clinical indicators of PCOS are hirsutism and acanthosis nigricans [30].

The study's findings revealed the number of PCOs cases for those females who untreated (not taken metformin treatment) were suffered from stomach pain more than

those females who treated cases were 28/50 (47.5%), 22/40 (37.3%), while the PCOs cases of both treated and untreated groups whose showed no stomach pain were 18/40 (25.4%),22/50 (31%) respectively, These variations were statistically significant (P-value 0.002).

The results agreed with polycystic ovary disorder (PCOS) are the foremost common endocrine clutter in regenerative matured ladies. Regularly, hyperandrogenism is used to describe it. Constant anovulation and polycystic ovaries. Ladies with PCOS frequently encounter dermatologic signs of hyperandrogenism, counting hirsutism, skin break out vulgaris, and androgenic alopecia [31].

With PCOS, excessive hair growth is more common than hair loss. Your face, neck, chest, and torso are among the areas where excessive androgens usually cause hair growth. For this kind of hair loss to occur, testosterone levels must be fairly high [32]. Symptom of *H. pylori* among cases (treated and untreaded) and control groups.

Levels of diabetic screening among PCOs groups (treated and untreated) according to CagA-IgG categories.

The data reveals that although FBS levels do not show significant differences related to CagA-IgG status in either group, both insulin levels and insulin resistance are markedly elevated in individuals with positive CagA-IgG status in both treated and untreated groups. This indicates a possible association between CagA-IgG positivity and metabolic disturbances, especially concerning insulin regulation and resistance. That results agreed with Buzásm,s study [33]. Globally, *H. pylori* continue to be the most prevalent infection. When this bacterium colonizes the stomach, it results in chronic gastritis, a low-grade inflammatory disease that can produce long-term symptoms as well as local ones including peptic ulcers, gastric cancer, and lymphoma. These extragastric symptoms are most likely caused by cytokines and acute phase proteins generated by the inflamed mucosa, even if *H. pylori* does not enter the bloodstream. There is conflicting and inconclusive epidemiological evidence linking *H. pylori* infection to metabolic alterations. Insulin resistance and *H. pylori* have been discovered to be most consistently associated with glucose metabolism; this is predicted proof that eradication reduces this prevalent metabolic problem. More active regimens should be discovered to achieve better results because diabetes individuals' eradication outcomes with standard regimens are noticeably poorer than those of non-diabetic patients [33].

There is growing evidence that the pathophysiology of *H. pylori* -induced mucosal alterations involves additional variables, such as the host's reaction to the infection. An elevated risk of gastric atrophy and/or gastric cancer has been associated with genetic variations in pro-inflammatory and immunoregulatory cytokines [26]. The strongest evidence that host immune responses influence clinical outcome comes from these investigations. The Th1 mucosal responses are polarized by cytokines like interleukin (IL)-12 and IL-18, which are elevated in *H. pylori* infection. Mice missing T cells have shown a significant correlation between the immune response and the outcome of stomach Helicobacter infection.

Serologic evidence of atrophic gastritis was linked to a higher prevalence of a similar trend reported in relation to CagA IgG antibody sero-positivity (difference of 0.14 g/dL in mean hemoglobin level), but of a lesser magnitude. Although there was no significant interaction between sex and either atrophic gastritis or CagA IgG sero-positivity, these differences were more pronounced in women [34].

Gastric acidity and ascorbic acid levels, which are critical for the absorption of dietary iron, are impacted by atrophic lesions in the stomach. Additionally linked to body gastric atrophy are reductions in intrinsic factor production and dietary vitamin B12 absorption, both of which can lead to pernicious anemia. Although CagA is linked to an inflammatory response in the stomach, it can also cause carcinogenesis regardless of inflammation. The prevalence of microcytic anemia was clearly higher in those with serological evidence of atrophic gastritis than in those without, and all three of the individuals with macrocytic anemia had positive CagA IgG serum antibody tests [35].

The results can explained by Jozkowiak, et al., study that saied The overproduction of acute-phase proteins like CRP and inflammatory cytokines like IL-8, IL-10, and IL-12 is frequently linked to the prognosis of IR. (36). Among adults, the frequency of IR with related metabolic problems has risen over the past few years, from 15.5% to 46.5%, especially as people age. Different changes in the hormones that control insulin metabolism, including gastrointestinal hormone, whose insufficiency is a common sign of *H. pylori* infection, were discovered to have an impact on IR [36].

Polycystic ovarian disorder (PCOS) is one of the promptly perceived endocrine organ sicknesses in ladies, being weak, and being overweight. Low-grade, persistent discomfort has emerged as a key factor contributing to PCOS. According to Indian research, female PCOS patients' Mononuclear Cells (MNC), which typically don't rely on fat, may react alarmingly to an increase in glucose levels, which may stimulate oxidative stress. Since MNC-derived macrophages are the primary source of cytokine mixture in massive fat tissue and also stimulate adipocyte cytokine synthesis, this is frequently necessary. In summary, research reveals the serious risks of affront resistance in healthy people suffering from PCOS. This lesson's findings, which ignored the nonappearance of BMI contrasts from other phenotypes, demonstrated that individuals with the typical PCOS phenotype were heavier and had higher degrees of affront and affront resistance [37].

Research shown infection with *H. pylori* can cause inflammation and the production of inflammatory cytokines, leading to the onset of diabetes [15] because chronic inflammatory response of *H. pylori* infection the neutrophils, T-cell and B-lymphocytes, macrophages, and plasma cells recruitment to gastric mucosa which promote continuous and localized inflammation [38].

Levels of diabetic screening among PCOs groups (treated and untreated) according to CagA-IgG categories.

The data reveals that although FBS levels do not show significant differences related to CagA-IgG status in either group, both insulin levels and insulin resistance are markedly elevated in individuals with positive CagA-IgG status in both treated and untreated groups. This indicates a possible association between CagA-IgG positivity and metabolic disturbances, especially concerning insulin regulation and resistance. That results agreed with Buzás's study [33] with *H. pylori* remains the most common infection worldwide. Colonization of the stomach with this bacterium causes chronic gastritis, a low-grade inflammatory disease with long-term symptoms and local consequences (peptic ulcer, stomach cancer, lymphoma). These extragastric symptoms are most likely caused by cytokines and acute phase proteins generated by the inflamed mucosa, even if *H. pylori* does not enter the bloodstream. There is conflicting and inconclusive epidemiological evidence linking *H. pylori* infection to metabolic alterations. Insulin resistance and *H. pylori* have been discovered to be most consistently associated with glucose metabolism; this is predicted proof that eradication reduces this prevalent metabolic problem. More active regimens should be discovered to achieve better results because diabetes individuals' eradication outcomes with standard regimens are noticeably poorer than those of non-diabetic patients [33].

## CONCLUSION

The most cases of PCOs were obese and overweight BMI (Kg/m$^2$) among the untreated (not taken metformin treatment) groups, observed the number of PCOs female groups who treated with metformin had positive cagA-IgG. Both insulin levels and insulin resistance are markedly elevated in female with positive CagA-IgG status in both treated and untreated groups, this indicates a possible association between CagA-IgG positivity and metabolic disturbances, especially concerning insulin regulation and resistance.

REFERENCES


1. **Li Y, Zhang J, Zheng X, et al.** Depression, anxiety and self-esteem in adolescent girls with polycystic ovary syndrome: a systematic review and meta-analysis. *Front Endocrinol.* 2024;15:1399580.
2. **Joham AE, Norman RJ, Stener-Victorin E**. Correction to Lancet Diabetes Endocrinol.
3. **Glueck CJ, Goldenberg N**. Characteristics of obesity in polycystic ovary syndrome: Etiology, treatment, and genetics. *Metabolism.* 2019;92:108-120.
4. **Norman RJ, Teede HJ.** A new evidence-based guideline for assessment and management of polycystic ovary syndrome. *Med J Aust.* 2018;209(7):299-300.
5. **Amisi CA**. Markers of insulin resistance in Polycystic ovary syndrome women: An update. *World J Diabetes.* 2022;13(3):129.
6. **Cheng L, Zhou J, Zhao Y, et al.** The associations of insulin resistance, obesity, and lifestyle with the risk of developing hyperuricaemia in adolescents. *BMC Endocr Disord.* 2024;24(1):220.
7. **Siemienowicz KJ, Coukan F, Franks S, et al.** Aberrant subcutaneous adipogenesis precedes adult metabolic dysfunction in an ovine model of Polycystic Ovary Syndrome (PCOS). *Mol Cell Endocrinol*. 2021;519:111042.
8. **Barber TM, Hanson P, Weickert MO, et al.** Obesity and polycystic ovary syndrome: implications for pathogenesis and novel management strategies. *Clin Med Insights Reprod Health*. 2019;13:1179558119874042.
9. **Darvishi M, Forootan M, Azmodeh O, et al.** Studying the frequency of *Helicobacter pylori* infection among women suffering from polycystic ovary resorting to hospital infertility center. *Biomed Pharmacol J.* 2017;10(1):75-80.
10. **Zhong X, Zheng H, Zhao S, et al.** Effects and mechanisms of *H. pylori* on cancers development and immunotherapy. *Front Immunol.* 2024;15:1469096.
11. **Elbehiry A, Marzouk E, Aldubaib M, et al**. *H. pylori* infection: Current status and future prospects on diagnostic, therapeutic and control challenges. *Antibiotics*. 2023;12(2):191.
12. **Denic M, Touati E, De Reuse H.** Pathogenesis of *H. pylori* infection. *Helicobacter.* 2020;25:e12736.
13. **Sabbagh P, Mohammadnia-Afrouzi M, Javanian M, et al.** Diagnostic methods for *H. pylori* infection: ideals, options, and limitations. *Eur J Clin Microbiol Infect Dis*. 2019;38:55-66.
14. **Stefano K, Rosalia A, Chiara B, et al.** Non-invasive tests for the diagnosis of *H. pylori*: state of the art. *Acta Bio Medica: Atenei Parmensis*. 2018;89(Suppl 8):58.
15. **Nodoushan SA, Nabavi A.** The interaction of *H. pylori* infection and type 2 diabetes mellitus. *Adv Biomed Res.* 2019;8(1):15.
16. **Takahashi-Kanemitsu A, Knight CT, Hatakeyama M.** Molecular anatomy and pathogenic actions of *H. pylori* CagA that underpin gastric carcinogenesis. *Cell Mol Immunol*. 2020;17(1):50-63.
17. **Talebi G, Saffarian P, Hakemi-Vala M, et al.** The effect of *H. pylori*-derived extracellular vesicles on glucose metabolism and induction of insulin resistance in HepG2 cells. *Arch Physiol Biochem*. 2024:1-2.
18. **Askar AA, Abdallah AA, Sedky A, et al.** Effect of *H. pylori* Infection on Insulin Resistance in non-Obese, non-Diabetic Patients. *Afro-Egypt J Infect Enem Dis.* 2021;11(4):382-388.
19. **de Melo FF, Marques HS, Pinheiro SL, et al.** Influence of *H. pylori* oncoprotein CagA in gastric cancer: A critical-reflective analysis. *World J Clin Oncol.* 2022;13(11):866.
20. **Jang DI, Lee AH, Shin HY, et al.** The role of tumor necrosis factor alpha (TNF-α) in autoimmune disease and current TNF-α inhibitors in therapeutics. *Int J Mol Sci.* 2021;22(5):2719.
21. **Cheang KI, Huszar JM, Best AM, et al.** Long-term effect of metformin on metabolic parameters in the polycystic ovary syndrome. *Diabetes Vasc Dis Res.* 2009;6(2):110-9.
22. **Shahebrahimi K, Jalilian N, Bazgir N, et al.** Comparison clinical and metabolic effects of metformin and pioglitazone in polycystic ovary syndrome. *Indian J Endocrinol Metab.* 2016;20(6):805-809.
23. **Akhtar N, Banu H, Morshed MS, et al.** Effects of metformin on polycystic ovary syndrome: a randomized, double-blind, placebo-controlled study. *IMC J Med Sci.* 2021;15(2):1-2.
24. **Alsaadi YL, Mohamad BJ.** Prevalence of hyperandrogenism in Iraqi women with polycystic ovary syndrome. *Iraqi J Sci.* 2019:2600-2608.
25. **Kshetrimayum C, Sharma A, Mishra VV, et al.** Polycystic ovarian syndrome: Environmental/occupational, lifestyle factors; an overview. *J Turk Ger Gynecol Assoc.* 2019;20(4):255.
26. **Jozkowiak M, Piotrowska-Kempisty H, Kobylarek D, et al.** Endocrine disrupting chemicals in polycystic ovary syndrome: the relevant role of the theca and granulosa cells in the pathogenesis of the ovarian dysfunction. *Cells.* 2022;12 (1):174.
27. **Fauser BC, Tarlatzis BC, Rebar RW, et al.** Consensus on women's health aspects of Polycystic Ovary Syndrome (PCOS): the Amsterdam ESHRE/ASRM-Sponsored 3rd PCOS Consensus Workshop Group. *Fertil Steril.* 2012;97(1):28-38.

28. **English RS, Barazesh JM**. Self-assessments of standardized scalp massages for androgenic alopecia: survey results. *Dermatol Ther*. 2019;9(1):167-178.

29. **Prasad S, De Souza B, Burns LJ, et al.** Polycystic ovarian syndrome in patients with hair thinning. *J Am Acad Dermatol.* 2020;83(1):260.

30. **Schmidt TH, Khanijow K, Cedars MI, et al.** Cutaneous findings and systemic associations in women with polycystic ovary syndrome. *JAMA Dermatol.* 2016;152(4):391-398.

31. **Burns LJ, De Souza B, Flynn E, et al.** Spironolactone for treatment of female pattern hair loss. *J Am Acad Dermatol.* 2020;83(1):276-278.

32. **Sachdeva S**. Hirsutism: evaluation and treatment. *Indian J Dermatol*. 2010;55(1):3-7.

33. **Buzás GM.** Metabolic consequences of *H. pylori* infection and eradication. *World J Gastroenterol.* 2014;20(18):5226.

34. **Muhsen K, Sinnreich R, Beer-Davidson G, et al.** Sero-prevalence of *H. pylori* CagA immunoglobulin G antibody, serum pepsinogens and haemoglobin levels in adults. *Sci Rep.* 2018;8(1):17616.

35. **D'Elios MM, Amedei A, Del Prete G.** *H. pylori* antigen-specific T-cell responses at gastric level in chronic gastritis, peptic ulcer, gastric cancer and low-grade Mucosa-Associated Lymphoid Tissue (MALT) lymphoma. *Microbes Infect*. 2003;5(8):723-730.

36. **Peña AS, Witchel SF, Hoeger KM, et al.** Adolescent polycystic ovary syndrome according to the international evidence-based guideline. *BMC Med*. 2020;18:1-6.

37. **Purwar A, Nagpure S.** Insulin resistance in polycystic ovarian syndrome. *Cureus.* 2022;14(10).

38. **Kim N**. Immunological reactions on H. pylori infection. In*H. pylori*, *Singapore: Springer Nature Singapore.* 2024: 39-59.