

Relation between Helicobacter Pylori Infection and Mild Pre-eclampsia

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ABSTRACT

Background: Infections were assumed as potential risk-factors for pre-eclampsia (PE). An exciting correlation was found among PE and Helicobacter pylori (HP) infections. HP is an infectious agent that was related to several complications throughout the gestation course, counting iron insufficiency anemia and hyper-emesis gravidarum. It is assessed to be existing in 46 percent of gestations.

Aim of the work: to show the role of HP infections in females with mild PE.

Patients and methods: This a prospective cohort study included a number of 100 women between 36th to full-term gestational weeks was conducted in obstetrics and gynecology department, El-Hussein Hospitals, Al-Azhar University. Lab investigation included Hb (%), RBCs, WBCs, platelets sCr. S.prolactine. Coagulation profiles (PT, aPTT, and fibrinogen. ldh level (LDH). C/A ratio in urine (uACr). Urine:albumin dipstick testing Thrombomodulin (TM). Serological tests using ELISA serology kits and UBT.

Results: A significant change was found among the study groups as regard BMI only. A significant change was found among the study groups as regard SBP and DBP. A significant change was found among the study groups as regard hemoglobin, PLT, ALT, AST, LDH, creatinine, 24h proteinuria UACR and TM. Positive anti HP anti-bodies were significantly more frequent in PE cases. Regarding to anti-HP anti-bodies in PE-group, a nonsignificant change was found among the study groups. A significant change was found among the study groups as regard birth weight only.

Conclusion: Considering the correlation among positive test and PE incidence we may utilize screening for elevated risk females and treatment for pre-eclampsia cases.

Keywords: Mild Pre-eclampsia ; Helicobacter Pylori, Pregnant .

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INTRODUCTION

Preeclampsia (PE) is a main contributor to motherly and embryonic morbidities and mortalities, as it affects from 2 to 8% of gestations. It is a multi-system condition and its complex pathophysiology still under study.¹ It is hypothesized that insufficient trophoblast invasions and poor spiral artery remodeling result in placental ischemia and oxidative-stress. This procedure indorses the releases of several intermediaries into the motherly circulations, causing elevated vaso-reactivity and generalized endothelial injury.²

The function of systematic inflammations is maintained by the fact that pre-eclampsia is accompanying with increased motherly circulating cytokines, particularly Tumor Necrosis Factor- α (TNF- α), Interleukin-6 (IL-6), Interleukin-10 (IL-10) and Interferon- γ (IFN- γ). There is rising indication that numerous infectious parameters are concerned in the pathogenesis of the disease, like

periodontal disorder, urogenital and parasitic infection.³

Helicobacter pylori is an infectious agent that was related to several complications throughout the gestation course, counting iron insufficiency anemia and hyper-emesis gravidarum. It is assessed to be existing in 46 percent of gestations.⁴ Cytotoxin associating gene-A (CagA) is a 120-145 kDa protein that was formerly related to the advance of gastric tumor.⁵

AntiCagA anti-bodies cross-reacts in vitro with placental p-actin, decreasing the intrusiveness of the cytotrophoblast. Exceeding 10 years ago, the same authors detected that antiCagA antibodies cross-reacts with antigens from ordinary to atherosclerotic blood vessel. The procedure includes vascular wall peptides and is supposed to cause activations of the inflammation cascades which was formerly concerned in the pathogenesis of pre-eclampsia. Although, experimental researches in this topic are still lost.⁶

In the previous 2 decades, the frequency of PE has increased in the Western Republics, perhaps because of an elevated prevalence of influencing parameters, like advanced motherly ages, chronic Hypertension (HPT), Diabetes Mellitus (DM), obese, and the growing usage of supported reproducing methods.⁷

In spite of this latter observations, numerous observational researchers have discovered H.pylori sero-positivity status with PE. But, up to the present time it still unidentified whether cases with H.pylori infections are at elevated of rising PE.¹

The aim of the current study was to illustrate the role of H.pylori infections in women with mild pre-eclampsia.

PATIENTS AND METHODS

This prospective cohort study enrolled a number of 100 women between 36th to full-term gestational weeks has been performed at obstetrics and gynecology dep, El-Hussein Hospital, Al-Azhar University, the interval between May 2020 to December 2020.

This study based on study carried out by Tersigni et al.⁷ Epi Info STATCALC was used to calculate the sample size by considering the following assumptions: - 95% two-sided confidence level, with a power of 80%. &a error of 5% odds ratio calculated= 1.115. The final maximum sample size taken from the Epi- Info output was 92. Thus, the sample size was increased to 100 cases to assume any drop out cases during follow up.

Written knowledgeable agreement was attained and the research was accepted by the Ethical Committee of Al-Azhar Faculty of Medicine.

Inclusion criteria: Gestational age between 36th to full-term gestational weeks according to a reliable date for the last menstrual period and ultrasound evaluation, and mild pre-eclampsia.

Exclusion criteria: Manifold gestations, embryonic irregularities, DM, chronic HPT, auto-immune diseases, early membrane ruptures, infections, systemic diseases as renal or hepatic disorders detected before gestation, and women in active labor.

All women were allocated into 2 groups: Group I: (Cases group): including 50 pregnant preeclamptic women with gestational age 36st weeks to full-term gestation, and Group II: (Control group): included 50 pregnant nonpreeclamptic women who are matched in age, and gestational age with the case group.

A PE diagnosing is performed if a BP of 140/90 mm-Hg was established by 2 measures done at 6 hours periods and in the existence of extra quantity of protein (100-300 mg/L) in a one day urine sample.

All patients were subjected to:

Complete history taking: Personal history. menstrual history, history Parity, present history: of chronic diseases and medication, past history of HTN, DM, family history of similar condition or diabetes, history of allergy to any medication, and surgical history of operation.

Examination: General examination and abdominal, local clinical examination, and vaginal examination.

Laboratory investigation: CBC: Hb (%), RBCs, WBCs, platelet count. S. ALT. AST. sCr. S.prolactine. Coagulation profiles (pro-thrombin time [PT], activated partial thromboplastin time [aPTT], and fibrinogen. Serum lactate dehydrogenase level (LDH). Urinary albumin creatinine ratio (uACr). Urine: albumin assessment by dipstick. Plasma Thrombomodulin (TM) was assessed with ELISA. Serological tests were performed for detection of anit-H. Pylori IgG using ELISA serology kits with sensitivity and specificity of 85% and 79%. Anti-H. pylori IgG remain for along time eve after treatment thus current infection was confirmed by Urea breath test (UBT), a highly accurate and reproducible test with near 95% sensitivity and specificity, was used for confirmation of current H. pylori infection by the urease activity of H. pylori. the ¹³C- labeled urea was ingested by the patient to be hydrolyzed into labeled CO₂ in stomach, then the labeled CO₂ absorbed in the blood and exhaled by breathing in which labeled CO₂ was measured.

Statistical Analysis:

Data analyzed via SPSS-20 (IBM, USA). Quantitative variables have been introduced as mean and SD. Qualitative variables have been introduced as numbers and percentages. For comparison between parametric quantitative variables of 2 groups, Student t testing has been utilized. Qualitative variables comparison has been performed via chi-square (X²) testing or Fisher's exact testing when frequencies were less than 5. Pearson correlation coefficients have been utilized to evaluate the associations among 2 variables with normal distribution. When a variable wasn't of normally distribution, At P< 0.05 the results had statistical significance

RESULTS

	Pre-eclampsia (n=50)	Normotensive (n=50)	t/X ²	p
Age (years) Mean ± SD	27.33 ± 4.28	25.77 ± 4.54	1.77	.081
BMI (kg/m ²) Mean ± SD	27.12 ± 3.64	26.34 ± 2.39	2.18	.032
Parity Mean ± SD	1.22 ± 0.95	1.38 ± 1.17	.751	.455
SBP (mmHg) Mean ± SD	147.13 ± 12.44	123.74 ± 11.48	9.77	.000
DBP (mmHg) Mean ± SD	92.13 ± 8.55	74.39 ± 9.22	9.98	.000

BMI: Body mass index. SBP: systolic blood pressure. DBP: Diastolic blood pressure.

Table 1: Demographic and clinical parameters among the study groups.

There was no significant difference between the 2 groups regarding Age or parity (P=0.081, 0.455). there was significant difference between the 2 groups regarding BMI, SBP and DBP which were increased in the preeclamptic group (P-Value=0.032, 0.000 and 0.000) (Table 1).

	Pre-eclampsia (n=50)	Normotensive (n=50)	t	P
Hb (g/dL) Mean ± SD	11.19 ± 1.21	11.68 ± 1.17	2.06	.042
TLC (x 10 ³ /L) Mean± SD	8.15 ± 2.32	8.41 ± 2.53	.536	.594
PLT (x 10 ³ /L) Mean± SD	287.54 ± 57.76	312.31 ± 45.14	2.39	.019
ALT (U/L) Mean± SD	49.22 ± 27.34	26.31 ± 7.76	5.7	.000
AST (U/L) Mean± SD	42.37 ± 26.76	23.47 ± 8.33	4.77	.000
RBS (mg/dl) Mean ± SD	137.75 ± 25.41	139.63 ± 26.88	.359	.721
LDH (U/L) Mean ± SD	364.52 ± 157.85	291.59 ± 103.69	2.73	.007
Creatinine (mg/dl) Median (Range)	0.82 (0.7 - 1.2)	0.75 (0.6 - 1.1)	3.75	.001
Urea (mg/dL) Mean ± SD	13.25 ± 3.83	12.47 ± 3.6	1.05	.297
Proteinuria (mg/dl per 24h) Mean ± SD	615.23 ± 142.46	137.57 ± 17.55	23	.000
UACR Mean ± SD	1.97 ± 1.14	0.113 ± 0.052	11.5	.000
TM (ng/mL) Mean ± SD	63.42 ± 7.53	42.31 ± 3.84	5.31	.000

Hb: Hemoglobin. TLC: Total lymphocyte count. PLT: Platelet count. ALT: Alanine transaminase AST: Aspartate aminotransferase. RBS: Random blood sugar. LDH: Lactate dehydrogenase. UACR: Urine Albumin-to-Creatinine ratio. TM: Tumor marker.

Table 2: Laboratory results between the study groups.

There was significant difference regarding ALT, AST, LDH, creatinine, proteinuria, UACR and TM which were increased in preeclamptic group (P-Value=0.000, 0.000, 0.007, 0.001, 0.000, 0.000 and 0.000 respectively). There was there was significant difference regarding Hb which was decreased in the preeclamptic group (P-Value=0.042) and there was non-significant difference regarding TLC, RBS and Urea between the 2 groups. (Table 2).

Anti H.pylori antibodies	Pre-eclampsia (n=50)	Normotensive (n=50)	χ ²	P
Positive	34 (68%)	23 (46%)	4.94	.026
Negative	16 (32%)	27 (54%)		

Table 3: Anti H.pylori antibodies between the two studied groups

There was significant difference regarding anti H. pylori Ab as 34 (68%) cases of the preeclamptic cases were positive compared to 23 (46%) cases from the normotensive group. There were 16 (32%) negative cases of the preeclamptic cases compared to 27 (54%) cases from the normotensive group (P-Value = 0.026). (Table 3).

	Anti H.pylori antibodies		t	p
	Positive (n=34)	Negative (n=16)		
Age (years) Mean ± SD	27.46 ± 4.27	26.3 ± 4.62	.873	.387
BMI (kg/m ²) Mean ± SD	26.84 ± 3.45	25.72 ± 3.14	1.1	.277
Parity Mean ± SD	1.29 ± 1.05	1.11 ± 0.964	.592	.557

Table 4: Demographic data distribution according to anti H.pylori antibodies in pre-eclampsia group

A nonsignificant change was found among the study groups regarding Age, BMI and parity. The mean age in cases with positive Anti H.pylori antibodies was 27.46 ± 4.27 years compared to 26.3 ± 4.62 years (P-Value=0.387). the mean BMI in cases with positive Anti H.pylori antibodies was 26.84 ± 3.45 kg/m² compared to 25.72 ± 3.14 kg/m² (P-Value=0.277). the mean parity in cases with positive Anti H.pylori antibodies was 1.29 ± 1.05 compared to 1.11 ± 0.964 (P-Value= 0.557) (Table 4).

	Pre-eclampsia (n=50)	Normotensive (n=50)	t	p
GA (weeks) Mean \pm SD	37.44 \pm 0.927	37.6 \pm 0.629	1.01	.315
Birth weight (kg) Mean \pm SD	2.84 \pm 0.435	3.02 \pm 0.314	2.37	.019
Apgar Score at 1 min Mean \pm SD	6.73 \pm 1.65	7.11 \pm 0.964	1.41	.163
Apgar Score at 5 min Mean \pm SD	9.71 \pm 0.499	9.86 \pm 1.21	.811	.419

GA: Gestational age.

Table 5: Neonatal outcomes between the studied groups

A significant change was found among the study groups as regard birth weight only with P-Value= 0.019. there was non-significant change in GA, Apgar score at 1 min and Apgar score at 5 min as P-Value= 0.315, 0.163 and 0.419 respectively. (Table 5).

Anti H. pylori antibodies	Mild preeclampsia (n=28)	Severe preeclampsia (n=22)	χ^2	P
Positive	15 (53.6%)	19 (86.4%)	6.09	0.014
Negative	13 (46.4%)	3 (13.6%)		

Table 6: Correlation between H. pylori and severity of preeclampsia.

A significant difference was found among the study groups regarding preeclampsia severity. There was increase in the severity of preeclampsia in correlation to the positivity of anti H. pylori antibodies observed in 19 (86.4%) cases compared to 15 (53.6%) cases with mild preeclampsia and positive anti H. pylori antibodies. The number of cases with severe preeclampsia decreased in patients with negative antibodies. (P-Value= 0.014).

DISCUSSION

There were statistical insignificant differences in basic data (age and parity) between two groups except in BMI which was significantly higher among women with pre-eclampsia.

These results were dissimilar from other reports as we omitted the patients of pre-eclampsia who had already impacted by other disorders as DM, essential HPT or any other medical disorders that happen more in elder group which rise the occurrence risk of PE.⁸

In the current study, systolic and diastolic blood pressure were significantly elevated in PE-patients in comparison to in control group. These findings are maintained by Maybury and Waugh⁹ and shows that PE is a multi-organ disorder (systemic endothelial dysfunctions impacting renal glomeruli resulting in elevated protein losing to the urine).

In this study a significant change was found among the study groups as regard hemoglobin, PLT, ALT, AST, LDH, creatinine, 24h proteinuria UACR and TM.

Severe PE shows elevated blood urea, s.creatinine and s.uric acid that represented renal dysfunctions because of ischemic variations as stated by Mustafa et al.¹⁰

This is consistent with Hasan and Alshami¹¹, study which study consisted of 100 gravid females, out of

them 50 controls, 17% had mildly PE and 33% had severely PE. sever PE there is significantly high blood urea, s.Cr, s.uric acid, SGOT, SGPT, and S.A.P, than other groups (pvalue<0.05). Severe PE exhibits lower Hb and plt count than other groups (pvalue<0.001), while there is nonsignificant change as regard total s.bilirubin (pvalue=0.399).

In the current study, positive anti HP anti-bodies were significantly higher frequent in PE cases (86%) than normotensive (46%) (p=0.026).

This is in agreement with another study which included 108 PE cases and 108 controls. The study revealed that 62% in the case group and 44.4 % were positive in the controls that has significance.¹²

The study by Cardaropoli et al.¹³ around the correlation among HP infections and its correlation with PE and low fetal growing, findings revealed that HP is accompanying with PE and low growing of embryonic.

These findings revealed the significant association among PE and HP infections which is mainly developed throughout childhood and it is life-long when not treated. This result maintained the speculations that HP positive cases can have original vascular damages; such sub-clinical dysfunctions may expand the inflammatory variations in gestation, consequently contributed to the signs of PE.¹⁴

Regarding neonatal outcome, the present study found that the mean birth weight was significantly lower among pre-eclampsia group (2.84 ± 0.435 kg) than normotensive group (3.02 ± 0.314 kg) ($p=0.019$). This is very significant to select the correct time for birth or terminations of gestation complicated by HPT and need more assessment.

Similarly, Hasan and Alshami¹¹, study found that regarding birth weight significantly lower in sever PE (2.1 ± 0.51 kg) and mild PE (2.49 ± 0.4 kg) than normal group (3.25 ± 0.34 kg) ($p < 0.001$).

This is in agreement with another study which reported that HSPA positivity was significantly high between cases with PE complicated with IUGR; of the 50 women with PE complicated with IUGR, 38 (76%) were HPSA-positive and 16 (32%) of the 50 women with normal uneventful pregnancy were HPSA-positive ($P < 0.001$).¹⁵

The findings in this work are comparatively reliable with Ponzetto et al.¹⁶, in which 94 cases were examined in Italy (47 cases with PE and 47 with healthy gestations) for s.antibodies versus HP by enzyme immuno-assays and CagA protein by immuno-blot assay and revealed that HP seropositivity frequency was elevated in moms with PE (51.1%) in comparison to cases with healthy gestation (31.90%) [OR = 2.67; 95% CI = 1.084-6.5; P value = 0.033].

The change was even higher for CagA sero-positivity (80.9 and 14.9%, resp.) (OR = 26.035; 95% CI = 8.2-82.7; P value < 0.001). They revealed that the correlation was stronger in patients of CagA-positive strain; the latter are more virulent, and consequently they are more possible to elicit the generalized inflammations and succeeding vascular damages typical of PE.¹⁷

Regarding severity of preeclampsia, there was significant difference with increased number of cases of severe preeclampsia with positive anti- H. pylori antibodies.

Our results were in line with Cardaropoli et al.¹⁸ study which enrolled 111 cases after allocating them into 2 groups: group-1 was the controls and included 49 uneventful gestations and the other group included 62 cases having pathological gestations with complication of embryonic growing restrictions (IUGR-only, n = 13), PE (PE-only, n = 17), or both (PE-IUGR, n = 32); it was revealed that HP seropositivity was statistically more common in PE cases with or with no FGR (85.70%) (P value < 0.001; OR = 9.2, 95 % CI = 2.8-30.0), while it didn't vary among IUGR-only (46.20 %) and controls (42.90 %). Additional sub-division of the PE group revealed a elevated prevalence of seropositivity between PE-IUGR patients (93.8 %) (P value < 0.001; OR = 35.5, 95% CI = 5.2-242.4) in comparison to control group, while in the PE-only group the percent of HP-seropositive cases was elevated, but nonsignificant (70.6%), comparative to control group.¹⁸

While definite blends of various antibiotics are operative in eradicating HP, antibiotic-resisting strains are already developing, consequently lessening the effectiveness of existing treatments.

Pharmacogenomics-built therapies seem to rise the curing rate, and new treating methods targeting HP virulence influences are essential.¹⁹

In the circumstance of gestation connected conditions, it may be better to avoid the worsened inflammations typical of PE, consequently evading pharmacologic treatments throughout gestation. Numerous clinical trials and animal research have concentrated on producing HP recombinant vaccines.¹⁸

Limitation of the study use of serology instead of stool antigen, lack of comparative group with negative H. pylori.

CONCLUSION

The findings revealed that the opportunity of exposures to HP in females with pre-eclampsia significantly more than the opportunity of exposures to HP in control cases .

In comparison the PE embryonic side effects between the PE patients with positive HP, the frequency of low delivery weight babies in the controls was elevated than the other group but among cases in the controls, with positive infections and healthy controls. In addition, there was a significant correlation between the H. pylori infection and severity of the disease.

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