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REVIEW ARTICLE

HYPEREMESIS GRAVIDARUM: A COMPREHENSIVE REVIEW OF PREGNANCY RELATED COMPLICATION AND ITS MANAGEMENT

Niraj Khatri Sapkota*, Prakasah Kumar Yadav, Ram Lochan Yadav

Department of Physiology, Chitwan Medical College, Bharatpur, Chitwan, Nepal.

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ABSTRACT

Nausea and vomiting are common symptoms in early pregnancy usually mild and self limiting, but less percentage of women experience severe symptoms known as hyperemesis gravidarum, outcomes have improved with intravenous rehydration therapy, consequences include decreased quality of life, time off work and secondary depression.This short review will focus on the outlines considering comprehensive information related to this pregnancy related complication.Treatment modalities are discussed together with evidence regarding use excluding other causes of nausea and vomiting, such as urinary tract infection and thyrotoxicosis. Assessment and management section succinctly explains the way of ameliorating symptoms from non-medication to therapeutics level to prevent symptoms.

Key words: Hyperemesis gravidarum, outcomes, depression, management, thyrotoxicosis

INTRODUCTION:

What was known?

1. HG (Hyperemesis Gravidarum) is a unique feature of pregnancy related complication of nausea and vomiting (morning sickness) occurring 6^{th} to 8^{th} week of pregnancy peaking at 11^{th} week and resolved by around 20 weeks of gestation.
2. In general fetal outcome is less fatal but maternal prognosis is worsened to mortality if untreated or treated inappropriately.

Hyper-emesis is a protracted emetic condition of the pregnancy which results into the severe weight loss (5% of the body mass) and ketosis. In severe cases wernicke's encephalopathy,central pontine myelinolysis and maternal death can occur.Moreover,fetal growth restriction and smaller birth results. About 1% of the pregnant population are affected from hyperemesis gravidarum, higher incidence is seen in multiple pregnancy and with hydatidiform moles both of which are associated with secretion of high amount of human chorionic gonadotrophin (hCG) suggesting its causative role in hyperemesis, interesting fact is that women with HG give birth to higher proportion of female infant.(1)

Patho- physiology:

Nausea and vomiting of pregnancy, commonly known as "morning sickness," affects approximately 80 percent of pregnant women, is generally a mild, self-limited condition that may be controlled with conservative measures, the exact cause of which remains unclear but research has implicated Helicobacter pylori as one possible cause, small percentage of pregnant women have a more profound course, with the most severe form being hyperemesis gravidarum, unlike morning sickness, hyperemesis gravidarum may have negative implications for maternal and fetal health.(2)Serious alarming state of nausea and vomiting during early pregnancy, is known as hyperemesis gravidarum and may result in dehydration, ketonuria, catabolism and require hospitalization. Etiological factors involves increased hCG and steroids, multiple gestation and vitamin B_6 deficiency (3) affecting 70-80 percent of pregnant mothers between weeks usually mild and self-limiting, however some mothers have a more profound course which lead to hyperemesis gravidarum posing health risk to both mother and baby, therefore prompt treatment should be initiated without delay.(4,5,6,7) Hyperemesis gravidarum cause sustained nausea and vomiting during the first trimester of pregnancy .

A prospective study comparing the hormonal status in women with hyperemesis gravidarum (5-18 weeks), with healthy pregnant controls, matched for gestational age demonstrated that only maternal age, free thyroxine and thyroid stimulating hormone were significantly independent variables. Human chorionic gonadotropin is not independently involved in the etiology of hyperemesis gravidarum but may be indirectly involved

*Corresponding author: Niraj Khatri Sapkota | E-mail: nirajkhatri22@yahoo.com

by its ability to stimulate the thyroid.(5) However early study reported that neither thyroid hormones,nor hCG contribute to the pathogenesis of the condition.(6)

Hyperemesis gravidarum and GTT (Gestational transient thyrotoxicosis):

Onset of pregnancy follows the physiological stimulation of thyroid gland sometimes, deviating thyroid hormone from the normal range, leading to a state which is referred to as gestational transient thyrotoxicosis (GTT). GTT has been observed in up to two thirds of women suffering from HG, total incidence of GTT increased significantly if serum hCG was more than 80,000 IU/L, subclinical GTT if serum hCG was 80,000-140,000 IU/L and clinical GTT if serum hCG was more than 180,000 IU/L the recovery of which do not require antithyroid therapy and thyroid function normalized by the second trimester, newborns of mothers with GTT had normal TSH levels, severity is related to serum hCG levels with HG and GTT, thyroid function normalized by the second trimester without antithyroid treatment, it doesn't affect pregnancy outcomes,(7) also the increase in thyroxine binding globulin, total triiodothyronine and thyroxine concentrations, thyroglobulin, and renal iodide clearance,(8) a study demonstrated about 60% of patients with hyperemesis gravidarum has GTT (9,10) peaks hCG at first trimester of pregnanc,as hCG has intrinsic mild thyroid stimulating activity, the increase in thyroid hormones is attributable to either higher hCG concentrations, or hCG hypersensitivity TSH receptor in an overactive thyroid,(11) or probable secretion of a variant of hCG with increased thyroid stimulating activity. (12) Generally, patients with GTT have no history of thyroid illness, goiter is usually absent, and thyroid antibodies are negative at the moment, however depicts feature of abnormal liver function test and electrolytes, degree of vomiting determines thyroid stimulation and the higher the concentration of hCG.(13)Transient hyperthyroidism may be responsible for 40%–70% of thyroid function abnormalities in pregnancy and resolves spontaneously by 18 weeks without treatment and sequelae,(14) only a small proportion of these patients have clinical thyrotoxicosis and may be these are the patients who secrete a more potent molecular variant of hCG besides hyperemesis gravidarum occurring during the first pregnancy, recurrence in two consecutive pregnancies has been reported.(15)

Hyperemesis gravidarum and LFT (Liver function test):

Liver function test abnormalities is 32% among pregnant women of all gestational ages with HG and was responsible for 94% of which is present in the first trimester of gestation.(16) Aminotransferase elevation (up to 200 U/l) is the most common laboratory report of LFT (liver function test) in HG, although increased alkaline phosphatase up to twice normal values and bilirubin up to 4 mg/dl is anticipated with rare incident of elevation greater than 1600 U/l, without any report of fulminant liver failure in HG ,the severity of nausea and vomiting in patients with HG and liver disease, as a general rule, correlates with the degree of liver enzyme elevation.(17,18,19) Liver function abnormalities usually return to normal levels within a few days of volume expansion and the cessation of vomiting.

Clinical features, maternal and fetal outcomes:

Nausea and vomiting of pregnancy ("morning sickness,") affects nearly 75%-80% of pregnant women where 50% experience vomiting alone, an alarming state of HG is exhibited by 1% resulting into adverse outcomes for the mother and fetus associated with increase in maternal adverse effects, including splenic avulsion, esophageal rupture, Mallory-Weiss tears, pneumothorax, peripheral neuropathy, and preeclampsia, as well as increases in fetal growth restriction and mortality.(20-24)

Severity of HG is characterized by extreme weight loss, suggesting that HG is a form of prolonged starvation in pregnancy included food aversions, muscle pain, nausea, and posttraumatic stress. The result is 16% of babies are reported to born prematurely and 8% weighed <2500 g, 9.3% was reported to have a behavioral disorder.(25)

Assessment and management:

Management of the HG can be done in different stages, initially adopted was non-pharmacological method where dietary and life style modification is applied to improve symptoms and quality of life, that includes nausea and vomiting electrolyte drinks are aided to maintain electrolyte balance by following nutrition changes such as small amount of fluids and food throughout the day in small binge that is enriched by carbohydrate with less fat and acid (26) rather in one full bout along with protein predominant meals are beneficial as they have eupeptic effect, other recommended supplements includes light snacks, nuts, dairy products and salty biscuits,(27)taking less stress with enough rest as lifestyle modification is advised.

Pharmacological management:

In severe case of HG that is unresponsive to dietary and lifestyle modification, optimum to low dose antiemetic is prescribed for administration which is proven to have safety, efficacious and cost effectiveness (28) in early stage of pregnancy antiemetic becomes quite effective , ondensetron is among the commonly used with few side effects,(29,30) other safe drugs recommended are metoclopramide that improves gastrointestinal motility and pyridoxine (vitamin B6) which is given at a dose of 10-25mg daily three times can be progressively increased

up to 200mg without any side effect that lowers symptoms and is quite effective,(30-34) though some study suggest this combination (Pyridoxine and metoclopramide (category A) first line in the treatment of hyperemesis gravidarum followed by ondansetron (category B1),(35) however more recent study did not show any improvement in vomiting frequency and nausea with this combined treatment,(36) other antiemetic superior for the treatments in pregnancy includes antihistamine and anti cholinergic drugs such as meclizine, promethazine, dimenhydrinate and diphenhydramine,(37) side effects of the mentioned antiemetics ranges from common dizziness, drowsiness, constipation to severe convulsions, diminished alertness, tachycardia or bradycardia, also now in recent period diazepam is also effective in the treatments in combination with antiemetic due to its sedative properties which reduces the challenge of hospitalization and improves patient satisfaction.(38)

Non pharmacological management:

It comprises acupressure on the interior of the wrist but the evidence for this treatment includes very less evidence (39,40) and other aid that can be used as a supplement involves ginger paste 1g/day without having any teratogenic effect to the fetus.(41- 46)

Psychosomatic therapy:

The talk between physician and pregnant women about her psychological condition of her marital relationship gives encouragement to accept the pregnancy, inpatient nursing support and relief from stress or strain ameliorate the symptoms without any therapeutic intervention. (47)

Quality of life during HG:

The pregnant women suffering from HG has psychological burden of not feeling well since several weeks and months that cause severe feeling, distress which disturb working schedule and reduce quality of life,(48) therefore support from family and spouse play important role in combating the symptoms as many women feel embarrassment and helpless due to misunderstanding by relatives.(49)

CONCLUSION:

Nausea and vomiting during pregnancy (NVP) or emesis gravidarum ,is of no pathological significance as long as the affected women do not feel unwell or restricted in their daily life however, different grades in the scope of NVP, which range from occasional morning-sickness to excessive vomiting that persists throughout the day. The most severe grade of NVP often leads to hyperemesis gravidarum,understanding its etiology is quite essential since the causal factors of HG are multifarious, treatments of this condition must be taken seriously of which management ranges are multimodal, ranging from dietary and lifestyle advice to psychosomatic counseling or psychoanalytic therapy, antiemetic drugs may be necessary, as well as IV fluid replacement. Since this condition is accompanied by a significant reduction in quality of life for the patient and high costs to the healthcare system. General practitioners and obstetricians should ensure that they are well informed about this condition that they are able to provide advice, counseling and effective medication to pregnant women to prevent the exacerbation of symptoms.

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