# INTRODUCTION

Nausea, vomiting and other gastrointestinal symptoms are common in pregnancy and affect almost all women with different severity ***(Goodwin, 2002).***

They can affect the women's quality of life and contribute significantly to health care costs and time lost from work ***(Attard et al., 2002).***

Although the majority of pregnant middle class women suffer from these complaints, but causes of symptoms are not clear ***(Weyermann et al., 2003).***

Numerous etiologies have been hypothesized including gestation associated hormone levels, psychological, and social factors ***(Shrinin et al., 2004).***

Helicobacter pylori is a gram-negative bacillus that colonizes the gastric mucosa. Approximately one half of the population is infected world wide meanwhile; H.pylori has been recognized as a cause of several gastroduodenal diseases, including peptic ulcer and gastric malignancies ***(Karaer et al., 2008).***

Recently the possible susceptibility to H.pylori infection in pregnancy has been reported. Although the presence of the H.pylori specific IgG antibodies as a marker for exposure to this bacterium. Yet the H.pylori

infection still defined as a positive serum immunoglobulin G (IgG) **(*Weyermann, 2003).***

It's recommended in most cases because of simplicity, low costs and high specificity and sensitivity (about 90%) ***(Debra et al., 2005).***

Recently the possible involvement of H. pylori in occurrence of gastrointestinal symptoms in early pregnancy has been reported by many studies but the role of H.pylori was contradictory ***(Karaer, 2008).***

Some studies have suggested to eradicate the infection of H.pylori in women preparing for pregnancy ***(Khayati et al., 2003).***

# AIM OF THE WORK

To investigate the relationship of helicobacter pylori infection with gastrointestinal symptom in early pregnancy.

# GASTROINTESTINAL DISEASE AND PREGNANCY

Gastrointestinal (GI) disorders are some of the most frequent complaints during early pregnancy. Some women have certain GI disorders that are unique to pregnancy. Other pregnant patients presented by chronic GI disorders that require special consideration during pregnancy. Understanding the presentation and prevalence of various GI disorders is necessary in order to optimize care for patients.

## • Nausea and vomiting

NVP occurs in 70% to 80% of pregnancies ***(Emeliano et al., 1999)***

In a large prospective multicenter study of pregnant women in the 1960s, vomiting (excluding hyperemesis gravidarum) occurred in 56% of women and was more common in the first pregnancy, in younger women, in women with less than 12 years of education, in nonsmokers, and in obese women ***(Klebanoff et al., 1985).*** Nausea and vomiting occurs significantly more frequently in the first trimester in multiple gestations than in single gestations (87% versus 73%, $p < 0.01$) ***(Brandes, 1967)***. In one study, nausea occurred in the first trimester in 91%, but occurred in the last trimester only in 3%. Nausea was reported by 50% of the patients in the morning whereas the

nausea peaked in the evening in 7% of the patients and 36% experienced nausea constantly ***(Jarnfelt et al., 1983)***.

A recent prospective study of 160 pregnant women revealed the impressive daily burden of these symptoms. In this study, 74% of women reported nausea. Morning sickness occurred in only 1.8% and 80% of the women reported that nausea lasted all day. The duration of the nausea averaged 36 days. Only one half of the women had relief of nausea by the $14^{th}$ week of gestation ***(Lacroix et al., 2000).***

**Table (1):** Factors affecting the incidence of NVP

| Factors increasing incidence | Factors decreasing incidence |
|---|---|
| Multiple pregnancies<br>Mothers or sister with nausea and vomiting in pregnancy<br>Previous pregnancy with nausea and vomiting<br>Hydatidiform mole<br>Nulliparity<br>Unplanned pregnancy<br>Female gender of the fetus<br>Non smoking<br>Low socio-economic status<br>Younger maternal age<br>Obesity<br>Stress | Smokers<br>Women who subsequently experience miscarriage |

***(Davis, 2004)***

Women with severe nausea and vomiting had more frequent depression and more often considered termination of pregnancy; they perceived that the symptoms could

affect their relationship with their spouse and adversely affect their baby. Women with mild nausea and vomiting also experienced these same psychosocial problems, indicating that categorizing these patients simply by the number of episodes of nausea or vomiting per day does not reflect the true suffering and dysfunction ***(Mazzotta et al., 2000).***

Prolonged nausea and vomiting was hypothesized as an interference with proper fluid intake and nutrition, leading to various blood chemistry abnormalities, such as increased blood urea nitrogen and ketones. Furthermore, hypothesized dietary protein level reductions for weeks during gestation could lead to subtle neurobehavioral defects apparent later in life.

Some nausea may indicate adequate levels of various pregnancy hormones or pregnancy related growth factors that influence cardiac development ***(Bonevars et al., 1999).***

Olfactory sensitivity may also play a role in NVP ***(Blum, 2000).***

Nausea during the first trimester may have different pathophysiologic mechanisms than vomiting. Metabolic and endocrine factors related to pregnancy affect gastrointestinal neuromuscular function. Gastroparesis or gastric dysrhythmias can disturb digestive activities. Metabolic,

endocrine, and gastrointestinal pathogenic factors are discussed in the next section.

**Endocrine factors:-**

***Human chorionic gonadotropin***

The HCG level rapidly rises and peaks during the first eight weeks of gestation, the time of increasing symptoms of NVP. The HCG level, however, does not correlate with NVP ***(Fairweather, 1968).***

***Estrogen and progesterone***

Elevated urinary and circulating estrogen levels may be risk factors for NVP. Because subsequent studies found no relationship between estrogen levels and NVP, the role of estrogen remains unclear ***(Depue et al., 1987).***

Progesterone, alone or in combination with estrogen, also may have a role in NVP. Progesterone decreases smooth muscle contractility and may cause gastric dysrhythmias or altered gastric emptying, thereby evoking nausea and vomiting ***(Walsh et al., 1996)***. Serum progesterone levels peak during the first trimester of pregnancy, when nausea and vomiting increase. Studies have not shown, however, a significant difference between progesterone levels in patients with or without NVP ***(Masson et al., 1985). Walsh et al.,1996*** found that physiologic levels of estrogen and progesterone elicited

postprandial gastric dysrhythmias and nausea in healthy women. The disruption of gastrointestinal neuromuscular function, evoked by various hormonal changes during pregnancy, likely contributes to NVP.

- **Esophageal and gastric neuromuscular dysfunction in NVP :-**

Gastric peristaltic contractions are driven by the gastric pacemaker region, located between the fundus and corpus on the greater curvature. Produce the rhythmic electric signals or pacesetter potentials that control the frequency and propagation of postprandial gastric contractions ***(Koh et al. 1998).***

***Gastric dysrhythmias, gastroparesis, and nausea and vomiting :***

Gastric dysrhythmias are associated with upper gastrointestinal symptoms, particularly nausea. The dysrhythmias can be bradygastrias (1-2.5 cpm) or tachygastrias (3.7-10.0 cpm) ***(Koch et al., 2003)***. Gastric dysrhythmias occur in nausea associated with motion sickness, diabetic gastroparesis, and idiopathic ***(Stern et al., 1987).***

Nausea and gastric dysrhythmias were significantly reduced by feeding patients high protein meals, but not by feeding them high fat or high carbohydrate meals. These data confirm an association between gastric dysrhythmias

and nausea, because the decrease in dysrhythmias with a protein meal paralleled the decrease in nausea ***(Jednak et al., 1999).***

***Gastric emptying and nausea of pregnancy*** **:**

Delayed gastric emptying correlates with prolonged gastric fullness and vomiting of undigested food, but does not correlate with nausea. Gastric emptying is difficult to measure during pregnancy because standard methods use radioisotopes in test meals ***(Stanghillini et al., 1996).***

- **Helicobacter pylori (H. pylori) infection:**

Has been found to be significantly associated with hyperemesis gravidarum ***(Shirin et al., 2004).***

The density of H. pylori could be correlated with the severity of symptoms and might be an explanation for the difference between ordinary morning sickness and severe vomiting.

By contrast ***Erdem et al. (2002)*** could not find a correlation between serum H. pylori IgG concentration and duration of HG symptoms although histological examination of mucosal biopsy was not used. Helicobacter pylori infection in pregnant women could be caused by changes in the gastric pH or pregnancy related changes in immune system.

A manifestation of subclinical H. pylori infection could be the result of a change in gastric PH because of an increased accumulation of fluid caused by elevated steroid hormones in pregnant women ***(Kocak et al., 1999)***. Changes in humoral and cell mediated immunity during pregnancy could cause an increased susceptibility to H. pylori infection in pregnancy, these effects possibly being more pronounced in HG patients ***(Lanciers et al., 1999).***

However, this hypothesis is susceptible to confounding factors such as lower socioeconomic status, which has been implicated in both NVP and H. pylori infection ***(Patel et al., 1994).***

***Karaca et al. (2004)*** found supportive evidence for a possible association between socioeconomic status and H. pylori infection in pregnant women with NVP in a prospective comparative study with asymptomatic pregnant women.

Another study which was done by ***Jacoby and Porter (1999)***, to describe an association of helicobacter pylori with emesis gravidarum. Three pregnant women were described with the diagnosis of emesis gravidarum unresponsive to standard therapy, but therapy with H. pylori treatment resulted in a complete relief of symptoms.

- **Psychosocial factors :**

NVP previously was associated with a woman's subconscious desire to reject an unwanted pregnancy, but this finding was not subsequently corroborated. Psychosocial problems may develop secondary to nausea and vomiting, persisting for weeks. Thus, psychosocial issues occur, particularly in patients with severe NVP ***(Atanackovic et al., 2001).***

- **Metabolic factors :**

Deficiencies of vitamin B6 have been noted in pregnant women and vitamin B6 use during pregnancy is associated with some improvement in the severity of nausea and vomiting ***(Jewell and Young, 2003).***

Abnormalities of liver function tests are common in women with hyperemesis gravidarum; however, it is possible that these are secondary to the condition ***(Conchillo et al., 2002).***

- **Immunological factors :**

Recently, several groups have investigated the role of cytokines in emesis gravidarum. The consistent finding has been an increased concentration of tumor necrosis factor-α ***(Kaplan et al., 2003).***

TNF-α is involved in regulation of the HCG production, suggesting a possible link to the HCG hormone

hypothesis. The normal shift in pregnancy to T helper cell 2 (Th2) over T helper cell 1 (Th1) dominance has been reported to be more exaggerated in women with hyperemesis gravidarum ***(Yoneyama et al., 2002).***

The increase in IL-4 secreting cells seen in this milieu also favors increased HCG production.

These changes and the increase in HCG point to increased activity in the trophoblast cells at maternal fetal interface. Consistent with this is the finding of increased cell free DNA in the plasma of women with emesis gravidarum attributed to trophoblats, damaged or destroyed by a hyperactive maternal immune response ***(Sugito et al., 2003).***

- **Allergic factors :**

It is claimed that the patient is allergic to her own corpus luteum hormones or to the by-products of early pregnancy. This theory is supported by the rapid and dramatic relief in early cases in response to anthihistaminic ***(Broussard and Richter, 1998).***

## Effect of emesis gravidarum on maternal and fetal conditions

### 1. Maternal effect:

Sleep disturbances may lead to increased fatigue and irritability ***(Davis, 2004).***

Time off work is needed by 35% of working women, who spend a mean of 62 hours away from their paid work as a result of the symptoms of nausea and vomiting ***(Gadsby et al., 1993).***

In more severe cases, hospitalization is required because dehydration, weight loss, electrolyte disturbance, and nutritional deficiency can occur.

Parenteral nutrition may also be necessary if the woman continues to loose weight.

Hyperemesis gravidarum may lead to serious complications due to vomiting itself as aspiration pneumonia, Mallory Weiss syndrome, esophageal rupture, pneumothorax, pneumomediastinum, fluid depletion which leads to dehydration which is reflected mainly by oligouria, constipation, heamoconcentration.

***a) Heart:***

It is atrophied (brown atrophy). The severity of the changes is proportionate to the duration of vomiting ***(Broussard and Richter, 1998).***

***b) Kidneys:***

Vomiting may be prolonged, frequent, and severe. Various degrees of acute renal failure from prerenal causes are encountered ***(Cunningham et al., 2005).***

***c) Liver:***

In a study, jaundice and cholestasis on liver biopsy were reported in a patient with hyperemesis gravidarum during three consecutive pregnancies with spontaneous resolution after delivery. It is claimed that the increased hormonal load during pregnancy compounded by the slow hepatic adaptation to this load may contribute to this cholestasis as the liver is the major site for steroid hormone inactivation ***(Broussard and Richter, 1998).***

***d) Brain:***

One of the most serious complications of hyperemesis gravidarum is Wernicke's encephalopathy ***(Togay et al., 2001).*** This form of central venous system dysfunction is due to a deficiency of thiamine (vitamin B1). Some patients presented with blindness ***(Goodwin, 2006).***

Other CNS complications include central pontine myelenolysis and peripheral neuropathy ***(Goodwin, 2006).***

***e) Coagulopathy:***

Another case report of coagulopathy complicated hyperemesis gravidarum was reported in the year 2000. Clotting profile was compatible with the diagnosis of vitamin K deficiency. Deficiency was secondary to lack of absorption of vitamin K due to severe nausea and vomiting and not by hepatic dysfunction ***(Julian et al., 2000).***

***The long term health consequences on women:***

Reports of post traumatic stress disorder, depression and a variety of neurological complaints are commonly mentioned by women but there has been no systematic follow up ***(Goodwin, 2006).***

Depression secondary to hyperemesis gravidarum, which may develop in up to 60% of women, with some women electing to terminate their pregnancy ***(ACOG, 2004).***

**2. Fetal effect:**

The effects on the fetus depend on the severity of the maternal symptoms. Overall, nausea and vomiting of pregnancy is associated with favorable pregnancy outcomes.

There is a decreased risk of miscarriage and a lower incidence of perinatal death, and preterm birth ***(Weigl and Weigl, 1989).***

With severe symptoms (abnormal electrolytes and weight loss) there may be an increased risk of low birth weight ***(Bailit, 2005).***