

# VOMITING OF FIRST PREGNANCY TRIMESTER: HOW TO ESTIMATE?

## INTRODUCTION

Nausea and vomiting are most frequent complaints of first pregnancy weeks. Emotional component, significant impact on wellbeing and quality of life has put these symptoms in the center of plenty of investigations. The majority of them deal with treatment methods and comparison of their effectiveness.

From 50 to 80% of all pregnant women have complains on vomiting or nausea or both, but only in 2–3% cases the severity of vomiting is a reason of hospitalization and an indication to parenteral nutrition [12]. This is very important to notice, that this diagnosis should be a one of exclusion – absence of other diseases; vomiting is a proper clinical symptom, as gastrointestinal inflammation or enteral infection.

Race, age, number of pregnancy and labor role in nausea and vomiting genesis was discussed [4], some authors proposed an influence of maternal, social and psychological status [5] and even educational status [14]. One investigation has proposed the less frequency of nausea and vomiting in multiparous women as a result of smaller placental volume [6]. Human chorionic gonadotropin is considered to be a main pathogenic factor of nausea, as it stimulates estrogen production in ovarian and thus provokes symptoms. That's why twin or molar pregnancy is in more risk of nausea and vomiting [6].

Thus, the real etiological factor of both nausea and vomiting are unknown, investigators have been concentrated for the search of association between this early pregnancy symptoms and more late pregnancy complications. Q. Zhou et al. (2019) reported about increased risk of low weight newborn by severe form of first-trimester vomiting. On the contrary, S. Hinkle et al. (2016) proved a strong association of vomiting and nausea with a reduced risk of clinical pregnancy loss. Discussing the absence of this association with losses on preclinical or preimplantation pregnancy, authors propose protective role of vomiting and nausea, but realized only after complete implantation. In 1986 F. Tierson et al. proposed an explanation, what is the reason of small newborn weight by first trimester nausea and vomiting. It may be caused by a more quick fetus maturation because of an increased protein intake. S. Poeran-Bahadoer et al. (2019) studied more longer the catamnesis of patients with vomiting of first trimester and their children till adulthood in population of Rotterdam. According to their results,

vomiting, not depending on its severity, increases the risk of obesity and excess body mass of an offspring in adulthood. Any other cardiovascular risk factor increasing was not revealed, in the same time authors cannot propose any explanation of this trend, in spite of possible risk of fetal growth restriction at these patients [10]. A. Ayycrevoo et al. (2013) have reported about decreased insulin sensitivity, revealed at offspring's of women with vomiting of first trimester. The number of cases in this report was less than 100, totally with control group, and authors dialed only with severe forms of disease, so the possibility of their application to all vomiting women is discussable.

The same difficult as an etiology question, the first trimester vomiting management problem is. I. Tsikiridis et al. (2019), reporting about evidence based recommendations for nausea and vomiting treatment, marked only two ones – frequent small meal and avoidance of iron supplementation [12]. Speaking about other popular remedies, they mentioned ginger, antihistamines, acustimulations, phenothiazines, dopamine, and serotonin 5-hydroxytryptamine type 3 receptor antagonists, those are often used, but do not have enough evidences of effectiveness. As an example of those methods, N. Michihata et al (2019) have demonstrated that use of one of Japanese herbal drug, leading not to decreasing frequency of vomiting, let to avoid staying in hospital for these patients.

Speaking about possible consequences of first trimester vomiting we performed a prospective investigation, devoted to electrolytic balance in first and second trimester. The goal was to reveal if vomiting in first 12 weeks of pregnancy leads to significant or non-significant changes in electrolytic balance and are there any changes in more late terms.

**Objective of the study** – to study changes in electrolyte balance and hematocrit concentration by vomiting of first trimester and by uncomplicated pregnancy.

## MATERIALS AND METHODS

109 women in first pregnancy trimester were investigated. All of them were nulliparous and had single-fetus pregnancy. They were divided in 2 groups, depending on having vomiting. 58 patients of group I had vomiting from 1 till 10 times a day; we excluded women with emesis gravidarum, as well as patients with other objective reasons of vomiting – severe gastrointestinal diseases, intesti-

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nal infections. As women with multipregnancy are more like to have vomiting, they also were not included in groups. The possible effect of ovulation stimulation on the vomiting appearance and heaviness, the patients after additional reproductive technology also didn't take part in investigation. Group II consisted of 51 pregnant that during first trimester did have neither nausea, nor vomiting. We didn't include to any of group patients with nausea as on only complication of first trimester, because it's impossible to measure its heaviness, as for vomiting.

In both groups the concentration of  $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{Ca}^{2+}$  and  $\text{HCO}_3^-$  ions was investigated on the beginning of study and in 20 pregnancy weeks. We had any case of miscarriage in both groups, so the quantity of tests was identical in both terms. The amperometric method was used for ions concentration definition, the material – venous blood, got from v. cubitalis early in the morning, before meal. For each electrolyte a corresponding ion-selected electrode was used. Laboratory investigations were provided in Kyiv Perinatal Center laboratory that has an international certificate. The results were compared in group borders (first and second trimester data) and between groups in equal terms. Also the division of patients by sodium-ion concentration and hematocrit volume in both terms was analyzed. The correlation between sodium-ion concentration and hematocrit volume was in both terms was calculated.

## RESULTS AND DISCUSSION

By pregnancy progress the female body undergoes significant overload due to the growing need of fetus-placental complex. One of the ways to achieve it is to make circulating blood volume according to persistently increasing volume of vascular bed. The mechanisms of this are still discovering, but scientists have no doubt, that the main one is an asymmetric change of circulation volume – while totally it is increased on 30%, the volume of plasma becomes bigger on 40% and volume of blood cells – only on 20%. The first result is physiological for pregnancy anemia. But the plasma itself also is not a homogenic medium; it contains a lot of non-polar molecules, proteins first of all. So, the next result of hemodilution is a relative hypoproteinemia that is not

Table. Ion concentrations in plasma of surveyed women

Electrolyte concentration (mmol/l)	Group I (n = 58)		Group II (n = 51)	
	10–12 weeks	20–22 weeks	10–12 weeks	20–22 weeks
$\text{Na}^+$	$138.5 \pm 2.80$	$141.1 \pm 4.57$	$144.1 \pm 2.91$	$142.1 \pm 4.05$
$\text{K}^+$	$4.0 \pm 0.22$	$4.1 \pm 0.19$	$3.7 \pm 0.27$	$3.7 \pm 0.11$
$\text{Ca}^{2+}$	$2.3 \pm 0.12$	$2.1 \pm 0.29$	$2.3 \pm 0.32$	$2.3 \pm 0.14$
$\text{HCO}_3^-$	$24.5 \pm 2.25$	$25.9 \pm 2.71$	$27.2 \pm 1.60$	$25.4 \pm 3.13$

corrected by significant increasing of fibrinogen concentration. So, changes in electrolyte balance are avoidless. But possible borders of these changes are very narrow, because electrolytic gradient on both sides of membrane is a base of cell wellbeing and function. An additional factor, that can influence this balance, is vomiting, being a reason of sodium-ion and chloride-ion loss.

Our previous researches have demonstrated, that women with severe forms of preeclampsia by detailed questioning in majority of cases didn't remind nausea and vomiting in first trimester of current pregnancy [15]. On contrast, women with uncomplicated pregnancy and labor in 67% testified about nausea and vomiting, mild, moderate or severe. That's why the group of patients with vomiting in first trimester was collected with the aim to find correlation between possible electrolyte changes and pregnancy progress.

As our results demonstrate, that medium concentrations of all studied ions didn't differ between groups on the start of investigation (Table).

So, vomiting of first pregnancy trimester does not lead to dramatically changes of electrolyte balance, and according

to good pregnancy results in most cases of vomiting women, cannot be considered as a serious complication. In any case, vomiting should lead to electrolytes losses, and sodium-ion is one of the first to lose. But the stability of electrolytes balance is so important for organism wellbeing, and regulating mechanisms, including aldosterone with its angiotensin activation, vasopressin and atrial natriuretic peptide, are very sensitive and thus – effective. This stability is a reason of non-effectiveness of different correcting solutions appointment for vomiting of pregnancy treatment (R. Boeliget al, 2015). Nevertheless, speaking not about moderate concentrations, but about distribution of patients with different sodium-ion concentration in first pregnancy trimester, we have found diversity (Fig. 1).

The majority of women, having vomiting in first pregnancy trimester, in the beginning of study showed lower concentrations of sodium-ion – 142–143 mmol/l, in group of non-vomiting women – 145 mmol/l. That can mean, that women with vomiting of first trimester have stronger tendency to hyponatremia, then patients of second group. Speaking about sodium as a main electrolyte of plasma, tendency to hyponatremia is a manifestation

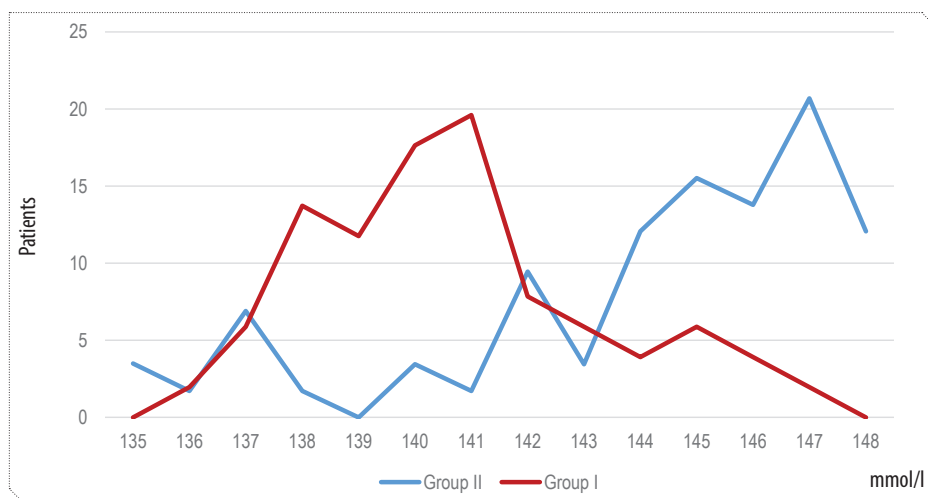


Figure 1. Distribution of patients by sodium-ion concentration

of physiological for pregnancy hemodilution, and this tendency is proper majority of women with vomiting of first trimester, albeit they are losing fluid. In the same time, part of women, despite absence of any complains during first trimester, are in a dangerous tendency of insufficient hemodilution.

Researchers are minded to consider hemodilution by pregnancy first of all from the point of view hemoglobin decreasing. Nevertheless, hemodilution is rather a reflection of normal regulation of electrolyte-protein balance by pregnancy. Initial hypo-proteinemia, that is considered to be one of possible pathogenic mechanisms of pre-eclampsia, and perhaps – other obstetrics complications, results an oncotic pressure decreasing. In this condition the increasing of sodium-ion concentration that does not exceed physiological borders, is well explained. It can be proposed, that vomiting in first pregnancy trimester is a possible way to confirm normal sodium-ion concentration in the beginning of gestation.

From this point of view a question of any kinds of infusion, used for nausea and vomiting treatment, becomes very discussable. The regulation of osmotic homeostasis may be very fragile, so excess volume of different electrolytes formula may be not only useless, but sometimes harmful for future pregnancy currency.

Hyponatremia is divided into absolute and relative. Absolute one is a result of profuse diarrhea or vomiting, excessive sweating, renal and adrenal insufficiency, hemorrhage and diabetic acidosis. Relative hyponatremia is a consequence of water delay in circulation, as it is necessary by physiological pregnancy [24].

Difference in concentration of other electrolytes between groups is not significant, as well as distribution patients by this concentration.

In the beginning of second pregnancy trimester the moderate concentrations of all studied ions also didn't have differences between groups. But discussing the direction of changes with pregnancy progress, they are opposite in two studied groups. Patients, that had vomiting of first trimester, till 20 weeks had registered decreasing of sodium-ion concentration. On the contrary, women, having any complain in first trimester, till second trimester demonstrates increasing of so-

dium-ion concentration. It means, first group of patients have more favorable changes in blood circulation, meaning more expressed hemodilution. The increasing concentration of sodium-ion in second group testifies the inadequate hemodilution in these patients.

To prove the idea of incomplete hemodilution at some patients without vomiting and nausea, we studied the moderate hematocrit value and distribution of patients for this criteria in the end of first trimester. For evaluation of hemodilution hematocrit is more favorable, than hemoglobin, because of possible influence of iron deficiency. The moderate hematocrit volume in first trimester was similar in both groups, hesitating in physiological measures –  $38.9 \pm 3.52\%$  for group I and  $36.7 \pm 4.53\%$  – for group II. The distribution of patients by this sign demonstrates difference, similar to the sodium-ion concentration (Fig. 2).

In spite of similar moderate value in groups, 35.3% patients of group II demonstrate hematocrit level 40% and more, in group I – only 18.9%. This deviation also can be considered as an argument of insufficient hemodilution at part of women without nausea and vomiting in first trimester. The hematocrit volume in first trimester correlates negatively with sodium ion concentration (correlation index – 0.7), that can prove the role of additional osmotic regulation by the vomiting.

In the middle of second trimester the trend of hematocrit level is also similar to sodium concentration – at patients, having vomiting in first trimester it has decreased from  $38.9 \pm 3.52\%$  to  $34.4 \pm 1.98\%$ , that argues hemodilution pro-

gressing. The group II (patients, having any nausea and vomiting in first 12 weeks), contrary demonstrate increasing of this parameter – from  $36.7 \pm 4.53\%$  to  $37.9 \pm 2.79\%$ . Some of these patients, having comfortable and uncomplicated passing of first trimester, really have inadequate adaptation of blood circulation, including lack of circulating volume. The decreasing of this parameter in 14–17 gestational weeks is proved as prognostication factor of early pre-eclampsia onset [13]. A. Stangret et al. (2017) tried to explain it by a significant dysfunction of renin-angiotensin-aldosterone system, occurring as a predictor of fetal growth restriction.

According to modern point of view, reduced blood flow in placenta leads to a specific kind of injury – hypoxia reoxygenation process caused by free radicals. They damage placental tissue, provoking excess releasing of placental vasoconstrictor factors to systemic maternal circulation. The activation of proinflammatory cytokines synthesis makes the pathological changes in endothelium deeper [7].

**CONCLUSION**

Vomiting of first pregnancy trimester does not lead to significant changes electrolyte balance. These patients in progress of pregnancy demonstrate adequate hemodilution, that mean decreasing of hematocrit value and sodium-ion concentration. At the same time, at some patients without vomiting and nausea the trend to incomplete hemodilution is revealed. This trend may result progressing of endothelial dysfunction, what will lead to different pregnancy complications.

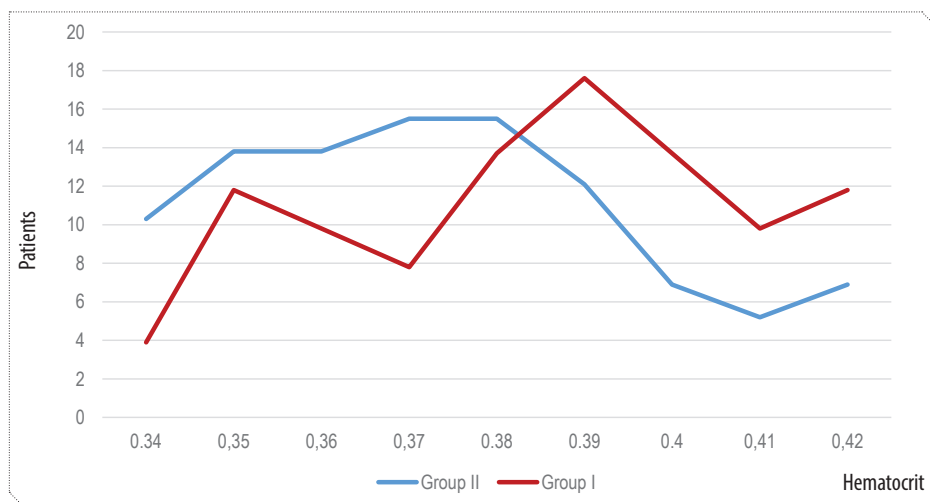


Figure 2. Distribution of patients by hematocrit concentration in first pregnancy trimester

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### VOMITING OF FIRST PREGNANCY TRIMESTER: HOW TO ESTIMATE?

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**Objective of the study:** to study changes of electrolyte balance and hematocrit in the first trimester vomiting and in uncomplicated pregnancy.

**Material and methods.** 109 women in the first trimester of pregnancy were divided into 2 groups. Group I consisted of 58 patients with complaints on vomiting from 1 to 10 times a day, group II – 51 women without complaints of nausea and vomiting. At the beginning of the study and at 20 weeks the concentrations of the main electrolytes in the serum, as well as the hematocrit index, were determined in all study participants. Groups were compared basing not only modern concentration level, but also distribution of each meaning in total.

**Results.** Despite the loss of fluid and electrolytes with vomiting, patients in group I did not differ from women with uncomplicated pregnancy in average ion concentrations and hematocrit. However, the distribution of the study participants by the indicators showed that the majority of women in group II had high levels of serum sodium and hematocrit. In addition, the dynamics of pregnancy progression in women of group I showed a decrease in sodium concentration and in pregnant women in group II – on the contrary, the tendency to increase this indicator.

**Conclusion.** Vomiting of the first trimester does not lead to significant changes in electrolyte balance. However, with the progression of pregnancy, such patients show adequate hemodilution, which implies a decrease in sodium concentration and hematocrit. At the same time, in some patients with uncomplicated course of the first trimester of pregnancy, there is a tendency for defective hemodilution. This can lead to endothelial dysfunction and associated obstetric complications, by the time patients with first pregnancy vomiting have more favorable changes of blood circulation.

**Keywords:** vomiting of pregnancy, hematocrit, sodium.

### БЛЮВАННЯ ПЕРШОГО ТРИМЕСТРУ ВАГІТНОСТІ: ЯК ОЦІНЮВАТИ?

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**Мета дослідження:** вивчити показники електролітного балансу і гематокриту при блювоті першого триместру і при неускладненому перебігу вагітності.

**Матеріали та методи.** Обстежено 109 жінок в першому триместрі вагітності, їх розділено на 2 групи. Групу I склали 58 пацієнток зі скаргами на блювоту від 1 до 10 разів на добу, групу II – 51 жінка без скарг на нудоту і блювоту. В усіх учасниць дослідження на початку його і в 20 тижнів були визначені концентрації основних електролітів у сироватці, а також показник гематокриту. Групи було порівняно між собою не лише за середніми значеннями показників, але й за розподілом по цих параметрах.

**Результати.** Всупереч втратам рідини і електролітів з блювотою, пацієнтки I групи не відрізнялися від жінок з неускладненим перебігом вагітності за середніми концентраціями іонів і показником гематокриту. Однак при розподілі учасниць дослідження за показниками виявлено, що велика частина жінок II групи мала високий вміст натрію в сироватці крові і високий рівень гематокриту. Крім того, в динаміці прогресування вагітності в жінок I групи відзначено зниження концентрації натрію, а у вагітних II групи – навпаки, тенденція до підвищення цього показника.

**Висновок.** Блювота першого триместру вагітності не призводить до значних змін електролітного балансу. Однак з прогресуванням вагітності такі пацієнтки демонструють адекватну гемодилуцію, що передбачає зниження концентрації натрію і показника гематокриту. В той же час у частини пацієнток із неускладненим перебігом першого триместру вагітності виявлена тенденція до неповноцінної гемодилуції. Це може призвести до ендотеліальної дисфункції і пов'язаних із нею акушерських ускладнень, тоді як пацієнтки з токсикозом першого триместру в динаміці вагітності демонструють більш сприятливі зміни мікроциркуляції.

**Ключові слова:** блювота вагітності, гематокрит, натріємія.

### РВОТА ПЕРВОГО ТРИМЕСТРА БЕРЕМЕННОСТИ: КАК ОЦЕНИВАТЬ?

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**Цель исследования:** изучить изменения электролитного баланса и гематокрита при рвоте первого триместра и при неосложненном течении беременности.

**Материалы и методы.** Обследованы 109 женщин в первом триместре беременности, разделенные на 2 группы. Группу I составили 58 пациенток с жалобами на рвоту от 1 до 10 раз в сутки, группу II – 51 женщина без жалоб на тошноту и рвоту. У всех участниц исследования в начале его и в 20 недель были определены концентрации основных электролитов в сыворотке, а также показатель гематокрита. Группы были сравнены между собой не только по средним значениям концентрации изученных параметров, но и по распределению в пределах группы.

**Результаты.** Вопреки потерям жидкости и электролитов с рвотой, пациентки I группы не отличались от женщин с неосложненным течением беременности по средним концентрациям ионов и показателю гематокрита. Однако при распределении участниц исследования по показателям установлено, что большая часть женщин II группы имела высокое содержание натрия в сыворотке крови и высокий уровень гематокрита. Кроме того, в динамике прогрессирования беременности у женщин I группы отмечено снижение концентрации натрия, а у беременных II группы – наоборот, тенденция к повышению этого показателя.

**Выводы.** Рвота первого триместра беременности не приводит к значительным изменениям электролитного баланса. Однако с прогрессированием беременности такие пациентки демонстрируют адекватную гемодилуцию, что предполагает снижение концентрации натрия и показателя гематокрита. В то же время у части пациенток с благополучным и неосложненным течением первого триместра беременности выявлена тенденция к неполноценной гемодилуции. Это может привести к эндотеліальної дисфункції и связанным с ней акушерским осложнениям. Вместе с тем женщины со рвотой первого триместра демонстрировали более благоприятные изменения микроциркуляции.

**Ключевые слова:** рвота беременных, гематокрит, натриемия.