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HELICOBACTER PYLORI INFECTION IN AMNIOTIC FLUID MAY CAUSE HYPEREMESIS GRAVIDARUM

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ABSTRACT

OBJECTIVES: Limited data are avaible from recent trials involving pregnant women to guide the diagnosis of Helicobacter pylori infection. There is no data about presence of H. pylori in the amniotic fluid as well. Furthermore, relation between amniotic fluid H. pylori and hyperemesis gravidarum (HG) has not been characterized yet.

MATERIALS AND METHODS: Pregnant women undergoing amniocentesis were enrolled in the study. Presence of H. pylori in amniotic fluid was assessed by stool antigen test. A perinatalogist independently performed amniocentesis. Obtained amniotic fluid was sent to the laboratory to assess H. pylori infection by stool H. pylori antigen assay. We determined the rate of H. pylori in amniotic fluid and assessed relations between H. pylori infection and pregnancy outcome including HG.

RESULTS: Between May 2017 - September 2017, we enrolled 48 pregnant women who underwent amniocentesis to detect possible fetal malformations. Among them, 28 (58.3%) were found to have positive for H. pylori in the amniotic fluid. The rate of HG was significantly higher (71.4%) in patients who tested positive for H. pylori in amniocentesis than H. pylori negative group (20%), ($p<0.001$).

CONCLUSIONS: The main new finding of the study is that presence of H. pylori in the amniotic fluid is possible. Our data suggest that H. pylori infected amniotic fluid is associated with experience of past HG. Current study may have important implications for detecting HG and may help identify patients who would derive the most benefit from future preventive strategies.

KEYWORDS

Helicobacter Pylori, Amniotic Fluid, Hyperemesis Gravidarum

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1. INTRODUCTION

H. pylori is a gram negative, spiral shaped, multiple unipolar flagellated and urease producing bacteria. Subjects diagnosed with H. pylori reported more comorbidity burden and higher use of healthcare services than those without H. pylori [1]. H. pylori effects over one billion people worldwide. Although patients often remain asymptomatic for years, chronic H. pylori infection is a leading cause of peptic ulcus, gastric cancer, gastric lymphoma and pregnancy-related clinical events including HG and preterm birth (PTB). It has been also showed that pregnant women with H. pylori infection experience substantially higher pregnancy-related diseases than those without H. pylori negative counterparts [2].

Many obstetric studies have been conducted the relationship between maternal H. pylori infection and HG during pregnancy. Presence of H. pylori infection was searched in maternal fecal content, fetal umblical cord as well as in maternal serum in pregnant women in those study[3-5]. There have been conflicting results the association between maternal H. pylori infection and HG. In a meta-analysis of 25 case–control studies showed that nearly half of them have not been found an association between HG and H. pylori [6]. On the other hand, the presence of H. pylori has never been examined from the amniotic fluid until now.

As a part of efforts to decline pregancy related diseases including HG, the many researchers conducted studies involving H. Pylori infection in pregnant women. Suspected H. pylori infection is best assessed by histopathological examination of gastric biopsy specimens. But, performing endoscopy in pregnant women has difficulties due to risk of PTB. Furthermore, these studies are not based on amniotic fluid that may not reflect H. pylori status among pregnant women. With the advent of the H. pylori treatment, it remains unclear whether the amniotic fluid contains H. pylori or not. Furthermore, the effect of H. pylori in amniotic fluid on pregnancy related diseases is also unknown. Therefore we conducted current study to detect the rate of hp infection in amniotic fluid, as well as rate of HG among those with HP infection.

2. MATERIALAND METHODS

This prospective trial was conducted between May 2017 - September 2017 at a university medical center, in a large metropolitan area near the Iranian border of Turkey where H.pylori infection are endemic. 48 pregnant women ages 16-35 from rural Turkish communities were enrolled for the study. Main goals of the current study are to describe H.pylori infection status in amniotic fluid and the association between amniotic fluid H. pylori infection and HG. Participants completed a comprehensive baseline examination that included detailed questionnaires as well as laboratory examination. We excluded samples from patients that had prior treatment with proton pump inhibitors and antibiotics, H. pylori status in amniotic fluid are confusing when used before the enrollment of the study subjects.

Evidence of HG of the study patients was extracted from hospital database. HG was also defined by a perinatalogist according to the presence of protracted vomiting and nausea in pregnancy, accompanied by

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weight loss, disturbance of electrolyte balance, ketonuria, and dehydration or hospitalization [7]. A perinatalogist performed all of the amniocentesis procedures according to guideline of Royal College of Obstetricians and Gynaecologists (RCOG) [8]. Amniotic fluid specimens from the baseline examination were processed within 2 hours of collection, transported to microbiology lab. Amniotic fluid samples are tested for H. pylori infection by using a commercial stool H. pylori antigen test kit (GI Supply® Camp Hill, PA, USA) which has 95% specifity for detecting H. pylori. Universally, at least 2 cc amniotic fluid sample is removed and wasted before the analysis of further examination. We used this wasted amniotic fluid material for examining H. pylori infection. Therefore we did not obtain an ethical approval for the current study.

We defined the presence of H. pylori infection, when stool test was positive in the amniotic fluid. Study subjects were also required to be medical treatment free for H. pylori infection at least 6 months from the time of study entry.

STATISTICALANALYSIS:

Analysis of the data collected in the study was performed using Statistical Package for the Social Sciences 21 statistical software package (IBM Corporation, Chicago, IL). Descriptive statistics for the continuous variables were presented as mean, standard deviation (SD), while count and percent for the categorical variables. Comparisions between H. pylori positive and negative group was performed by Chi-square test. The differences were considered statistically significant at $p < 0.05$.

3. RESULTS:

Totally, 53 patients who underwent to amniocentesis were included to the study. 5 patients were excluded due to the insufficient amniotic fluid. Finally, 48 pregnant women's amniotic fluid were evaluated for the study. H. pylori infection was observed in 28 of 48 (58.3%) patients who underwent amniocentesis. The rate of HG was significantly higher (20/28, 71.4%) in patients who tested positive for H. pylori in amniocentesis than H. pylori negative group (4/20, 20%), ($p<0.001$), (table I).

Table I. Frequency of HG between H. pylori positive and negative group

	HG positive	HG negative	Total	P value
H. pylori positive	20	8	28	<0.001
H. pylori negative	4	16	20	
Total	24	24	48	

Abbrevations: HG; Hyperemesis gravidarum

There was no significant difference between the H. Pylori positive group and H. pylori negative group with respect to the baseline characteristics and laboratory parameters of 48 amniocentesis-performed pregnant women (table II and table III).

Table II. Baseline characteristics of the patients

	H. pylori (+) group (N=28) Mean±SD	H. pylori (-) group (N=20) Mean±SD	P value
Age	27,5±6,1	26,9±5,7	P >0,05
Gravida	2,4±1,1	2,4±1,2	P >0,05
Parity	1±0,9	1,1±1	P >0,05
BMI	27,3±5,5	25,8±4,7	P >0,05

Abbrevations: BMI; body mass index, SD; standard deviation

Table III. Laboratory parameters of the patients

	H. pylori (+) group (N=28) Mean±SD	H. pylori (-) group (N=20) Mean±SD	P Value
Hemoglobin (g/dL)	11,8±1,2	11,9 ±1,3	P >0,05
Hematocrite (%)	35,9±3,2	36,2±3,1	P >0,05
AST (UI/L)	20,5±10,7	18±8,9	P >0,05
ALT (UI/L)	14,2±5,4	16±3,2	P >0,05
Creatinine (mg/DL)	0,52±0,28	0,56±0,19	P >0,05
TSH (mIU/L)	2,3±1,4	2,1±1,7	P >0,05

Abbrevations: AST; aspartate aminotransferase, ALT; alanine aminotransferase TSH; thyroid stimulating hormone. SD; standard deviation

4. DISCUSSION

In the current study, we tried to find out whether H. pylori may be detected from amniotic fluid by stool antigen test in pregnant women. We also searched for the association between amniotic H. pylori infection and HG. To our knowledge, there is no previous study of H. pylori in the amnion fluid and this is the first report in the literature.

In our study involving 48 pregnant women, 28 (58.3%) of the patients had positivite antigen test from amniotic fluid. When compared to H. pylori negative pregnant women, positive counterparts had statistically significant higher rates of HG. ($p<0.001$)

H. pylori is a gram-negative bacterium that induces chronic inflammation of the underlying gastric mucosa [9]. H. pylori infection is acquired early in childhood and if not treated is caused many gastric diseases including peptic ulcus, gastric cancer and gastric mucosa-associated lymphoid-tissue (MALT) lymphoma [10]. Recent studies show that H. pylori infection in pregnant women may cause HG and PTB as well as pregrancy-related diseases [11].

Nausea and vomiting in pregnancy affects more than half of pregnant women and causes low life quality and restricted social functions during early pregnancy [12,13]. The situation worsens with the increase in the number and severity of vomiting in some pregnant patients. This situation is characterised by weight loss, dehydration, electrolyte disturbance and it is referred to as hyperemesis gravidarum (HG) and requires hospitalization [7]. HG occurs in approximately 0.3-2% of pregnancies and is the single most frequent reason for hospital admission in the first half of pregnancy [14]. Several studies have shown that pregnancies with severe nausea and vomiting or HG have demonstrated negative effects on birthweight, SGA, and prematurity rates [15,16].

Many case-control studies [3, 17-21] demonstrated significant positive association between HG and Helicobacter pylori (HP) infection in pregnancy. Also in a systematic review of 14 case-control studies, found higher prevalance of HG in H. pylori-infected pregnant women than uninfected ones (pooled OR = 4.45; 95%CI:2.31-8.54) [22]. H.pylori serology or stool antigen test were used to detect H.pylori in these studies. Despite that, a meta-analysis of 25 case–control studies included 14 studies that found an association between HG and H. pylori and 11 studies that did not [2].

In our study, the risk of HG differed significantly between patients who had a positive result for HP in amniotic fluid and those who had not. Although it could be argued that HG might be a result of multifactorial causes and not only due to H. pylori infection, there have been several studies involving H. pylori infection-related HG, it was found even in patients with acute H. pylori infection. Therefore we concluded that presence of H.pylori infection in amniotic fluid may have been caused HG in study patients.

There are both invasive and non-invasive diagnostic methods, which are being used to determine the H. pylori infection status. Invasive methods are endoscopy, culture, rapid ureas test, histology, and molecular methods while non-invasive methods are urea breath test, stool antigen test and h.pylori serology [23]. It has been showed that stool antigen test has 90.1% sensitivity and 92.4% specificity, that is a result comparable to the other invzive or non- invazive tests. For detecting HP infection It is a cheap, automated, and minimally labor-intensive method [24]. Although stool antigen test has been developed for detecting H. pylori microorganism of gaita, there are no published data to detect H. pylori in pregnant women undergoing amniocentesis.

Volume - 3 | Issue - 4 | December - 2019 | ISSN No. Online : 2663 - 1199 | ISSN No. Print : 2663 - 1180

Despite many obstetric studies implicating H. pylori-related HG, little is known about amniotic fluid H. pylori infection. So we used stool antigen test to detect H. pylori infection in the amniotic fluid. At the first time, our analysis of amniotic fluid from 28 patients shows that, HP infection in pregnant woman may be detected by stool H. pylori antigen test in amniotic fluid. The likely explanation for presence of H. pylori in amniotic fluid is fetal gastric infection with H. pylori. Another possible explanation is that maternal H. pylori infections are fully penetrant into the amniotic fluid.

A limitation of this study is the low number of patients that were included in the study. This could bias the results, since rate of HG may have been affected in the analysis. Also, potantial biases are the possible confounding effects on amniotic fluid by the normal bacterial flora which can be effect stool H. pylori antigen test. Finally we did not assess the accuracy of the H. pylori stool antigen test in combination with ELISA method.

5. CONCLUSION

In our study, we showed that H. pylori infection in amniotic fluid may be detected by H. pylori stool antigen test. Moreover a positive association was found between the presence of H. pylori in amniotic fluid and HG. Furthermore, prospective studies involving the role of H.pylori infection in the amniotic fluid and its eradication in the treatment of HG may be neccesary, taking into account the role of confounding factors such as non-H. pylori infectious agents in the amniotic fluid.

6. REFERENCES

1.. Weyermann M, Rothenbacher D, Brenner H. Acquisition of Helicobacter pylori infection in early childhood: independent contributions of infected mothers, fathers, and siblings. Am J Gastroenterol 2009; 10: 182–89.
2.. Sandven I, Abdelnoor M, Nesheim B, Melby KK. Helicobacter pylori infection and hyperemesis gravidarum: a systematic review and meta-analysis of case– control studies. Acta Obstet Gynecol Scand 2009; 88: 1190–2000.
3.. Guven MA, Ertas IE, Coskun A, Ciragil P. Serologic and stool antigen assay of Helicobacter pylori infection in hyperemesis gravidarum: which test is useful during early pregnancy? Taiwan J Obstet Gynecol 2011; 50: 37-41
4.. Kuo FC, Wu CY, Kuo CH, Wu CF, Lu CY, Chen YH, et al. The utilization of a new immunochromatographic test in detection of Helicobacter pylori antibody from maternal and umbilical cord serum. Biomed Res Int. 2014; 2014: 568410. doi: 10.1155/2014/568410. Epub 2014 Aug 7.
5.. Boltin D, Perets TT, Elheiga SA, Sharony A, Niv Y, Shamaly H, et al. Helicobacter pylori infection amongst Arab Israeli women with hyperemesis gravidarum—a prospective, controlled study. Int J Infect Dis. 2014 Dec; 29: 292-95. doi:10.1016/j.ijid.2014.10.005. Epub 2014 Oct 30.
6.. Sandven I, Abdelnoor M, Nesheim B, Melby KK. Helicobacter pylori infection and hyperemesis gravidarum: a systematic review and meta-analysis of case– control studies. Acta Obstet Gynecol Scand 2009; 88: 1190–2000.
7.. Niebyl JR. Clinical practice. Nausea and vomiting in pregnancy. N Engl J Med 2010; 363: 1544-50.
8.. Royal College of Obstetricians and Gynaecologists (2010) Green Top Guideline Amniocentesis and chorionic villus sampling. RCOG; Green top guideline no.8 June 2010
9.. Everhart JE. Recent developments in the epidemiology of Helicobacter pylori. Gastroenterol Clin North Am 2000; 29: 559-79.
10.. Kenneth EL, McColl MD. Helicobacter pylori Infection. N Engl J Med 2010; 362: 1597-1604.
11.. den Hollander WJ, Schalekamp-Timmermans S, Holster IL, , Jaddoe, V. W., Hofman, A., Moll, HA, et al. Helicobacter pylori colonization and pregnancies complicated by preeclampsia, spontaneous prematurity, and small for gestational age birth. Helicobacter. 2017; 22: e12364.
12.. Jarvis S, Nelson-Piercy C. Management of nausea and vomiting in pregnancy. BMJ 2011;342:d3606.
13.. Lacasse A, Rey E, Ferreira E, Morin C, Bérard A. Nausea and vomiting of pregnancy: what about quality of life? BJOG 2008; 115: 1484-93.
14.. Bailit JL. Hyperemesis gravidarium: epidemiologic findings from a large cohort. Am J Obstet Gynecol 2005; 193: 811-14.
15.. Veenendaal MVE, van Abeelen AFM, Painter RC, van der Post JAM, Roseboom TJ. Consequences of hyperemesis gravidarum for offspring: a systematic review and metaanalysis. BJOG 2011; 118: 1302-13.
16.. Bolin M, Åkerud H, Cnattingius S, Stephansson O, Wikström AK. Hyperemesis gravidarum and risks of placental dysfunction disorders: a population-based cohort study. BJOG 2013; 120: 541-547.
17.. Frigo P, Lang C, Reisenberger K, Kölbl H, Hirschl AM. Hyperemesis gravidarum associated with Helicobacter pylori seropositivity. Obstet Gynecol 1998; 91: 615-17.
18.. Kazerooni T, Taallom M, Ghaderi AA. Helicobacter pylori seropositivity in patients with hyperemesis gravidarum. Int J Gynaecol Obstet 2002; 79: 217-20.
19.. Salimi-Khayati A, Sharami H, Mansour-Ghanaei F, Sadri S, Fallah MS. Helicobacter pylori aeropositivity and the incidence of hyperemesis gravidarum. Med Sci Monit 2003; 9: CR12-CR15.
20.. Cevrioglu AS, Altindis M, Yilmazer M, Fenkci IV, Ellidokuz E, Kose S. Efficient and non-invasive method for investigating Helicobacter pylori in gravida with hyperemesis gravidarum: Helicobacter pylori stool antigen test. J Obstet Gynaecol Res 2004; 30: 136-41.
21.. Koçak I, Akcan Y, Ustün C, Demirel C, Cengiz L, Yanik FF. Helicobacter pylori seropositivity in patients with hyperemesis gravidarum. Int J Gynaecol Obstet 1999; 66: 251-54.
22.. Golberg D, Szilagyi A, Graves L. Hyperemesis gravidarum and Helicobacter pylori infection: a systematic review. Obstet Gynecol 2007; 110: 695-703.
23.. Mégraud F, Floch P, Labenz J, Lehours P. Diagnostic of Helicobacter pylori infection. Helicobacter 2016; 21 [Suppl.] 1: 8–13.
24.. Ramirez-Lazaro MJ, Lite J, Lario S, Pérez-Jové, P., Montserrat, A., Quílez, M. E et al. Good diagnostic accuracy of a chemiluminescent immunoassay in stool samples for diagnosis of Helicobacter pylori infection in patients with dyspepsia. J Investig Med. 2016; 64: 388–91.