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SYSTEMATIC REVIEW

Nausea and vomiting in pregnancy: A Systematic Review of socio-demographic risk factors.

Short title: Socio-demographic risk factors for NVP.

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Abstract

Objective: Nausea and vomiting in pregnancy are two of the most prevalent symptoms and may have an unfavorable effect on a pregnant's daily life. The aim of this systematic review was to identify studies which assessed the risk of socio-demographic factors for nausea and vomiting in pregnancy.

Materials and Methods: This study was conducted according to the PRISMA guidelines and the PubMed, Scopus, and Google Scholar databases were reviewed. The Newcastle-Ottawa Scale (NOS) for non-randomized studies for the assessment of the studies' quality was used. The socio-demographic risk factors reviewed were age, educational level, income, employment, marital status, alcohol intake and smoking.

Results: Finally, 718 articles were found, of which 13 matched the eligibility criteria. The studies' sample sizes varied from 116 to 81.486 participants. The findings showed that results are conflicting for the majority of the risk variables studied. The majority of the studies did not identified age, educational level and alcohol consumption as risk factors for nausea and vomiting in

pregnancy. The relationship between income, employment and marital status, smoking and nausea and vomiting in pregnancy remains ambiguous because of the existence of conflicting conclusions.

Conclusion: The emergence of nausea and vomiting in pregnancy is influenced by socio-demographic variables. Obstetric health care providers should be conscious of several socio-demographic characteristics which may act as risk factors for the occurrence of nausea and vomiting in pregnancy and they should use a holistic and sensitive approach to identify pregnant women who might have greater risks to experience these symptoms.

Keywords: socio-demographic; nausea; pregnancy; risk factors; vomiting.

Introduction

During pregnancy, nausea and vomiting (NVP) are two of the most prevalent symptoms, affecting 35-91% of pregnancies [1]. While, according to a recent systematic review, these percentages ranges to 50–90% of all pregnant women [2]. Previous studies have also reported that the prevalence rate for nausea is 50–80% and for vomiting and retching is 50% [3]. NVP frequently starts at the beginning of the first trimester (6-8 weeks) and usually diminishes at 16-20 weeks of gestation [4]. The most severe form of NVP, hyperemesis gravidarum, looks to be on the far side of the spectrum of NVP [5,6] and affects about 0.3–3% of pregnancies [3]. Hyperemesis gravidarum is the most prevalent reason for hospitalization in the first trimester of pregnancy [6,7] because of a severe weight loss and dehydration [6,8].

The cause of NVP is uncertain and inadequately comprehended. Several hypotheses have been suggested and it is considered to involve a number of factors such as a hormonal stimulus, evolutionary adaptation, and psychological predisposition [2,6,9,10]. According to a study, the levels of human chorionic gonadotropin and estrogen are responsible since they coincide with the peak of symptoms of nausea and vomiting [11,12]. The severity of NVP is linked to a worse quality of life and negative consequences on numerous aspects of daily life, social and professional functioning [13,14,15] as well as to birth outcomes [11,16]. Because of its frequency, it is possible to be underestimated by obstetric care providers, and to that may contribute a woman’s perception of the severity of her symptoms. Early detection and treatment of NVP may contribute to the avoidance of the development of hyperemesis gravidarum [6] and of more serious problems, such as hospitalization [6,17].

Although the cause of NVP is doubtful, risk factors for it have aroused the research interest of the scientific community. Definite answers are still being sought around the question of whether socio-demographic characteristics can act as risk factors for NVP and furthermore which of them can actually be considered as risk factors for the occurrence of it. The recognizing and studying NVP's socio-demographic risk factors can be an effective step in the identification of women at risk. Moreover, adequate knowledge of the socio-demographic risk factors for NVP is essential for the planning of effective strategies focusing on supporting these pregnants. Therefore, the present study aimed to systematically review and identify studies which assessed the risk of socio-demographic factors for NVP.

Methods

The PRISMA statement's (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines were followed in conducting this systematic review [18].

Eligibility criteria

Only cohorts and case controls, peer-reviewed, in English-language published studies between the years 2000 and 2020 were considered, with no limitations on geographic area. We considered studies that described or reported any diagnostic criteria for NVP and with samples not having hyperemesis gravidarum. The primary or one of the outcomes of the studies had to be the assessment of risk socio-demographic factors for NVP (i.e. age, education level, income, employment and marital status, alcohol intake and smoking). Studies were excluded if they were unrelated to the study's goal and if they were not cohorts or case controls studies.

Search strategy

Studies were identified by searching in PubMed, Scopus, and Google Scholar databases, and this search has been completed in December 2021. Searched terms and filters were used for each database. Table 1 summarizes the databases search strategy.

Study selection

The titles and abstracts of possibly relevant studies were separately assessed by the two researchers (VP, DA) according to eligibility and exclusion criteria. The full texts of selected studies were retrieved for additional assessment. Consensus was used to resolve disagreements among reviewers.

Data extraction

The two authors (VP and DA) worked individually to extract data from relevant studies using a pre-made piloted extraction template. Each study's data extraction was comprised: first author, year of publication, location of study, type of study, sample size and results given in terms of frequencies percent, OR (unadjusted or adjusted), 95% CIs and p values when accessible.

Quality assessment

The authors (VP and DA) assessed the quality of the included articles by using Newcastle Ottawa Scale (NOS) for non randomized studies [19]. The NOS checklist evaluates studies in three areas based on their quality: selection of the study groups; comparability of the groups; and ascertainment of either the exposure or outcome of interest for case-control or cohort studies, respectively. The NOS "star system" has a minimum score of 0 and a maximum score of 9. We gave the studies a star rating based on their quality; low ratings imply low quality and a significant risk of bias. Studies with a score of less than six stars were deemed low-quality, those with a score of six to seven stars were deemed moderate-quality, and those with a score of seven stars or more were deemed high-quality.

Results

A systematic search resulted in the identification of 718 studies. After removing duplicates (n=127), the remaining 591 studies were screened. After exclusions with reasons (i.e. title, abstract, full-text, review articles, and not English-language papers), 13 full-text studies remained to be assessed and all of them were included in this systematic review. The Prisma flow diagram of the selection process is shown in Fig. 1.

Characteristics of the Studies

Twelve studies had a cohort design and one study had a case control design. The included studies were published between 2000 and 2020. Six studies were conducted in the USA, two in Canada, one in Germany, one in Sweden, one in Nepal, one in Finland and one in Korea. The sample size of the studies ranged between 116 and 81.486 participants. Six studies were of moderate quality

and seven studies were of low quality. Table 2 shows the main features and characteristics of the included studies.

Age

The connection between age and NVP was studied in twelve studies [20-31]. The majority of the studies (7/12) did not identified age as a risk factor for NVP [20,24,25,26,29,30,31]. Younger women were more likely to experience NVP in the studies of Louik et al. [23], Naumann et al. [27], and Temming et al. [28]. These findings are in agreement with Kallen's findings which showed that the major increase in risk occurred in women aged younger than 25 years [21]. Lindseth &Vari found that women who experienced NVP were older than those without NVP. However, the mean age of their sample was 26.3 years [22].

Income

Two studies examined the association between income and NVP with contradicting results. Louik et al. reported in their study that the incidence of NVP did not differ noticeably between groups [23]. In contrast, Lacasse et al. found that women having a lower family income (<40000 cdn$/y) were more likely to have NVP in the first trimester of pregnancy than women with higher household income (between 40000 and 79999 cdn$/y) [25].

Education

Seven studies investigated the link between educational level and NVP [20,22,23,25,26,29,31] . The level of education has not been found to be a risk factor for NVP in the studies of Lindseth &Vari [22], Louik et al. [23], Lacasse et al. [25], Chan et al. [26], Choi et al. [29], and Regodón et al. [31]. Louik et al. mentioned that though there was a statistically significant increase in risk among women having higher educational level, the difference was not considerable and they did not verify relationships between overall occurrence of NVP and low educational level [23]. In addition, Regodón et al. [31] reported that when comparing women with symptoms vs. without symptoms in the third trimester, specifically, they observed a statistically significant lower proportion of literate women in the symptomatic group. However, generally, there were no significant variations in the percentages of the categories [31]. Nevertheless, the findings of the study of Weigel et al. do not support the previous results. In their study nausea and vomiting were more common in women who had fewer than six years of formal schooling [20].

Employment status

The relationship between employment status and NVP was studied in seven studies [20,21,23,25,29,30,32]. No association between employment status and NVP was found in the studies of Louik et al. [23], Lacasse et al. [25], and Choi et al. [29]. These results match those observed in the study of Ellilä et al. in which working status was not associated with the severity of NVP [30]. As opposed to the above findings are those of Kallen et al. who found that women who worked outside the home had a lower risk for NVP than housewives/women on maternity leave or who were not working [21]. Similarly, Kramer et al. stated that women who were unemployed were twice as likely to report moderate and severe NVP in the first/early second trimester of pregnancy [32]. Interestingly, Weigel et al. demonstrated that vomiting but not nausea was more frequent in women who were employees earning higher salaries in average doing highly skilled work (white collar or professionals) [20].

Marital status

Overall seven studies looked into the relationship between marital status and NVP. Two of the studies did not find any association between of them [26,29] and one study found that marital status was not associated with the severity of NVP [30]. Oppositely, Markl et al. observed that being single raised the risk of NVP, compared to women who lived with a partner [24]. Likewise,

women reporting NVP were more likely to be unmarried in the study of Temming et al. [28]. In addition, Lacasse et al. stated that women living alone were more likely to have NVP in the first trimester of pregnancy, but there was not a statistical significance [25]. Also, informal marriage retained its positive association with NVP according to the study of Weigel et al. [20].

Alcohol intake

Alcohol consumption as a possible risk factor for NVP, was examined by five studies. The majority of the studies (3/5) did not find any association between alcohol and NVP [25,26,27]. In the study of Choi et al. alcohol consumption was associated with decreased odds of NVP [29]. However, Lindseth & Vari demonstrated that women who experienced late NVP were found to have significantly more alcohol intakes during their pregnancy [22].

Smoking

On the whole ten studies examined the association between smoking and NVP. Three of them did not find any association between smoking and NVP [22,29,31] and in another one smoking was not associated with the severity of NVP [30]. Four studies [21,23,24,32] suggested that smokers were less likely to experience NVP than non smokers. These findings are consistent with those of Lacasse et al. who found that smokers during the first trimester were less likely to have NVP, but with no statistical significance [25]. In contrary to the above results Temming et al. found that women reporting NVP were more likely to smoke [28].

Discussion

The purpose of this systematic review was to compile the evidence from observational studies and synthesize it regarding the socio-demographic risk factors of NVP. The current systematic review's results indicate that existing findings are contradictory for the most of the risk factors examined.

The results of the most studies have failed to identify the age as a risk factor for the occurrence of NVP. However, studies have shown that younger women are more likely to experience NVP. The existence of conflicting findings makes it difficult to reach an absolute conclusion. It is not easy to explain why younger ages were associated with NVP, but perhaps we can assume that younger women cope with pregnancy in a more stressful way. According to the literature, the hormones involved in the stress response (e.g. cortisol) are positively related to the severity of nausea [33].

The findings of the current study cannot establish the generalizability of the association between income and symptoms of NVP, due to the fact that only two studies examined the above mentioned association, and furthermore, they used different definitions of household income categories (i.e. cdn$/yr and $/year). A comparative interpretation would be easier and clearer if the number of the studies were more extended and the currency was the same. The educational level did not found to be a risk factor for NVP in the majority of the studies. Any possible pathway leading to a positive association remains unclear. It is apparent from the above results that there are contradicting findings relatively the association between employment status and NVP. Although not all studies have shown that unemployment can be a risk factor for NVP, the fact that it was found to be positively related in some of them cannot be ignored. It is not easy to interpret the significance of this association without knowing how many women were unable to work as a result of the NVP or this was of their own choice. This finding suggests that psychological variables may be important as well. The link between better health and consistent, high-quality work is well documented [34,35]. It is not entirely definite whether marital status is a risk factor for NVP since there are findings that contradict each other. Single pregnant women may be more likely to experience nausea and vomiting, perhaps due to the existence of low social support or due to a stressful status affecting their health status [36]. For some pregnants the absence of a partner may reflect financial and emotional insecurity which in turn it is possible to make them more fragile

and vulnerable. Conflicting results exist regarding the link between alcohol consumption and NVP, thus making it difficult to determine whether alcohol is indeed a risk factor for NVP or not. Although the majority of the studies did not find any association between alcohol and NVP, there are studies with conflicting results. In one study alcohol use was linked with a lower risk of NVP [29], and in another one woman who was shown late NVP was found to use considerably higher alcohol amounts during her pregnancy [22]. Some authors have considered that alcohol consumers women compared to those of no consumers would be nausea or vomiting tolerant [29]. Another possible explanation for this is that alcohol intake lowers the hormone levels of estradiol and of human chorionic gonadotropin, which in turn lower the risk of developing NVP [37]. Unknown factors may lead to the above inconsistency between the studies of Lindseth & Vari [22] and Choi et al. [29]. The existence of inconsistencies among studies' results regarding whether or not smoking is a risk factor for NVP, makes it complicated to find the answer. Interestingly, there are studies which demonstrated that smokers were less likely to experience NVP than non smokers [21,23,24,32]. These data support the protective effect of smoking against NVP and not that smoking may be a risk factor for NVP. Authors of previous studies have pointed out their suggestions on the subject. Kallen et al. hypothesized that "If NVP is an expression of a well-functioning placenta, the negative association with smoking may be because of a negative effect of maternal smoking on early placenta development" [21]. Also, the sense of odor [38] and taste [39] have been associated with increases in NVP and these senses may be decreased as a result of maternal smoking [32]. A variety of negative pregnancy outcomes have been associated with smoking during pregnancy, including placental abruption, miscarriage, stillbirth and preterm birth [40,41,42]. Health care professionals, and especially midwives, should encourage and support smoking cessation among all smoker pregnant women.

Interpretations regarding the presence of conflict findings might be described in part. The main reason can be considered to be the lack of homogeneity among the studies. Differences in methodological designs or the use of different NVP measures may have led to dissimilar conclusions. Furthermore, the samples' features and the confounding variables taken into account in the statistical analysis are also factors to consider.

One of the study's strengths is that it has been followed known recommendations (PRISMA) for systematic reviews of this type. In addition, it was used a reliable checklist for the assessment of the studies' quality. The present systematic review considered seven risk factors and the two reviewers worked separately based on predetermined criteria. The current review is limited by the lack of information in non-English papers and therefore some information might be missing. Another source of weakness that could have affected the findings is that solely three databases were used for the literature search.

Summarizing, the present review doubtless provides proof that socio-demographic factors do play a role in the emergence of NVP. The majority of the studies did not identified age, level of education and alcohol consumption as a risk factor for NVP. The association between income, employment and marital status, smoking and NVP remains obscure since there are contradicting findings.

Conclusion

Nausea and vomiting in early pregnancy are common symptoms well-known to health care practitioners. Obstetricians, midwives and other health care providers should be conscious of several socio-demographic characteristics may act as risk factors for the occurrence of NVP. Therefore they should be informed and up to date on the subject. Since there are conflicting research results more studies are needed. Future research will likely be able to bring to light

answers by minimizing the divergences that already exist about socio-demographic risk factors for NVP. Furthermore, the findings of future research will add to the growing body of evidence indicating specific socio-demographic traits are indeed risk factors for NVP. More study data is needed by the scientific community in order to create supportive techniques for pregnant women who are more likely to experience NVP. Until further understanding and verification through scientific data on which socio-demographic factors and to what extent they are indeed risk factors for NVP, health professionals should use a holistic and sensitive approach to identify pregnant women who may have greater probabilities to experience these symptoms.

Compliance with Ethical Standards

Authors contribution:

PV: Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Project administration, Writing – original draft.

AD**:** Data curation, Formal Analysis, Investigation, Methodology, Project administration, Supervision,Writing – review & editing.

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Table 1: Databases search strategy

Pubmed	(nausea) AND (vomiting)) AND (pregnancy)) AND (risk factors)	Humans English Female Adult:19+years From: 2000-2020
Scopus	nausea AND vomiting AND pregnancy AND risk AND factors	From: 2000-2020 English Publication STAGE : final
Google Scholar	nausea AND vomiting AND pregnancy AND risk factors	2000-2020

Table 2: Characteristics of the studies included in the systematic review of sociodemographic risk factors for NVP

First Author, (Year), Country	Type of study	Sample size (n)	Main results	NOS Quality score
Weigel et al (2000), USA (20)	Cohort study	n=1000	Age: Maternal age was not associated with the risk for developing NVP. Education: NVP was more common in women who had < 6 years of education Nausea: < 6 years: Adj OR:1.32, 95% CI:1.03-1.60 ≥ 6 years: Adj OR:1 Vomiting: < 6 years: Adj OR:1.47,95% CI:1.20-1.74 ≥ 6 years: Adj OR:1 Employment: Vomiting but not nausea was more frequent in women who were white collars or professionals Vomiting: white collars or professionals : Adj OR: 1.55, 95% CI: 1.15- 1.95. Housewife: Adj OR: 1 Blue collar: AdjOR: 0.86, 95% CI: 0.63- 1.10 Nausea: white collars or professionals : Adj OR: 1.26, 95% CI: 0.85- 1.67. Housewife: Adj OR:1 Blue collar: AdjOR: 0.96, 95% CI: 0.73- 1.21. Marital status: NVP was more common in women who were involved in informal marriages, Nausea: Common law union: Adj OR: 1.31, 95% CI:1.09- 1.53 Single: Adj OR: 1 Legally married: Adj OR: 0.84, 95% CI: 0.62- 1.06. Vomiting: Common law union: Adj OR: 1.36, 95% CI: 1.15-1.57 Single: Adj OR: 1 Legally married: AdjOR: 0.81, 95% CI: 0.59- 1.02.	7 moderate
Kallen et al (2003), Sweden (21)	Cohort study	n= 3675 NVP group: n=2906 No NVP group: n=769	Age: The major increase in risk for NVP has been identified in women aged younger than 25 years. age < 19 : AdjOR: 1.64, 95% CI: 0.68–3.94 age 20–24: Adj OR: 1.34, 95% CI: 1.03–1.75 age 25–29: Adj OR: 1.12, 95% CI:0.94–1.33 age 30–34: Adj OR: 0.92, 95% CI:0.78–1.09 age 35–39: Adj OR: 0.76, 95% CI:0.61–0.95 age 40>:Adj OR: 0.77, 95% CI:0.44–1.33 Employment: Women who worked outside home had a lower risk for NVP than housewives/women on maternity leave or who were unemployed Working outside home: Adj OR: 1.00 Housewife or unemployed: Adj OR: 2.86, 95% CI:1.49–5.46 Other/unknown (students and women who for reasons had leave of absence from work): Adj OR: 2.02, 95% CI:0.79–5.14 Smoking: Smokers before pregnancy had a lower risk for NVP No smoking: Adj OR:1.00 <10 cig./day: Adj OR: 0.78, 95% CI:0.60–1.00 10 +cig./day: Adj OR: 0.70, 95% CI: 0.55–0.88	5 low
Lindseth & Vari	Cohort study	n=116	Age: Women who reported NVP were older (t = 2.4, p =0 .02) than those not experiencing NVP.	4 low

(2005), USA (22)			Education: No difference between the NVP group and the non NVP group (t=0.47, p = ns). Alcohol intake: Women with higher late NVP scores were found to be significantly more severe alcohol users (r=0.26, p=0.04) during their pregnancy. Smoking: no significant difference between the groups.	
Louik et al (2006), USA (23)	Case-control study	NVP group: n=14998 No NVP group: n=7489	Age: There was a strong inverse relationship between age and the risk of NVP. Compared with younger women, the adjusted OR for women 40 or older was lower (Adj OR: 0.47, 95% CI:0.37-0.60). Income: No difference in the incidence of NVP, <10 000$/year: Adj OR: 1.03, 95% CI:0.88-1.21 vs 10 000–45 000$/year: Adj OR: 1.09, 95% CI:1.00-1.20. Employment: No difference in the incidence of NVP, Adj OR: 1.05, 95% CI: 0.98- 1.13. Education: There was a statistically significant elevation in risk among more educated women but the difference was not substantial, 12–15 years : Adj OR:1.09, 95% CI:1.01- 1.17 vs >15 years : Adj OR:1.11, 95% CI:1.03-1.21. Smoking: Women who smoked during pregnancy were significantly less likely to experience NVP than those who discontinued smoking or had never smoked, during pregnancy: Adj OR: 0.80, 95% CI: 0.74-0.86 vs before pregnancy: Adj OR: 1.06, 95% CI:0.98-1.13.	5 low
Markl et al (2008), Germany (24)	Cohort study	n=3624	Age: No association between age and NVP was found, Adj OR: 0.97, 95% CI:0.94–0.99. Marital status: Being single raised the risk of NVP, living with partner: Adj OR: 1.00 living alone: Adj OR: 1.49, 95% CI: 1.24–1.79. Smoking: Smokers were less likely to have NVP than non-smokers, smokers Adj OR: 1 non-smokers Adj OR:2.03, 95% CI: 1.02–4.05.	7 moderate
Lacasse et al (2009), Canada (25)	Cohort study	n = 367 NVP group: n=288 No NVP group: n=79	Age: No association between age and NVP was found, Adj OR:0.95, 95% CI:0.88-1.02 Income: Women with lower household income were more likely to have NVP in the 1st trimester of pregnancy Less than 40000 CDN$/yr: Adj OR: 1 Between 40000 & 79999 CDN$/yr: Adj OR: 0.35, 95% CI: 0.13-0.93. Employment: No association between employment status and NVP was found, Student/ not working: Adj OR: 1 Working: Adj OR: 0.56, 95% CI:0.22-1.42. Education: No association between education level and NVP was found, University completed:Adj OR: 1 University not completed: Adj OR: 0.61, 95% CI: 0.31-1.21. Marital status: Women living alone were more likely to have NVP in the 1st trimester of pregnancy, but with no statistical significance With spouse or with someone (family or cotenant): Adj OR: 1	6 moderate

			Living alone:Adj OR: 1.63, 95% CI:0.15-18.31. Alcohol intake: No association between alcohol and NVP was found, Use of alcohol before pregnancy: Adj OR: 1.13, 95% CI: 0.50-2.54 Use of alcohol during 1st trimester:Adj OR: 0.80, 95% CI:0.28-2.26. Smoking: Smokers during the 1st trimester were less likely to have NVP, but with no statistical significance Smoking before pregnancy: Adj OR: 1.07, 95% CI:0.37-3.05. Smoking during 1st trimester: Adj OR: 0.28, 95% CI: 0.05-1.50.	
Chan et al (2011), USA (26)	Cohort study	NVP group: n=1274 No NVP group: n=279	Age: No association between age groups and NVP was found, Age < 25: Adj OR:1.1, 95% CI:1.0- 1.2 Age 25–29: Adj OR: 1.0 Age 30–34: Adj OR: 1.0, 95% CI:0.9-1.1 Age ≥ 35: Adj OR: 0.8, 95% CI:0.7- 0.9. Education: No association between education years and NVP was found, < 12 years: Adj OR: 1.0, 95% CI:0.9- 1.1 ≥12 to < 16 years: Adj OR: 1.1, 95% CI:1.0-1.2 ≥ 16 years: Adj OR:1.0. Marital status: No association between marital status and NVP was found, Married: Adj OR:1.0 Other: Adj OR:1.0, 95% CI: 0.9-1.0. Alcohol intake: No association between alcohol use and NVP was found, Any: Adj OR: 0.9, 95% CI: 0.7-1.1 None : Adj OR: 1.0	6 moderate
Naumann et al (2012), USA (27)	Cohort study	NVP group: n=2174 No NVP group: n=557	Age: Younger maternal age was found to be an independent risk factor for NVP, age 21–24:Adj OR: 0.72, 95% CI:0.54- 0.97, age 25–29:Adj OR: 0.73, 95% CI:0.54- 0.98, age 30–34:Adj OR:0.69, 95% CI: 0.49-0.98, age 35–39:Adj OR: 0.44, 95% CI:0.27- 0.72, age 40+ : Adj OR: 0.18, 95% CI:0.05- 0.60. Alcohol intake: Any alcohol consumption during the 1st trimester was not significant predictor of NVP (NVP group vs no NVP group, p=0.06).	5 low
Kramer et al (2013), Canada (32)	Cohort study	Early pregnancy: n = 551 Late pregnancy: n = 575	Employment: Not working women were twice as likely to report moderate and severe NVP in the early pregnancy Moderate NVP- not working: Adj OR: 2.16, 95% CI:1.28- 3.65, p= 0.004 Severe NVP- not working: Adj OR: 2.06, 95% CI: 1.08-3.93, p=0 .028. Smoking: NVP was less common or less severe at late pregnancy in women who smoked Moderate NVP-smoking: Adj OR: 0.57, 95% CI: 0.22-1.49, p= 0.252 Severe NVP- smoking: Adj OR: 0.24, 95% CI: 0.11-0.52, p= < 0.001.	5 low
Temming et al (2014), USA (28)	Cohort study	NVP group: n=5207 No NVP group: n=76 279	Age: Women reporting NVP were more likely to be younger NVP group: Mean:26.8, SD: ±5.1 No NVP group: Mean: 28.1, SD: ± 5.0 , p= < 0.001. Marital status: Women reporting NVP were more likely to be single	6 moderate

			Unmarried: NVP group: 25.7% No NVP group: 19.0% OR :1.47, 95% CI: 1.38- 1.57, p=< 0.001. <u>Smoking</u>: Women reporting NVP were more likely to smoke Smoking: NVP group: 3.3% No NVP group: 2.2% OR:1.51, 95% CI: 1.29- 1.78, p=< 0.001.	
Choi et al (2018), Korea (29)	Cohort study	n=472 NVP group: n= 381 No NVP group: n= 91	<u>Age:</u> No significant differences were observed between the study groups <35 age: NVP group: n=225 (59.1%) No NVP group: n= 61 (67.0%) ≥35 age: NVP group: n=156 (40.9%) No NVP group: n= 30 (33.0%), p=0.160. <u>Marital status:</u> No significant differences were observed between the study groups Unmarried: NVP group: n= 4 (1.0%) No NVP group: n= 1 (1.1%), Married: NVP group: n=377 (99.0%) No NVP group: n= 90 (98.9%) p =1.000. <u>Employment:</u> No significant differences were observed between the study groups Unemployed: NVP group: n=156 (40.9%) No NVP group: n= 43 (47.3%) Employed: NVP group: n=225 (59.1%) No NVP group: n= 48 (52.7%), p= 0.270. <u>Education:</u> No significant differences were observed between the study groups Up to high school: NVP group: n= 34 (8.9%) No NVP group: n= 14 (15.4%) College/university or higher: NVP group: n= 347 (91.1%) No NVP group: n= 77 (84.6%), p=0.067. <u>Alcohol intake:</u> Alcohol consumption was associated with decreased odds of NVP No alcohol: Adj OR: 1 Alcohol: Adj OR: 0.36, 95% CI: 0.14–0.93, p = 0.035. <u>Smoking</u>: Smoking was not associated with the NVP No smoking: Adj OR: 1 Smoking: Adj OR: 2.69, 95% CI: 0.26–28.01, p= 0.410.	5 low
Ellilä et al (2018), Finland (30)	Cohort study	n= 2381 moderate NVP: n= 1243	<u>Age:</u> No association between age and NVP was found No NVP:OR:1 Mild NVP: OR:1 , 95% CI: 0.97–1.03 Moderate NVP: OR: 0.99, 95% CI: 0.96–1.02	6 moderate

		mild NVP: n = 700 severe NVP: n = 152 no NVP: n = 286	Severe NVP: OR: 0.97, 95% CI: 0.93–1.01, p= 0.370. Marital status: No association between cohabited or single and NVP was found No NVP:OR:1 Mild NVP: OR: 1.55, 95% CI: 0.70–3.4 Moderate NVP: OR:0.81, 95% CI: 0.41–1.61 Severe NVP: OR: 0.59, 95% CI: 0.24–1.49, p= 0.078. Employment: Working status (working/not working) was not associated with the severity of NVP No NVP:OR:1 Mild NVP: OR:1.19, 95% CI: 0.79–1.78 Moderate NVP: OR: 1.19, 95% CI: 0.81–1.75 Severe NVP: OR: 1.40, 95% CI: 0.80–2.46, p=0.684. Smoking: Smoking was not associated with the severity of NVP No NVP:OR:1 Mild NVP: OR: 0.74, 95% CI: 0.50–1.09 Moderate NVP: OR: 0.74, 95% CI: 0.51–1.06 Severe NVP: OR: 0.79, 95% CI: 0.45–1.39, p=0.387.	
Regodón et al (2020), Nepal (31)	Cohort study	1st trimester: NVP group: n=731 No NVP group: n=475 2nd trimester: NVP group: n=1137 No NVP group: n=2186 3d trimester: NVP group: n=517 No NVP group: n=2884	Age: No association between mean age and NVP was found, NVP group: Mean: 22.5, SD: 4.7 No NVP group: Mean: 22.6, SD: 4.7. Education: Overall it was not observed significant differences between the proportions of groups. Literate: NVP group: n=1027 (59.7%) No NVP group: n= 1076 (61.6%) No education: NVP group :n= 736 (42.8%) No NVP group: n= 738 (42.3%). When comparing women with symptoms vs. without symptoms in the third trimester specifically, it was observed a statistically significant lower proportion of literate women in the symptomatic group (53.8% vs. 62.4%, p= <0.001). Smoking: Overall it was not observed significant differences between the proportions of groups. NVP group: n=70 (3.9%) No NVP group: n=76 (4.2%).	4 low

Fig. 1: PRISMA flow diagram showing the selection process for the studies inclusion