ABSTRACT
Gastroesophageal reflux disease (GERD) in pregnancy is more common among women who become pregnant at an early age, suffered from reflux during previous pregnancies, have had reflux before pregnancy even though the extent of reflux had been limited, and had multiple pregnancies. GERD is multifactorial and is rare during the first trimester and after delivery. Progesterone plays a major role, whereas the involvement of mechanical factors is minor. Serious reflux complications are rare. Extra-esophageal symptoms (cough, hoarseness, precordial pain, laryngitis, tooth damage) do not become more frequent. GERD may have a prevalence of 45% and may be asymptomatic. GERD may occur only on some days. Regurgitation is more common than heartburn. GERD is 3.79 times more common during pregnancy in women who had GERD prior to pregnancy. GERD may be different in each pregnancy woman. Raft-forming-antireflux agents are safe and effective in GER treatment during pregnancy.

INTRODUCTION
Gastroesophageal reflux (GER) is the passage of stomach's contents to the esophagus. Presence of structural changes in the esophagus and occurrence of symptoms affecting individuals’ quality of life indicate gastroesophageal reflux disease (GERD) [1-6]. Gastroesophageal reflux develops in 30 to 50% of pregnant women but the incidence may be as high as 80% in some patient groups [1-4]. In Asian countries, the incidence varies between 2.5 to 7.5% [6]. Many studies indicate that the frequency of its symptoms increases from the first through the third trimester, resolving postpartum [3-5]. GERD tend to recur with subsequent pregnancies and affects multiparous and nulliparous women similarly. Pregnancy may precipitate or worsen GERD symptoms [7-9].

The root causes include decreased esophageal sphincter pressure due to the effects of the hormones, increased intra-abdominal pressure due to enlarged uterus, prolonged passage of food from the intestine due to hormonal causes, and decreased lower esophageal tone. This high prevalence of reflux in pregnancy is due to both hormonal and mechanical causes. Manometer studies have demonstrated progressively declining basal lower esophageal sphincter (LES) pressure.

Increased progesterone hormone levels in pregnancy lead to more frequent and higher relaxation of the lower esophageal sphincter. Esophageal movements are also slowed down and gastric emptying time is prolonged. While this provides maximal food absorption for the developing fetus, the gastric pressure remains high and escape back is facilitated due to this effect. Enlarging fetus, hence the uterus, during the later phases of pregnancy lead to a gradual increase in intra-abdominal pressure, which produces pressure on the stomach, increasing reflux. Increased intra-abdominal pressure due to enlarged uterus is not considered to be adequate per se to provoke GER. A compensatory increase in LES pressure is observed in other conditions that elevate intra-abdominal pressure, such as abdominal ascites. This compensatory mechanism does not come into play in pregnancy. Sensitivity to acid contact in the esophagus may also be increased (hypersensitivity, sensitization), which is involved in reflux development. Studies in experimental animals have shown that estradiol lead to LES relaxation by impairing motility over potassium channels in the G protein-coupled estrogen receptor (GPER) [7].

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the involvement of mechanical factors is minor. Serious reflux complications are rare. Extra-esophageal symptoms (cough, hoarseness, precordial pain, laryngitis, tooth damage) do not become more frequent. GERD may have a prevalence of 45% and may be asymptomatic. GERD may occur only on some days. Regurgitation is more common than heartburn. GERD is 3.79 times more common during pregnancy in women who had GERD prior to pregnancy [8, 9].

Risk Factors
Reflux in pregnancy is more common among women who become pregnant at an early age, suffered from reflux during previous pregnancies, have had reflux before pregnancy even though the extent of reflux had been limited, and had multiple pregnancies. Reflux in pregnancy is less common in advanced maternal ages. The frequency may decline with multiparity, gestational age and presence of reflux symptoms before pregnancy and advanced ages. GERD may be different in each pregnancy woman. Weight gain is a minor contributor [10]. Hormonal changes in pregnancy lead to relaxation of the LES muscle. Hormonal changes result in deceleration of esophageal motility and delayed descend of food to the stomach. Enlargement of the uterus during the second and third trimesters also lead to a gradually increasing pressure on the stomach by increasing intra-abdominal pressure. Some authors describe the role of this as a minor contribution. Reflux in pregnancy is frequent, but extra-esophageal complications are less common. Reflux symptoms diminish after delivery.

Diagnosis
Presence of reflux is understood through patient’s history. Upper gastrointestinal endoscopy is reliable and endoscopic is not risky in pregnancy. However, gastroenterologist still avoid this procedure in expectant mothers as far as possible. Endoscopy is indicated if reflux symptoms persist despite medical treatment and lifestyle changes or if additional symptoms including hematemesis or dysphagia are present. Manometer and pH-meter can be used safely but are seldom indicated.

Differential Diagnosis
Gallstones, stomach/esophageal cancer, peptic ulcer, esophageal motility disorders, drug-related esophagitis and eosinophilic esophagitis should be considered.

TREATMENT
Diet and lifestyle changes
Eating in 3-hour intervals and as small meals is important. Eating should also be slow and food should be thoroughly chewed. Water should not be drunk while eating and should be reserved to between meals, and all eating should be stopped 3 hours before bedtime. Chocolate, fatty/oily food, acidic drinks and food, caffeine, citrus fruits and tomato, ketchup and fizzy drinks should be avoided. Sitting up straight and walking slowly for one hour after meals provide relief. Individuals should wear comfortable clothes, maintain a healthy bodyweight, consume yoghurt or a glass of warm milk or chew sugar-free gums (increases salivation, thus neutralizing the acid that enters the esophagus) to suppress the symptoms. Food and drinks which are unlikely to increase reflux and are recommended include apples, bananas, baked potatoes, broccolis, cabbages, carrots, green beans, sweat peas, steak, chicken breast, egg whites, fish meat, cheese, goat cheese, bran, oat, corn bread, rice, mineral water, and oil-free salad [11, 12].

Individuals should drink chamomile tea or a glass of warm milk with some honey added, and should consult a physician for alternative medicine (e.g. yoga) treatments. Besides, raising bedhead or sleeping on the left side provides significant relief.

Medical Treatment
Antacids or sucralfate should be used first. Symptomatic treatments without systemic effect or absorption should be preferred. Antacids, which are non-systemic drugs, should be initiated in pregnant women who do not respond to lifestyle changes, and they should be used as the first choice in treatment. They offer the required relief in many women with mild symptoms. Preferably, the antacid + alginic acid combination is more beneficial. Medicinal products containing antacid plus alginic acid act by forming a layer over the stomach content, neutralizing the existing acid and preventing the effect of the refluxing material on the esophageal mucosa (picture 1). It is recommended to take 15-30 ml of these products 15 minutes after meals and before bedtime. Suspension forms are particularly efficacious. Being affordable and readily available are the advantages of these medicines [13, 14].

Long-term and high-dose Mg++ trisilicate should be avoided, especially in the third trimester, as it may lead to contractions. Na+ bicarbonate should be avoided since it may lead to edema and hypertension. Those that contain aluminum may result in constipation.

Sucralfate
As an aluminum salt that acts by inhibiting pepsin activity, sucralfate seems to be safe since it is not absorbed from the gastrointestinal tract [11,12]. Sucralfate is taken orally as 1 g three times daily but should this proves inadequate, it may be combined with lifestyle changes together with antacid + alginic acid treatment. No maternal or fetal side effects associated with sucralfate have been reported.

H2 receptor antagonist: Of the H2 receptor antagonists, ranitidine is FDA category B, while information on others is limited,
and they may possibly be safe.

**Prokinetic agents**

Data on their efficacy and safety in pregnancy is insufficient.

**PPI**

The most efficient medical treatment choice in relieving reflux symptoms and treating esophagitis in the general population is currently the proton-pump inhibitors and they are commonly used. There are, however, some side effects associated with their long-term use. Omeprazole is a FDA category B drug, while information on others is limited, and they may possibly be safe [14-17].

Herbal methods: Ginger, chamomile, thymus, valerian, fenu-greek, green tea, olibanum (oil derived from the sweetgum tree native to tropical zones) and quince sauce can be used. One study investigated quince sauce and ranitidine, and obtained comparable results [18].

In conclusion, gastroesophageal reflux in pregnancy is common but is well-managed with appropriate diet and medical treatment.

**REFERENCES**