

ORIGINAL PAPERS

Prevalence and persistence of nausea and vomiting along the pregnancy

Pluvio J. Coronado¹, María Fasero², Ángel Álvarez-Sánchez³ and Enrique Rey³

¹Department of Obstetrics and Gynecology. Instituto de Salud de la Mujer Botella Llusía. Hospital Clínico San Carlos. Madrid. Universidad Complutense de Madrid. Spain. ²Service of Obstetrics and Gynecology. Hospital Sanitas La Zarzuela. Madrid, Spain. ³Department of Digestives Diseases. Instituto de Investigación Sanitaria del Hospital Clínico San Carlos. Madrid (IdISSC). Universidad Complutense de Madrid. Spain

ABSTRACT

Background/aims: Nausea and vomiting of pregnancy (NVP) impact in the pregnant woman's quality of life, especially when are persistent or severe. The objective is to estimate the prevalence and factors associated with the persistence of NVP in each trimester of pregnancy.

Methods: We studied a cohort of 263 pregnant women with gestational age < 12 weeks. Data were collected using the Gastro-Esophageal Reflux Questionnaire validated for use in the Spanish population. Data were collected through telephone interviews at the end of each trimester of pregnancy. The main variable was the presence of NVP in each trimester and their persistence along the pregnancy.

Results: The prevalence of nausea in the each trimester was 63.5 %, 33.8 %, 26.2 %, and vomiting was 29.3 %, 22.1 %, 14.1 %, respectively. Factors associated with nausea in the first trimester were Latin-American origin (OR: 3.60, 95 %CI 1.61-80.5) and primary education (OR: 0.31; 0.13-0.73); vomiting was associated with Latin-American origin (OR: 13.80, 1.82-104.4) and was inversely associated with weight gain (OR: 0.58, 0.35-0.97). Persistence of NVP were only associated with suffering the symptom in the previous trimester ($p < 0.01$), and did not find other predictor factors.

Conclusions: NVP's prevalence declines along pregnancy, is associated with race and inversely with weight gain, and its persistence over time cannot be predicted.

Key words: Nausea. Vomiting. Hyperemesis gravidarum. Persistence. pregnancy.

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Correspondence: Pluvio J. Coronado-Martín. Departamento de Obstetricia y Ginecología. Hospital Clínico San Carlos de Madrid. c/ Martín Lagos, s/n. 28040 Madrid, Spain
e-mail: pcoronado@sego.es

INTRODUCTION

Gastrointestinal symptoms are very common during pregnancy. Hormonal changes in pregnancy usually alter the normal function of the digestive tract, even may aggravate or induce a previous gastrointestinal dysfunction (1). Nausea and vomiting of pregnancy (NVP) affect up to 90 % of all pregnant women, and have been considered so physiological that their absence has been associated with an increased risk of early pregnancy loss (2). Nevertheless, this physiological symptom can significantly impact in the pregnant woman's quality of life, especially when is persistent or severe (3-5). Hyperemesis gravidarum is a distinct entity, and has been defined when the vomiting is uncontrollably, is accompanied by weight loss, dehydration and even hospitalization. Fortunately, it affects to less than 2 % of pregnancies (6,7).

The etiology of pregnancy-related NVP remains unclear, but appears to be positively correlated with the serum levels of estrogens and human chorionic gonadotropin (8). Different studies have reported some factors associated to these symptoms, but data have not been consistent. Race/ethnicity seems to have an important influence, since Black and Asian women have fewer symptoms in the first trimester of pregnancy than Caucasians (9). Younger primigravid women are more likely to be affected than older multiparous women (10), as are women with multiple gestations (11). The higher sensibility of the vestibular system to the movements, the changes in the taste and olfactory sensibility and the psychological aspects are factors to consider in the study of nausea and vomiting during pregnancy (8).

Studies about epidemiology and risk factors of NVP have generally included small number of affected women, have analyzed usually the first/second trimester, but not until the end of pregnancy, there are not able to identify clearly the predictor factors of persistence and the clinical course of symptoms. For this reason, we conducted a prospective study in a cohort of pregnant women to estimate

the prevalence of NVP in each trimester of pregnancy and evaluate the existence of possible factors of their presence and evolution.

MATERIAL(S) AND METHOD(S)

We have conducted a prospective longitudinal study of upper gastrointestinal symptoms in a cohort of consecutive pregnant women since 2009 to 2011. They were recruited at the Hospital Clínico San Carlos, Madrid, Spain; an academic center which provides assistance to a population around 250,000 people, of which 9.4 % are immigrants from Latin America (12). This study was approved by the local ethics institutional board.

The study population included pregnant women with gestational age less than 12 weeks of pregnancy (estimated by the last menstrual period). The recruitment was performed coinciding with the first obstetric check. The inclusion criteria were: Healthy women aged between 18 and 45 years old, with singleton pregnancies, no pregnancies in the preceding last year, no history of gastro-esophageal surgery, prior esophageal dilation or gastrointestinal disorders, telephone at home, Spanish as a maternal language, and sign the informed consent. Patients with gastrointestinal disorders, detected in the anamnesis at first contact or during the pregnancy, were excluded from the study. Women with twin pregnancy, from non-Spanish spoken countries, that did not perform all interviews and had a severe medical disease diagnosed during the pregnancy, were excluded from the study.

Methodology has been described in detailed previously (13,14). Briefly, upon their acceptance to participate, they were contacted by phone and interviewed by experienced professional interviewers. Data were collected using the Gastro-Esophageal Reflux Questionnaire (“GERQ”) (15) validated and adapted for telephone use in the Spanish population. The validation of the questionnaire was performed in 40 pregnant women. The questionnaire includes questions about the presence and frequency of upper gastrointestinal symptoms and a measure of psychological distress. Phone calls and interviews were done at the end of each trimester of pregnancy (week 12 ± 1 , week 24 ± 1 and week 36 ± 1). In the first trimester of pregnancy, “GERQ” was administered twice: the first with questions referred to the year before pregnancy, and the second to the first weeks of the current pregnancy.

Severity of NVP were classified as mild (less than once a week), moderate (more than once a week, but not daily) and severe (daily symptoms). In the statistical analysis, only moderate-severe NVP was considered.

The pregnant women with NVP were treated as the Spanish Society of Gynecology and Obstetrics (SEGO) guidelines suggest (16). In general, it was recommended an adequate dietary regimen with vitamin supplements, and use of oral antiemetic drugs as doxilamine and met-

rocloramide if was necessary. Antacid and antisecretive therapy was prescribed if necessary. In case of persistent of NVP, beside the previous management, a psychological counselling was added. In case of incoercible vomiting with ketonuria, the pregnant was hospitalized and was treated with intravenous fluid, reposition of electrolytes and endovenous antiemetic drugs. The gastroenterologists attended to the pregnant when a severe NVP or hyperemesis was present. The other cases were managed by the obstetricians.

The main variable was the presence of nausea or vomiting in each trimester of the pregnancy. The variables studied as factors potentially associated with NVP were: a) Socio-demographic factors (age, ethnicity/origin, marital status, employment status and educational level); b) biological characteristics such as self-reported weight and height, and self-reported weight gain in each trimester; c) psychological distress at the beginning of the study (psychosomatic symptoms score-PSS-); and d) tobacco and alcohol consumption.

Statistical analysis

The prevalence of NVP for each trimester of pregnancy was calculated. Chi-squared test or the Fisher’s exact test in case of small cell comparisons was used to compare the differences between prevalence in each trimester. A logistic regression analysis for each trimester was performed to find the factors associated with the presence of NVP. Association is reported as adjusted odds ratio (OR) with its 95 % confidence interval (CI). “GERQ” validation was made in 30 cases using kappa coefficient. All statistical tests were two-sided and statistical significance was defined as p value less than 0.05. All computations were performed using IBM SPSS Statistic software version 19.

RESULTS

We invited 447 pregnant women to participate, and 365 were finally included. Only 263 women (72.05 %) completed all interviews. The figure 1 displays a flow-chart of subjects and reasons for withdrawal. There were no significant differences between those completing and not completing all interviews regarding age, origin, number of previous pregnancies, marital status, working situation, educative level, BMI and PSS. “GERQ” validation was made in consecutively 30 pregnant (kappa coefficient > 0.45 in all questions, $p < 0.001$). Demographic features of series are shown in table I.

The prevalence of NVP in each trimester is shown in table II. The prevalence of nausea was 63.5 % in the first trimester, 33.8 % in the second and 26.2 % in the third. For vomiting, the prevalence was 29.3 % in the first trimester, 22.1 % in the second and 14.4 % in the third. Moderate

and severe NVP were significantly decreasing along the pregnancy ($p < 0.001$).

One hundred twenty (45.6 %) women completed their obstetric follow-up until delivery at our center. Eight women (6.7 %) required at least one hospitalization before delivery and only one case was due to hyperemesis gravidarum (a woman of 14 weeks with incoercible vomiting, ketonuria, electrolyte imbalances and need for intravenous fluids), representing a prevalence of 0.8 %.

In the first trimester of pregnancy, nausea were directly associated with Latin-American origin (OR: 3.60, 95 %CI 1.61-80.5; $p = 0.002$) and inversely with education level and weight gain. Vomiting in the first trimester were directly associated with Latin-American origin (OR: 13.80, 95 %CI: 1.82-104.4; $p = 0.011$) and inversely with weight gain (OR: 0.58, 95 %CI: 0.35-0.97; $p = 0.039$) (Table III).

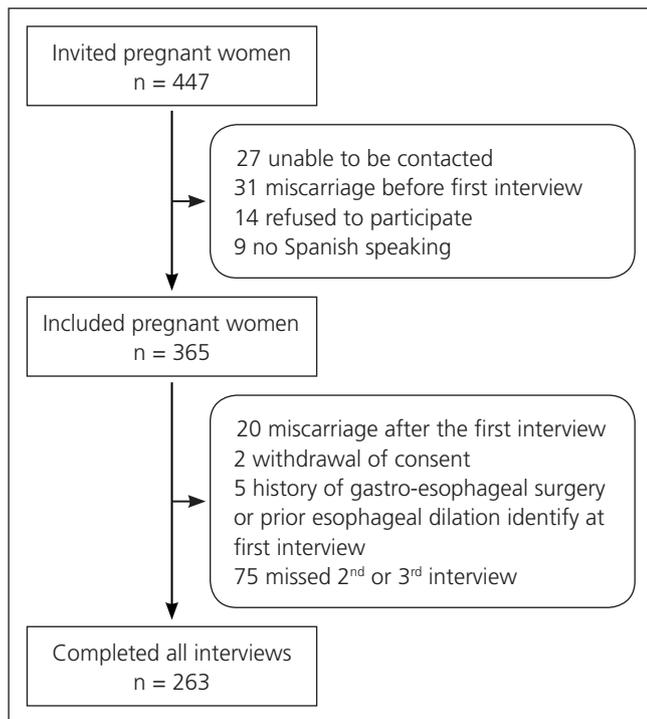


Fig. 1.

In the second trimester, nausea was associated with a higher psychosomatic symptom score, (OR: 1.04, 95 %CI: 1.00-1.07, $p = 0.026$), and the reporting of nausea in the first trimester (OR: 5.85, 95 %CI: 2.63-12.98; $p < 0.001$). The unique factor associated with vomiting was the report-

Table I. Series description

	Median (standard deviation) / Number (%)	Range
Age (years)	30.5 (4.7)	18-42
<i>Origin</i>		
Spain	189 (71.9)	
Latin-American	74 (28.1)	
<i>Previous gestations</i>		
No	126 (47.9)	
Yes	137 (52.1)	
No. previous gestations	1.4 (0.7)	1-4
No. abortions	0.5 (0.7)	0-4
No. vaginal deliveries	0.7 (0.6)	0-3
No. cesarean	0.2 (0.4)	0-2
<i>Marital status</i>		
Married/stable partner	251 (95.4)	
Single	12 (4.6)	
<i>Education</i>		
Basic	59 (22.4)	
Medium	115 (43.7)	
High	89 (33.8)	
<i>Employment situation</i>		
Working	203 (77.2)	
Unemployed	32 (12.2)	
Housewife	26 (9.9)	
Student	2 (0.8)	
<i>Body mass index (kg/m²)</i>	23.3 (3.5)	15.8-36.5
<i>Tobacco</i>		
No	170 (64.4)	
Current	82 (31.2)	
Past user	11 (4.2)	
<i>Alcohol intake (glass per week)</i>		
Nondrinker	142 (54.0)	
1 to 6 glass	110 (41.8)	
7 or more glass	11 (4.2)	

Table II. Prevalence of nausea and vomiting according to severity of symptom

<i>n</i> = 263	<i>Nausea</i>				<i>Vomiting</i>			
	<i>No n (%)</i>	<i>Mild n (%)</i>	<i>Moderate* n (%)</i>	<i>Daily* n (%)</i>	<i>No n (%)</i>	<i>Mild* n (%)</i>	<i>Moderate* n (%)</i>	<i>Daily* n (%)</i>
1 st trimester	59 (22.4)	37 (14.1)	79 (30.0)	88 (33.5)	120 (45.6)	66 (25,1)	52 (19,8)	25 (9,5)
2 nd trimester	110 (41.8)	64 (24.3)	65 (24.7)	24(9.1)	148 (56.3)	57 (21,7)	43 (16,3)	15 (5,7)
3 rd trimester	135 (51.3)	59 (22.4)	48 (18.3)	21 (8.0)	176 (66.9)	50 (19,0)	26 (9,9)	11 (4,2)

Mild: Less than once a week; Moderate: At least once a week, but not daily; Severe: Daily. *Chi-square for linear trend along the pregnancy compared with absence of symptoms, $p < 0.001$.

Table III. Socio-demographic variables related with nausea and vomiting in the first trimester

	Nausea		Vomiting	
	OR (95%CI)	p	OR (95%CI)	p
Age (per year)	0.93 (0.87-1.01)	0.106	1.20 (0.96-1.51)	0.108
<i>Latin-American origin</i>		0.002		0.011
Yes	3.60 (1.61-80.5)		13.80 (1.82-104.4)	
No	1		1	
<i>Previous gestations</i>		0.468		0.066
Yes	1.28 (0.65-2.51)		0.18 (0.03-1.12)	
No	1		1	
<i>Marital status</i>		0.318	NC	-
Married/stable partner	1			
Single	0.45 (0.09-2.17)			
<i>Education</i>				
Basic	1		1	
Medium	0.31 (0.13-0.73)	0.007	4.03 (0.39-41.15)	0.239
High	0.56 (0.21-1.49)	0.249	1.26 (0.12-13.71)	0.848
<i>Employment situation</i>				
Working	1		1	
Unemployed	1.19 (0.45-3.10)	0.605	9.54 (0.44-206.5)	0.150
Housewife	0.77 (0.27-6.17)	0.627	NC	-
Student	0.15 (0.01-3.40)	0.233	NC	-
<i>Baseline BMI (per unit kg/m²)</i>	0.97 (0.89-1.06)	0.504	1.01 (0.79-1.28)	0.925
<i>Weight gain (per kg)</i>	0.87 (0.76-1.00)	0.054	0.58 (0.35-0.97)	0.039
<i>Psychosomatic symptoms (per score unit)</i>	1.01 (0.98-1.05)	0.391	1.01 (0.934-1.08)	0.855
<i>Tobacco</i>				
No	1		1	
Current	0.67 (0.29-1.51)	0.335	0.49 (0.06-4.04)	0.513
Past user	0.86 (0.38-1.98)	0.732	0.42 (0.05-3.49)	0.422
<i>Alcohol (per glass a week)</i>	NC	-	NC	-
<i>Nausea previous to pregnancy</i>		0.196		0.165
Yes	5.15 (0.43-61.65)		34.56 (0.23-5148.4)	
No	1		1	

NC: Not calculable because of small sample.

ing of vomiting in the first trimester (OR: 16.74, 95 %CI 1.78-157.50; $p = 0.013$) (Table IV).

In the third trimester, the unique factor associated to nausea was the presence of the symptom in the preceding trimester (OR: 5.61; 95 %CI: 2.78-11.30; $p < 0.001$). There were no data respects to vomiting in this trimester due to a small sample (only 37 cases) (Table V).

DISCUSSION

This study provide the prevalence of NVP in a prospectively cohort of pregnant women until late pregnancy. The statistical power to detect differences in NVP between first and second trimester was 100 %, and 52 % between second and third trimester. Previous estimations of the prevalence

of NVP have mainly focused on the first trimester (17-21). Our data confirms that NVP are common complaints during the first trimester, and their prevalence decreases along of pregnancy. The prevalence of NVP in the first trimester were 63 % and 29 % respectively, in agreement with others studies reported in the international literature (22), and in Spanish population (19,20). A recent review has suggested that NVP usually disappear in the second trimester, but may continue until the third trimester in 15 to 20 % (5). These findings have been observed in two Spanish series (19,20), which showed an increase of vomiting in the third trimester after its reduction in the second trimester. Contrarily, our data suggest that presence and severity of NVP declines regularly along the pregnancy. This disagreement between the studies may be explained by two methodological differences. First, the longitudinal nature of our study

Table IV. Socio-demographic variables related with nausea and vomiting in the second trimester

	<i>Nausea</i>		<i>Vomiting</i>	
	<i>OR (95%CI)</i>	<i>p</i>	<i>OR (95%CI)</i>	<i>p</i>
Age (per year)	1.01 (0.93-1.10)	0.782	0.89 (0.63-1.25)	0.491
Latin-American origin		0.306		0.490
Yes	1.46 (0.71-3.00)		2.74 (0.56-48.40)	
No	1		1	
Previous gestations		0.166		0.506
Yes	1.68 (0.81-3.49)		2.39 (0.18-31.27)	
No	1		1	
Marital status		0.318	NC	-
Married/stable partner	1			
Single	0.52 (0.10-2.70)			
Education				
Basic	1		1	
Medium	0.59 (0.24-1.45)	0.250	8.49 (0.47-152.40)	0.147
High	0.84 (0.31-2.25)	0.727	1.34 (0.10-17.39)	0.823
Employment situation				
Working	1		1	
Unemployed	0.45 (0.14-1.43)	0.176	0.41 (0.02-7.11)	0.544
Housewife	0.84 (0.28-2.54)	0.760	NC	-
Student	NC	-	NC	-
Baseline BMI (per unit kg/m ²)	1.02 (0.92-1.12)	0.692	1.09 (0.84-1.42)	0.496
Weight gain (per kg)	0.97 (0.88-1.07)	0.568	0.76 (0.52-1.09)	0.677
Psychosomatic symptoms (per score unit)	1.04 (1.00-1.07)	0.026	1.01(0.934-1.08)	0.855
<i>Tobacco</i>				
No	1		1	
Current	1.19 (0.42-2.90)	0.833	0.36 (0.02-7.67)	0.512
Past user	7.58 (0.69-83.17)	0.097	NC	-
Alcohol (per glass a week)	0.23 (0.02-2.48)	0.226	NC	-
Nausea previous to pregnancy		0.558		0.383
Yes	1.59 (0.33-7.59)		9.25 (0.06-1366.1)	
No	1		1	
First trimester nausea		< 0.001		0.013
Yes	5.85 (2.63-12.98)		16.74 (1.78-157.50)	
No	1		1	

NC: Not calculable because of small sample.

avoids any referral bias; secondly, we previously validated a questionnaire which is able to discriminate clearly between gastroesophageal reflux symptoms and nausea/vomiting. In fact, we have previously reported the dynamic of gastroesophageal reflux symptoms (GERS) in this cohort, showing that incidence of GERS is similar across the three trimesters of pregnancy (13). Uterus at the end of the pregnancy might compress and displace the fundus and increase of intra-abdominal pressure promoting GERS (5). Clinical relevance of differentiating GERS from NVP is critical since treatment is completely different. We have not applied any of the current classifications (PUQUE/Rhode's score) (23,24), because they only refer to the symptoms in the 12 hours

preceding the interview, and is not suitable for evaluation of the pregnant woman in each trimester.

Our results have found an association of NVP with Latin-American origin, although only in the first trimester. In agreement with our findings, a recent prospective study of 2,470 pregnant women observed a higher risk for having nausea or vomiting in the first trimester in non-Hispanic Black (RR = 4.3, 95 %CI: 1.6-11.6) and Hispanic origin (RR = 2.3, 95 %CI: 0.4-11.5) compared with Caucasian (25). These differences may be explained because Latin-American women living in Spain usually get pregnant younger and have a lower socio-economic and educational level than native Spanish women.

Table V. Socio-demographic variables related with nauseas in the third trimester

	OR (95%CI)	p
<i>Age (per year)</i>	1.01 (0.93-1.11)	0.749
<i>Latin-American origin</i>		0.541
Yes	1.27 (0.59-2.75)	
No	1	
<i>Previous gestations</i>		0.513
Yes	1.29 (0.60-2.79)	
No	1	
<i>Marital status</i>		0.979
Married/stable partner	1	
Single	1.03 (0.15-6.96)	
<i>Education</i>		
Basic	1	
Medium	1.61 (0.64-4.03)	0.307
High	1.09 (0.40-3.01)	0.858
<i>Employment situation</i>		
Working	1	
Unemployed	0.89 (0.31-2.57)	0.829
Housewife	0.38 (0.10-21.45)	0.157
Student	NC	-
Baseline BMI (per unit kg/m ²)	1.07 (0.97-1.17)	0.171
Weight gain (per kg)	0.94 (0.86-1.03)	0.166
Psychosomatic symptoms (per score unit)	0.97 (0.94-1.01)	0.161
<i>Tobacco</i>		
No	NC	
Current	NC	-
Past user	NC	-
<i>Alcohol (per glass a week)</i>	1.44 (0.18-11.68)	0.731
<i>Nausea previous to pregnancy</i>		0.408
Yes	1.90 (0.41-8.74)	
No	1	
<i>First trimester nauseas</i>		0.087
Yes	2.03 (0.90-4.61)	
No	1	
<i>Second trimester nauseas</i>		< 0.001
Yes	5.61 (2.78-11.30)	
No	1	

NC: Not calculable because of small sample.

The gain weight along the pregnancy was inversely related to NVP. However, this affirmation should be interpreted with caution, as it was more likely to be due to the effect of NVP on appetite and food intake, resulting in weight loss (or less increase) and in nutrient deficiency, which can produce more symptoms (26). We found no statistically significant results between baseline BMI and NVP during pregnancy as it was previously published by Ben-Aroya et al. (27). Authors found that patients with more frequent NVP (2 or more vomiting episodes per day)

during the first trimester of pregnancy had lower BMI at baseline than the group of pregnant women with lower frequency (0-1 vomiting episodes per day). The differences with our series may reside in the Jewish ethnicity of their sample and the inclusion of patients that presented any gynecological emergency or clinic during the first trimester of pregnancy, and not previously healthy pregnant as ours.

Psychological factors may be relevant in the presence and persistence of NVP. In our series, women with high psychosomatic score had increased the risk of having nauseas. This is in agreement with previous studies reporting that some psychological factors, as somatization or conversion disorders, and stress have been correlated with NVP (28-30). Moreover, they suggested that the psychological response to persistent NVP may exacerbate the symptomatology.

The main factor to predict the maintenance of NVP in the second and third trimester was reporting these symptoms during the previous trimester. This is the first study in describing a cause of maintenance of nauseas and vomiting. Women with NVP have a tendency to prolong the symptoms until late in pregnancy, probably because there are an intrinsic predisposition in these pregnant to maintain the nauseas and vomiting in the next trimester.

In our series, the previous gestation had a slight protective effect on the risk of having vomiting during the first trimester. Contrarily, other series has found these symptoms more commonly in multigravidae, which were more likely to suffer them beyond the first trimester with each additional pregnancy (24). Consumption of tobacco or alcohol were no associated with nauseas and vomiting in our study. However, some series have found that women who consumed alcohol and tobacco prior to conception, were at decreased risk for NVP (31,32).

We observed a unique case of hyperemesis gravidarum, so we could not perform any analysis about this disorder. A recent study found no association between hyperemesis gravidarum and age, parity, number of artificial pregnancy, and smoking. In addition, no statistical association were found between the rates of small for gestational age birth, preterm birth, gestational diabetes, pregnancy-induced hypertension, cesarean section rate and adverse fetal outcome and hyperemesis gravidarum (6).

The gastroenterologist has an important role in the management of the pregnant woman with hyperemesis and severe NVP. In the other situations, the management by the obstetrician is enough. Pregnant women must be orient to the gastroenterologist when the obstetrician suspects a secondary gastro-esophageal disease that cause the NVP, or when the NVP are not well managed using the standard therapies. In addition, due to the high prevalence of nauseas found in this study, we suggest discard a pregnancy when a diagnosis of nauseas in a young women without a clear etiology is done, independently that it is performed by either general practitioners, gastroenterologists or gynecologists.

The telephonic interview can present some bias because of some data, such as the tall, weight, tobacco and alcohol consumptions, etc., frequently are altered or underestimated by the interviewed. To minimize the possible bias we used a validated questionnaire to telephone interviews in Spanish population.

In conclusion, our longitudinal study confirms that nausea and vomiting are frequent in the first trimester of pregnancy and tends to decrease along the pregnancy without disappearing completely. Our data emphasize the importance of race for these symptoms and suggest that have an impact on weight gaining. Although NVP are somewhat unpredictable, psychological distress seems to play a role in their persistence.

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