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Abstract

Thrombocytopenia is one of the health problems that faced pregnant women. The formation of antibodies against some of viral and bacterial infection leads to molecular mimicry with the surface of platelets. Hence, it leads to thrombocytopenic purpura. In current study, 421 women including 388 pregnant and 33 non-pregnant women, aged between 18 - 44 years participated in this study. Complete blood count (CBC) and anti H. pylori tests were performed for all participants. A total number of seropositive women for anti H. pylori Ab test (IgG) was 253 (60.1%) including 237 pregnant women and 93 of them were with history of abortion. The results showed significant differences ($p < 0.000$) in mean platelet count between seropositive results for Anti H. pylori Ab test (IgG) and women with seronegative results. Among 253 seropositive women, 199 (78.65%) of them have low platelet count, while only (4.76%) of seronegative women were thrombocytopenic. The cutoff of platelet count for thrombocytopenia set on (150,000 cell/cmm³). ROC analysis revealed good prognostic value of thrombocytopenia for H. pylori infection. This finding concluded that thrombocytopenia can be one of biomarker for H pylori infection among pregnant women.

Keywords

H. pylori, Thrombocytopenia, Pregnant women.



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ABSTRACT

Thrombocytopenia is one of the health problems that faced pregnant women. The formation of antibodies against some of viral and bacterial infection leads to molecular mimicry with the surface of platelets. Hence, it leads to thrombocytopenic purpura. In current study, 421 women including 388 pregnant and 33 non-pregnant women, aged between 18 - 44 years participated in this study. Complete blood count (CBC) and anti H. pylori tests were performed for all participants. A total number of seropositive women for anti H. pylori Ab test (IgG) was 253 (60.1%) including 237 pregnant women and 93 of them were with history of abortion. The results showed significant differences ($p < 0.000$) in mean platelet count between seropositive results for Anti H. pylori Ab test (IgG) and women with seronegative results. Among 253 seropositive women, 199 (78.65%) of them have low platelet count, while only (4.76%) of seronegative women were thrombocytopenic. The cutoff of platelet count for thrombocytopenia set on (150,000 cell/cmm³). ROC analysis revealed good prognostic value of thrombocytopenia for H. pylori infection. This

finding concluded that thrombocytopenia can be one of biomarker for H pylori infection among pregnant women.

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INTRODUCTION

The prevalence of *Helicobacter pylori* (*H. pylori*) infection is extremely common among peoples around the world. One third of north European and North American populations have infection with this bacteria, while its prevalence more than half among south and east Europe, South America, and Asia whereas in some developing countries, it reaches three-quarter (Eusebi, 2014). The risk of *H. pylori* appears in its relationship with thrombocytopenia. Studies in Japan showed that the eradication therapy in immune thrombocytopenic purpura was appeared after healing from *H. pylori* infection (Kuwana, 2014, Martinez, 2014, Mihăilă R. G., 2014). The mechanism how *H. pylori* leads to thrombocytopenia is unclear, however some studies referred to the relation of bacterial eradication to the genetic factors and the strain of bacteria. A portion of the structure of *H. pylori* mimics the platelets cell membrane, this similarity associated with the damage of PLTs by same Abs that formed initially against *H. pylori* (Kuwana, 2014).

Although most of infections are asymptomatic but the infection with *H. pylori* still considered as an important problem among pregnant women. The symptoms include many adverse effects such as hyperemesis gravidarum, congenital malformations, pre-eclampsia with intrauterine fetal growth restriction and miscarriage, and thrombocytopenia (Gasim, 2014, Howden, 2014). Idiopathic thrombocytopenic purpura (ITP) is a type of organ-specific autoimmune disease; it is mediated by anti-platelet autoantibodies that can react with platelets and megakaryocytes and leads to accelerate the destruction of platelet, this mechanism due to the decreasing in the platelet production. HIV and hepatitis C virus considered other causes of ITP (Kuwana, 2014).

The immune thrombocytopenia can be affected by some chronic infections and caused health problem especially during the pregnancy. The chronic infection with hepatitis B, C virus, cytomegalovirus and human immuno deficiency virus, (HBV, HCV, CMV and HIV) and *H. pylori* are the most common that lead to the secondary ITP. Moreover, systemic lupus erythematosus, Antiphospholipid syndrome, autoimmune thyroiditis or Evans syndrome), myeloproliferative syndromes, chronic lymphoid leukemia also has been associated with secondary ITP. While, using of some medicine also enhance secondary ITP. (Mocanu, 2014). Another study concluded a positive relationship between thrombocytopenia and the infection with mumps, rubella, varicella,

Parvovirus, and infectious mononucleosis by Epstein-Barr virus among children and adults (Palumbo, 2008).

In addition of thrombocytopenia, *H. pylori* also related to iron deficiency anemia and vitamin B12 deficiency (Tiwari, 2009, TanandK, 2012, Yeh, 2010, Apagiannakis, 2013) Among pregnant women the rate of anemia is high, they are more susceptible to anemia (especially iron-deficiency anemia), and its observed among different ages of pregnant women (Ahmed, 2013) and its observed among different ages of pregnant women, and it's sometimes leading to cause of maternal – fetal morbidity and mortality (Kalsoom, 2013).

Finally, there are few published data on *H. pylori* infection among pregnant women in Iraq, and also none are available in Erbil. Such data would be useful to care givers and health planners, and would add to our knowledge of anemia and its risk and prevention, and of how best to manage the condition during pregnancy in order to enhance maternal and prenatal outcomes (i.e. to minimize maternal anemia, still birth, low birth weight, and maternal and prenatal mortality). Therefore the current study was conducted to investigate the epidemiology (prevalence and predictors) of *H. pylori* infection and its effect – if any – on anemia, together with its association with thrombocytopenia among women.

MATERIALS AND METHODS

In this study, the ethical approval and permission to perform the work was granted by the local scientific committee of Health Technical College. Furthermore, consent was obtained from each participant prior to the study. Four hundred and twenty one women comprising 388 pregnant and 33 non-pregnant women, aged between 18 - 44 years, were randomly selected. Peripheral blood samples were collected by intra-venous puncture and aspiration from the cubital vein. The blood samples prepared for testing complete blood count (CBC) which performed by using Erma, the Japanese full automatic blood counter. Anti *H. pylori*. Investigations were done by using Vitek Immuno Diagnostic Assay System (VIDAS).. The interpretations of tests were performed at the Department of Medical Laboratory Technology, Health Technical College / Erbil Polytechnic University.

The assay principle of *H. pylori* detection combines a 2-step enzyme immunoassay sandwich method with a final fluorescent detection (ELFA). All of the assay steps as well as the assay

temperature are controlled automatically by the instrument. Anti-human IgG antibodies conjugated with alkaline phosphatase are cycled in and out of the Solid Phase Receptacle (SPR) and will attach to any human IgG bound to the SPR wall. At the end of the assay, results are automatically calculated by the instrument, a test value is generated and a report is printed for each sample (bioMérieux, 2004).

Statistical Analysis

The data were expressed as mean \pm SE and percent values depending on the nature of the data itself. The analyses were performed using SPSS version 21. Independent t-test was used for finding the significant differences between the treatments. Receiver-operating characteristic (ROC) curve was applied for determination the biomarker of *H. pylori* infection. $P < 0.05$ was set as significant critical level.

RESULTS:

The result in Table 1 shows that the minimum was 18 years while, the maximum was 44 years with mean value = 28.95. Table 1 also shows that 163 (38.7%) of women who participated in this study has history of abortion, while 258 (61.31%) of them haven't history of abortion.

Table 1: Demographic characteristics of the participants

Age group/ year	Minimum		Maximum	
	18		44	
	Mean = 28.95			
Number of Abortion	No. abortion	One Abortion	Two Abortion	Three Abortion
	n= 58(61.3%)	n=112 26.6%	n=46 (10.9%)	n=5(1.2%)
Platelet count	Normal $\geq 150.00 \text{ cell.cm}^3$		Abnormal (low) $< 150.00 \text{ cell.cm}^3$	
	365 (86.69%)		56 (13.31%)	
Anti <i>H. pylori</i> Ab test (IgG)	Negative		Positive	
	168 = 39.9%		253= 60.1%	

Figure.1: shows that number of pregnant women who participate in this study recorded 388 (92.16%). It is clear that 237 (61.08%) from 388 (92.16%) pregnant women have positive

result for anti *H. pylori* Ab test class IgG, and 151 (38.92%) of total pregnant women who participate in this study have negative result for anti *H. pylori* Ab test class IgG.

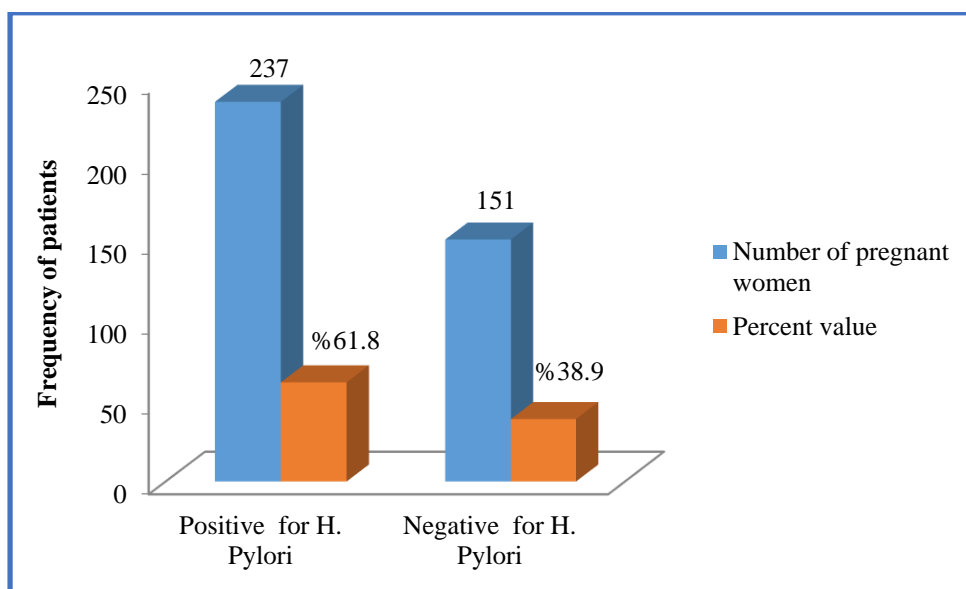


Figure. 1: Sero prevalence of anti *H. pylori* Ab test class IgG among pregnant women.

Figure. 2 shows that total number of women (pregnant and non-pregnant) who have positive result for anti *H. pylori* Ab test (IgG) was 253(61.08%) and 160 (63.24%) of them have no history with abortion while, 54 (21.43%) of them have one abortion, 37 (14.62%) have two abortion and 2 (~ 0.1%) have history with three abortion.

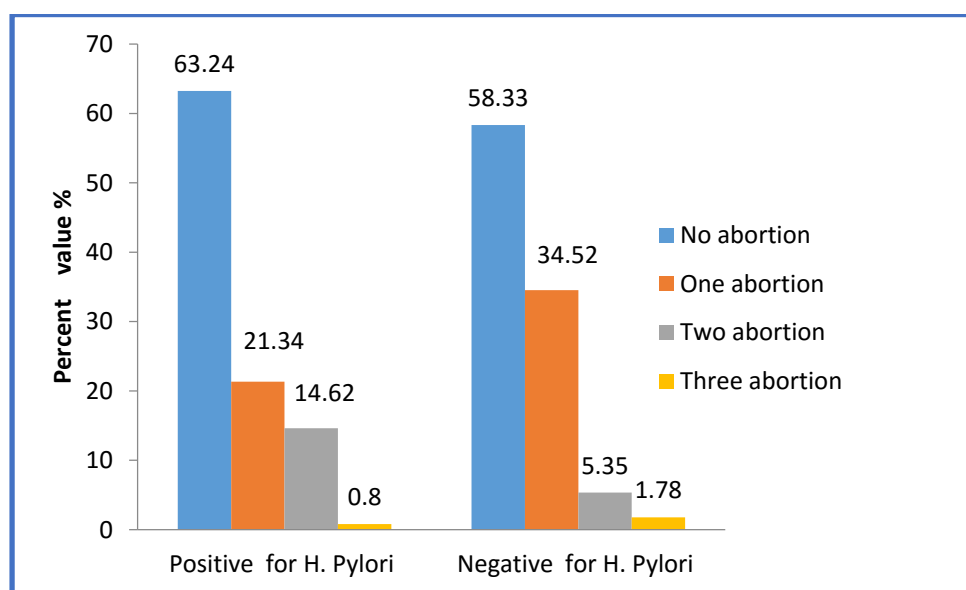


Figure. 2: distribution of Anti *H. pylori* test class IgG according to frequency of abortion.

Figure. 3 gives a no significant change in mean concentration of hemoglobin among women who have seropositive and seronegative for anti *H. pylori* Ab test (IgG). The result showed that the mean \pm SE hemoglobin concentration who have seropositive result for Anti *H. pylori* Ab test (IgG) were (11.452 ± 0.072 g/dl) when compared with its concentration in the body of women who have seronegative result for anti *H. pylori* Ab test (IgG) (11.502 ± 0.098 g/dl) and (P-value < 0.680).

Furthermore, same figure showed significant in mean \pm SE in the platelet count of participators. The result showed that the mean \pm SE platelets who have seropositive result for Anti *H. pylori* Ab test (IgG) were (157.529 ± 3.214 cell/cm³) when compared with its count in the blood circulation of women who have seronegative result for anti *H. pylori* Ab test (IgG) (212.851 ± 4.512 cell/cm³) and (P-value < 0.000). Figure no. 3 showed also no significant in mean \pm SE in the WBC count of participators. The result showed that the mean \pm SE WBC who have seropositive result for Anti *H. pylori* Ab test (IgG) were (9.060 ± 0.153 cell/cm³) when compared with its count in the blood circulation of women who have seronegative result for anti *H. pylori* Ab test (IgG) (8.831 ± 0.170 cell/cm³) and (P-value < 0.328).

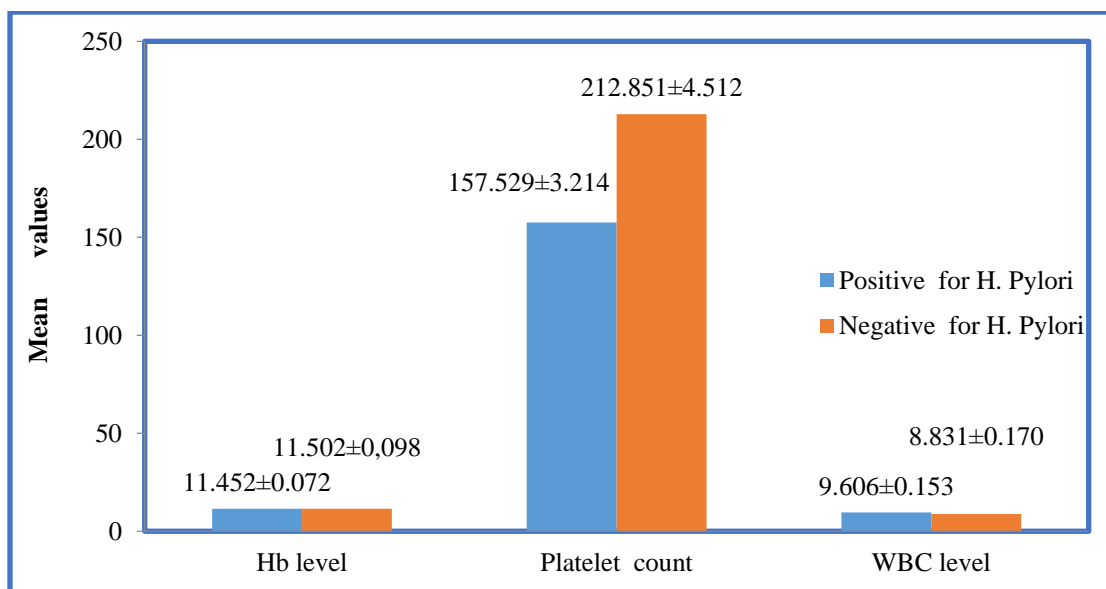


Figure. 3: Mean Hb, PLT, and WBC in pregnant women in relation with anti *H. pylori* Ab test class IgG serostatus.

Table 2; describes the level of hemoglobin, platelet and white blood cells among women who have seropositive and seronegative for anti *H. pylori* Ab test (IgG). The result shows that (73.12 %) of participators who have positive result for anti-*H. pylori* Ab test (IgG) has normal concentration of Hb, while (26.87%) of them have a low concentration of Hb. In the same time (72.02%) of participators who have sero-negative result for anti-*H. pylori* Ab test (IgG) have normal concentration of Hb, and 27.97%) of them have low concentration of Hb.

Moreover, table 2, shows that (21.35%) of participators who have sero-positive for anti-*H. pylori* Ab test (IgG) have normal account of PLTs and (78.65%) of them have low account of PLTs. While, (95.23%) of participators who have sero-negative for anti-*H. pylori* Ab test (IgG) have a normal account of PLTs, and (4.76%) of them have low account of PLTs.

On the other hand, same table shows that (74.30%) of participators who have sero-positive result for anti-*H. pylori* Ab test (IgG), have normal account WBCs, and (25.69%) of them have high number of WBCs. While, it shows that (84.52%) of participators who have sero-negative result for anti-*H. pylori* Ab test (IgG) have a normal account for WBCs, and (15.47%) have high account of WBCs.

Table 2: Hb, PLT and WBC test finding according to anti *H. pylori* Ab test class IgG serostatus among group study.

Anti <i>H. pylori</i> IgG serostatus	Hb level		PLT		WBC	
	Normal	Low	Normal	Low	Normal	High
Sero- positive n= 253	(73.12 %)	(26.87 %)	(21.35 %)	(78.65)	(74.30 %)	(25.69 %)
Sero- negative n= 168	(72.02 %)	(27.97 %)	(95.23 %)	(4.76 %)	(84.52 %)	(15.47 %)

Figure 3, shows result of viral infections among women who participate in this study. It shows that the number of participators who have sero-positive result for anti CMV Ab test (IgG) was 136 and 18 of them have a low account PLTs and 38 of 285 participators who have sero-negative for anti-CMV Ab test (IgG) have low number of PLTs. On the other hand, the result for

anti-rubella Ab test (IgG) shows that 97 of women have sero-positive result, 14 of them have below normal range of PLT count while, 324 of total participators have sero-negative for anti-rubella Ab test (IgG) and only 42 of them have low count of PLTs.

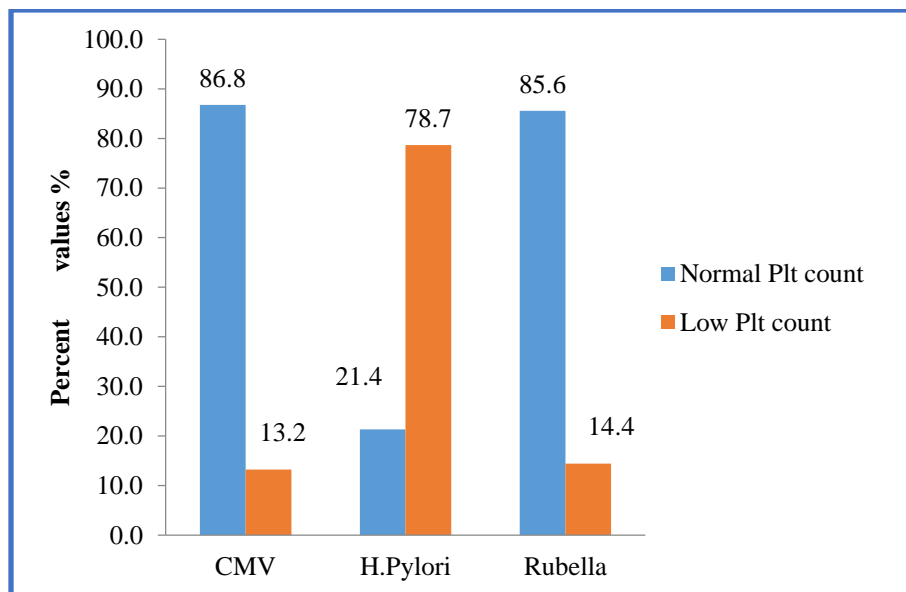


Figure 4: Comparison among the positive sera of CMV, *H. pylori* and Rubella regarding the normal and low PLT count.

Receiver-operating characteristic (ROC) curve revealed a significant ($p=0.0001$) diagnostic value of thrombocytopenia or PLTs reduction in *H. pylori* infection among the pregnant women. The Area under the curve AUC was 0.8063, with standard error value 0.02165. The confidence interval 95% was 0.7637-0.8487 (Figure 5)

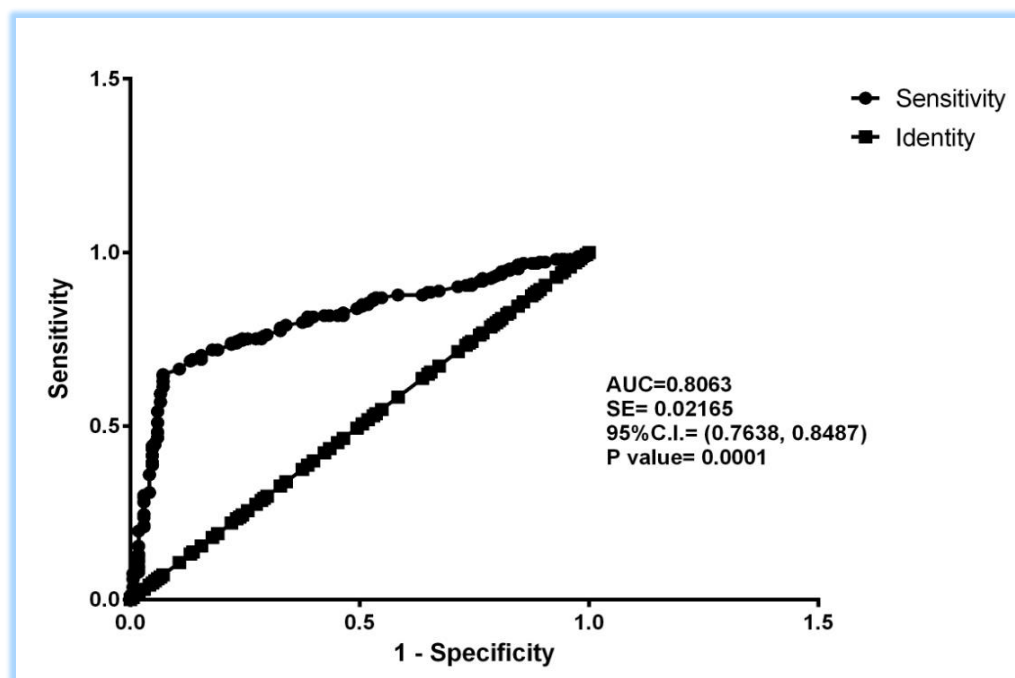


Figure5. Receiver-operating characteristic (ROC) curve for detection of diagnostic value of thrombocytopenia in *H. pylori* infection.

DISCUSSION:

The incidence of *Helicobacter pylori* (*H. pylori*) infection is extremely common among peoples around the world, but the rate different between counties. The findings of this study from the demographic point revealed the thrombocytopenia is one of the problems that face women in Iraq which might be almost idiopathic. Results of the current investigation showed that 13.31 % women suffer from thrombocytopenia. This finding was agreed with (Özçimen, 2016) who recorded 9.9% of gestational thrombocytopenia in Konya-Turkey and (Boehlen et al., 2000) who found 11.6 % among maternal in Switzerland. The finding of this study shows that more than half of patients who participate in this study have positive result of anti *H. pylori* Ab test (IgG). Thus, this result going with result of (Eusebi, 2014). This explains the presence of high number patients with gestational thrombocytopenia and *H.pylori* infection (Kuwana, 2014, Martinez, 2014, Mihăilă R. G., 2014). The finding of this study showed that the presence of anti *H. pylori* Ab is common in the blood circulation of the pregnant women, thus leads to destruction of platelets causing thrombocytopenia and decreasing in the Fe level in the erythrocytes (Roesler, 2015). On the other hand, the result of current study showed that there are one third of participants who have history abortion also have the presence of anti *H. pylori* Ab (IgG), but there were no relation found

between history of abortion and *H. pylori* infection. This agrees with result of (Leonardo H. Eusebi, 2014). Finally, our findings showed that 13.2 % of patients who participate in this study recorded positive result for anti CMV Ab test (IgG) and 14.4% of them has positive result anti - rubella Ab test. Thus, the results show a size the relationship between these types of viral infection and thrombocytopenic purpura. This result agrees with (Mădălina Mocanu) and (Owatanapanich et al., 2014).

CONCLUSION

This study concluded that thrombocytopenia demonstrated among Erbilian pregnant women and supports earlier research that reported on thrombocytopenia in the presence anti *H. pylori* Abs and claim that this results in thrombocytopenic purpura through immune disturbances.

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