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Full length article

Prolonged hospitalization and readmissions for hyperemesis gravidarum – Associations with personal and family history of nausea

Venla S. Lindström [a,*,5], Linda M. Laitinen [b,c,1], J.Miina A. Nurmi [d,2], Mari A. Koivisto [e,3], Päivi Polo-Kantola [a,4]

[a] Department of Obstetrics and Gynecology, Turku University Hospital and University of Turku, Turku, Finland
[b] Department of Obstetrics and Gynecology, University of Turku, Turku, Finland
[c] The Wellbeing Services County of Central Finland, Department of Obstetrics and Gynecology, Hospital Nova of Central Finland, Jyväskylä, Finland
[d] Department of Public Health, University of Turku, Turku, Finland
[e] Department of Biostatistics, University of Turku, Turku, Finland and Turku University Hospital, Turku, Finland

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ABSTRACT

Objectives: Hyperemesis gravidarum (HG) is characterized by severe nausea and vomiting in pregnancy and often requires hospitalization. Risk factors for severe HG remain poorly investigated. We aimed to identify risk factors for more severe HG, defined by prolonged and recurrent hospitalizations.

Methods: This cross-sectional study included 102 women hospitalized for HG. Data from medical records and questionnaires covered history of motion sickness, nausea related to migraine, and family history of nausea and vomiting in pregnancy (NVP). Women were categorized using three criteria: (1) hospitalization length ($\leq$3 days vs. $>$ 3 days), (2) readmissions (none vs. $\geq$ 1), and (3) combined HG severity: milder vs. more severe HG ($\leq$3 days and no readmissions vs. $>$ 3 days and $\geq$ 1 readmission). Logistic regression was adjusted for age, body mass index, parity, and marital status.

Results: Women with more severe HG (longer hospitalizations and readmissions) were hospitalized earlier in pregnancy than those with milder HG (8.0 vs. 10.0 gestational weeks, $p = 0.002$). After adjustment, readmissions were more common among women with a history of motion sickness (71%) than among those without (49%, $p = 0.029$). Nausea related to migraine and a family history of NVP showed no association with readmissions. None of the nausea-related factors were associated with longer hospital stays or combined HG severity.

Conclusion: Earlier hospitalization may indicate a more severe HG phenotype, emphasizing the importance of timely recognition and sufficient medical care. Although personal history of nausea and family history of NVP are known HG risk factors in general, they did not strongly predict more severe HG.

Introduction

Hyperemesis gravidarum (HG) affects up to 3.6% of pregnancies [1] and is the most common reason for hospitalization in the first trimester [2]. The symptoms include nausea, vomiting and inability to eat and/or drink normally, strongly limiting the daily life. [3] Signs of dehydration and electrolyte disturbances are often involved. [3] Recognizing and treating HG is important as it causes significant burden to the pregnant woman both physically and mentally [2,4,5]. Furthermore, HG has been shown to be associated with poorer perinatal outcomes [5,6]. Additionally, the burden of the disease has led women to termination of pregnancy or to postpone or to avoid future pregnancies [7–9].

Severe and prolonged HG is particularly burdensome. Even though no consensus exists about the definition of prolonged HG, definitions like prolonged hospitalization due to HG [10] or duration of HG symptoms until delivery [11] have been used. Also, the definition of

* Corresponding author.
E-mail address: vesali@utu.fi (V.S. Lindström).
[1] ORCID: 0000-0002-8589-4714.
[2] ORCID: 0000-0001-8186-4860.
[3] ORCID: 0000-0002-6106-1427.
[4] ORCID: 0000-0003-0665-0306.
[5] ORCID: 0000-0001-6381-7227.

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severe HG varies, but it is commonly used to describe a more serious form of the condition that typically necessitates medical interventions such as hospitalization [4]. Studies evaluating risk factors for prolonged or severe HG are limited. In a US questionnaire study, younger age, higher pre-pregnancy weight, allergies, and restrictive diet were associated with HG symptoms lasting until delivery [11]. Women whose HG symptoms persisted until delivery reported having more posttraumatic stress, motion sickness, and muscle weakness when completing the questionnaire postpartum [11]. An Israeli study found an increased risk of readmission if the initial hospitalization occurred before gestational week (gwk) nine, lasted longer than two days, and if the woman had a previous history of HG [12]. In a UK study, risk factors for readmission included a prior HG pregnancy, Asian or Black ethnicity, maternal comorbidities, such as hyperthyroid disorders, and multiple pregnancy [13].

One of the most prioritized challenges regarding HG includes recognition of risk factors involved in prolongation of the symptoms [14]. We have previously shown that maternal personal history of nausea in different situations, and a family history of NVP are associated with HG [15,16]. The purpose of the present study was to evaluate whether these risk factors are associated also with prolonged hospitalization and readmissions due to HG.

Methods

Subjects

The participants were enrolled in Turku University Hospital, Turku, Finland between January 2011 and March 2019. Women hospitalized due to HG were asked for their voluntary participation. Finnish language skills were required to give an informed consent to participate, and to answer the study questionnaire which was only available in Finnish. During the enrolment time span, there were 32 to 68 admission periods due to HG per year, including also possible readmissions of the same woman. This resulted in 433 admission periods, with an estimated participation rate of 37%. The number of deliveries during that time period in Turku University Hospital varied from 3708 to 4214, which gave an estimated admission rate due to HG of 0.8%–1.7%. HG diagnosis was set according to the current clinical guidelines (ICD-10 codes O21.0, O21.1, O21.9 [World Health Organization, ICD-10 version 2010]) [17]. At the time of our study, there were no national guidelines for admission and discharge for HG. The admission criteria were based on the hospital guidelines and the clinical judgment of a specialist in obstetrics and gynecology, including assessment of the severity of nausea and vomiting symptoms, woman's general wellbeing, clinical or laboratory signs of dehydration, and presence of urine ketones. During the hospitalization, all women received intravenous fluids and were offered antiemetic medication. Other potential causes of nausea and vomiting were clinically excluded. At discharge, both the overall alleviation of HG symptoms and the woman's self-reported improvement were evaluated. The laboratory measurements typically also improved, but their normalizing was not a prerequisite for discharge. Altogether 105 women participated, but because of incomplete questionnaires, data of 102 women were eligible for analysis. Other potential causes of nausea and vomiting were clinically excluded.

The basic characteristics (gwk according to the last menstrual period at admission, parity, pre-pregnancy body mass index (BMI, kg/m^2), smoking (yes/no), and marital status (cohabited/single), as well as the length of the first admission and the number of hospitalizations were collected from the medical records. Age was determined subtracting the date of birth from the date of hospitalization.

Three different group divisions were performed, and the women were divided accordingly:

1. Length of hospitalization:
   a. ≤3 days
   b. >3 days.
2. Readmission:
   a. No readmissions
   b. At least one readmission
3. Severity of HG:
   a. 'Milder HG': hospitalization for ≤ 3 days with no readmission.
   b. 'More severe HG': hospitalization for > 3 days and readmission.

Risk factors for prolonged hospitalization and readmissions due to HG

We evaluated personal history of nausea in various situations ('motion sickness','seasickness','nausea with migraine','nausea with other kind of headache','nausea after anesthesia','nausea during the use of contraception' and'other kind of nausea' [yes/no]), and family history of NVP ('first-degree' [mother, sister; yes/no] and'second-degree' [more distant] relatives; yes/no]). Previously we have found a relationship between HG/NVP and motion sickness and migraine, as well as between HG/NVP and family history of NVP [15,16], and therefore only those risk factors were included in the present study.

Statistical analysis

Continuous variables (age, gwk, pre-pregnancy BMI) are presented using means and standard deviations (SDs) or medians and interquartile ranges (IQRs). Categorical variables (parity, smoking, marital status, history of motion sickness, history of nausea related to migraine, and family history of NVP) are characterized with percentages and frequencies. Participants with missing data were excluded from the analysis. Fisher's exact test, two-sample *t*-test and Mann–Whitney U tests were used within group comparisons. Two-sample *t* test was used with continuous normally distributed variables and Mann–Whitney *U* test with continuous variables with skewed distribution. Having a personal history of motion sickness, migraine and family history of NVP were evaluated separately with univariate analysis in the three categories: 1) women hospitalized for ≤ 3 days vs. > 3 days, 2) women with no readmissions vs. at least one readmission and 3) 'milder HG' (hospitalized for ≤ 3 days and no readmission) group vs. 'more severe HG' (hospitalized for > 3 days and readmission) group using logistic regression analysis. Thereafter, the results of predictive factors (history of motion sickness, migraine, family history of NVP) were adjusted for age, parity, pre-pregnancy BMI and marital status. Results are reported using odds ratios (ORs) with 95% confidence intervals (CIs) with a significance level of $p = 0.05$ (two tailed). SAS Institute Inc. version 9.4. for Windows was used in the statistical analysis.

Results

Basic characteristics

Of all women, 54% (n = 55) were hospitalized for ≤ 3 days and 46% (n = 47) women > 3 days. Furthermore, 66% (n = 67) were hospitalized only once and 34% (n = 35) twice or more. Accordingly, 46% (n = 47) were categorized into the 'milder HG' group (≤3 days of hospitalization and no readmissions), and 26% (n = 27) into the 'more severe HG' group (>3 days of hospitalization and at least one readmission). Women with longer hospital stays (>3 days), readmissions, and both, were hospitalized in earlier gwks than those with shorter stays and no readmissions (milder HG gwk 8.0 vs. more severe HG gwk 10.0, p = 0.002). Otherwise, the groups did not differ in their basic characteristics. (Table 1).

Associations between prolonged hospitalization and readmissions due to HG and history of nausea

Altogether 56% (n = 51) women reported experiencing motion sickness and 45% (n = 41) had nausea related to migraines. Additionally, 71% (n = 55) women had a family member with a history of NVP

Table 1
Basic characteristics.

	Length of hospitalization							Readmissions							HG severity						
	≤ 3 days *n* = 55			> 3 days *n* = 47				No *n* = 67			Yes *n* = 55				Milder HG *n* = 47			More severe HG *n* = 27			
	n	Mean ± SD or % (n)	Range	n	Mean ± SD or % (n)	Range	*P*-value	n	Mean ± SD or % (n)	Range	n	Mean ± SD or % (n)	Range	*P*-value	n	Mean ± SD or % (n)	Range	n	Mean ± SD or % (n)	Range	*P*-value
Age (years)	55	29.1 ± 4.2	18.6–38.8	47	29.9 ± 5.8	18.9–42.7	0.448[a]	67	29.7 ± 4.6	19.5–42.6	35	29.0 ± 5.9	18.5–42.7	0.520[a]	47	29.4 ± 4.0	20.2–38.8	27	29.6 ± 6.0	18.9–42.7	0.913[a]
Parity	55			47			0.231[b]	67			35			0.401[b]	47			27			0.150[b]
Nulliparous		36.4 (20)			48.9 (23)				38.8 (26)			48.6 (17)				40.4 (19)			59.3 (16)		
Multiparous		63.6 (35)			51.0 (24)				61.2 (41)			51.4 (18)				59.6 (28)			40.7 (11)		
Gestational weeks*	55	9.0 (8.0–12.0)	6.0–20.0	47	8.0 (7.0–10.0)	6.0–15.0	**0.015**[c]	67	10.0 (8.0–12.0)	6.0–20.0	35	8.0 (7.0–9.0)	6.0–13.0	**0.004**[c]	47	10.0 (8.0–13.0)	6.0–20.0	27	8.0 (7.0–10.0)	6.0–13.0	**0.002**[c]
BMI* (kg/m^2)	54	24.0 (21.4–27.7)	18.0–40.6	46	22.9 (21.0–29.8)	18.0–37.6	0.615[c]	66	23.7 (20.9–28.0)	18.0–36.8	34	22.9 (21.2–28.4)	18.0–40.6	0.805[c]	46	23.8 (21.4–27.6)	18.0–36.5	26	22.5 (21.2–26.2)	18.0–37.6	0.673[c]
Smoking	55			44			0.999[b]	66			33			0.599[b]	47			25			0.606[b]
Non-smokers		96.4 (53)			95.5 (42)				97.0 (64)			93.9 (31)				95.7 (45)			92.0 (23)		
Smokers		3.6 (2)			4.6 (2)				3.0 (2)			6.1 (2)				4.3 (2)			8.0 (2)		
Marital status	55			46			0.090[b]	67			34			0.401[b]	47			26			0.126[b]
Married/ cohabited		98.2 (54)			89.1 (41)				95.5 (64)			91.2 (31)				97.9 (46)			88.5 (23)		
Single		1.8 (1)			10.9 (5)				4.5 (3)			8.8 (3)				2.1 (1)			11.5 (3)		

*BMI and gestational weeks reported using median and interquartile range.
Abbreviations: BMI = Body mass index, HG=Hyperemesis gravidarum, NVP=Nausea and vomiting of pregnancy, SD=Standard deviation
Milder HG: women who were hospitalized for ≤ 3 days and had no readmissions due to HG.
More severe HG: women who were hospitalized for > 3 days and had at least one readmission due to HG.
[a] Two sample *t*-test.
[b] Fisher's exact test.
[c] Mann-Whitney *U* test.

Table 2
Associations between severity of HG and personal history of nausea and family history of NVP.

	Length of hospitalization						Readmissions						HG severity							
	≤ 3 days		> 3 days				No		Yes				Milder HG		More severe HG					
	n = 55		*n* = 47				*n* = 67		*n* = 55				*n* = 47		*n* = 27					
	% (n)	OR	% (n)	OR (95% CI)[a]	AOR (95% CI)[b]	*P*-value[a]	P-value (AOR)[b]	% (n)	OR	% (n)	OR (95% CI)[a]	AOR (95% CI)[b]	*P*-value[a]	P-value (AOR)[b]	% (n)	OR	% (n)	OR (95% CI)[a]	AOR (95% CI)[b]	*P*-value[a]	P-value (AOR)[b]
Motion sickness	53.1 (26)	1	59.5 (25)	1.3 (0.57–2.99)	1.17 (0.45–3.07)	0.536	0.746	49.2 (31)	1	71.4 (20)	2.58 (0.99–6.72)	3.69 (1.14–11.92)	0.052	**0.029**	51.2 (22)	1	72.7 (16)	2.55 (0.84–7.74)	2.57 (0.68–9.62)	0.100	0.163
Migraine	45.7 (21)	1	43.5 (20)	0.92 (0.40–2.08)	0.80 (0.32–1.96)	0.834	0.621	42.6 (26)	1	48.4 (15)	1.26 (0.53–3.01)	1.14 (0.44–2.93)	0.599	0.794	43.9 (18)	1	46.2 (12)	1.10 (0.41–2.94)	0.90 (0.26–3.12)	0.857	0.865
Family history of NVP	69.1 (29)	1	74.3 (26)	1.30 (0.48–3.53)	1.14 (0.39–3.31)	0.613	0.813	67.3 (35)	1	80.0 (20)	1.94 (0.62–6.07)	2.03 (0.61–6.77)	0.253	0.250	73.0 (27)	1	90.0 (18)	3.33 (0.65–17.03)	2.89 (0.53–15.72)	0.148	0.220

Abbreviations: AOR = Adjusted odds ratio, CI=Confidence interval, HG=Hyperemesis gravidarum, NVP=Nausea and vomiting of pregnancy, OR=Odds ratio.
Note: The percentages are counted as the number of affirmative responses divided by the total number of responses in each question.
Milder HG: women who were hospitalized for ≤ 3 days and had no readmissions due to HG.
More severe HG: women who were hospitalized for > 3 days and had at least one readmission due to HG.
[a] Univariate analysis (logistic regression analysis).
[b] Adjusted for age, parity, pre-pregnancy body mass index and marital status.

(Table 2). The examined risk factors (motion sickness, nausea related to migraine, and family history of NVP) were equally common among women with shorter (≤3 days) and longer (>3 days) hospital stays and were not associated with the length of the hospitalization after adjustment for age, parity, BMI, and marital status. When categorized for readmissions (no readmission vs. at least one readmission) and adjusted for the same factors, women with a history of motion sickness were more likely to be readmitted (p = 0.029). When categorized into 'milder HG' (≤3 days of hospitalization and no readmission due to HG) and 'more severe HG' (>3 days of hospitalization and at least one readmission due to HG), no associations with the examined risk factors were found either before or after adjustment (Table 2).

Discussion

Severe HG, characterized by prolonged hospitalization or hospital readmissions, not only causes significant physical and psychosocial distress for pregnant women and their close relations, but also increases demands on healthcare resources. Therefore, research of risk factors is essential. Contrary to our previous results [15,16], only personal history of motion sickness was associated with more severe HG, reflected by readmissions. In addition, women admitted to the hospital earlier in pregnancy had longer hospitalization and more readmissions. This pattern may reflect differences in the clinical course and phenotypes of HG, with more severe manifestations emerging earlier in pregnancy and consequently leading to prolonged and recurrent need for inpatient care.

Morris et al. reported that hospitalization due to HG before gwk nine was associated with an increased risk of readmissions [12]. To add to their study [12], we found that earlier hospitalization was associated also with prolonged hospital stay. We hypothesize that earlier-onset HG is characterized by a more rapid and severe deterioration in the woman's general condition, leading to earlier, longer, and recurrent hospitalizations. It should be noted that because these women became ill earlier in pregnancy, they also had a longer period during which multiple admissions could occur. Nevertheless, their individual hospital stays were longer, even though they received guideline-based care. Therefore, these findings suggest that earlier-onset HG denotes a distinct phenotype, characterized by peracute and serious symptoms.

Nausea and vomiting in different situations are multifactorial conditions [18]. General nausea and vomiting and HG share overlapping biological pathways, including vestibular, olfactory, hormonal, and gastrointestinal mechanisms [2,18–20]. Nausea commonly occurs in conditions such as migraine, motion-related disorders, and similar vestibular disturbances have also been observed in HG [18,21]. Given these shared mechanisms, this relationship has been examined, and evidence indicates that HG is associated with a woman's previous susceptibility to nausea [15,16].

We aimed to examine whether a general predisposition to nausea in various situations and a family history of NVP are associated also with a more severe form of HG, which we characterized by prolonged and recurrent hospitalization. To the best of our knowledge, only one previous study has evaluated this association. Mullin et al. found that women who had HG symptoms lasting until delivery were more likely to report having motion sickness [11]. Our results were partly similar as we found that women with higher occurrence of motion sickness had more readmissions due to HG. However, we evaluated the history of motion sickness at the time of admission due to HG, whereas Mullin et al. [11] assessed it retrospectively after pregnancy. Also, they studied prolonged HG lasting beyond gwk 27 [11], while in our study most women were hospitalized in early pregnancy.

The potential associations between migraine-related nausea and prolonged hospitalization or readmissions due to HG remain unexplored in previous literature. The predominance of migraine among women and its variation across reproductive milestones, such as menstruation, pregnancy and menopause, suggest that sex hormones play an important role in its pathophysiology [22]. Estrogen receptors are present in the

central nervous system and fluctuations in female sex hormone levels, as well as variations in their receptor binding, are known to influence migraine occurrence [23]. Nausea with migraine has been found to be associated both with NVP and HG in previous studies [15,16,24]. However, based on our results, neither prolonged hospitalization nor readmissions due to HG were associated with migraine-related nausea. Thus, a history of migraine-associated nausea did not appear to predispose to a more severe form of HG.

Recent advances suggest that the familial aggregation of HG may be partly explained by genetic factors such as variation in GDF15, a placenta-derived cytokine recognized as a key driver of nausea and vomiting in pregnancy [25]. GDF15 acts on brainstem vomiting centre to induce nausea, appetite loss, and emesis, and both maternal and fetal genetic variants in the GDF15 locus have been shown to be strongly associated with susceptibility to HG [25]. Women with genetically lower baseline GDF15 levels appear particularly susceptible to the steep rise in circulating concentrations during early pregnancy, which may help explain these familial patterns [25]. In our study, however, a positive family history of NVP was not associated with longer or recurrent hospitalizations. Because a positive family history was common across all HG patients, differences between the groups may have been too small to reach statistical significance. In addition, a positive reporting bias may have contributed to the high prevalence of reported familial symptoms, as individuals are more likely to recall or report symptoms that are pronounced, distressing, or relevant to their own experiences.

Our study was one of the first to explore factors associated with prolonged hospitalization and readmissions due to HG. While ethnic differences are known to be important in HG, this bias was minimized in our study, because participants were predominantly Finnish, as being able to read and write in Finnish was a requirement for inclusion. However, this homogeneity limits the generalizability of our findings to populations with different ethnicity. The definitions of severe HG and prolonged HG lack consensus. For instance, McCarthy et al. [4] defined severe HG as requiring hospitalization, whereas in our study, more severe HG was classified as more than three days of hospitalization and at least two hospital admissions. We believe that our stricter classification better distinguishes severe cases from milder ones.

Nevertheless, our study has certain limitations, including relatively small sample size, which may interfere with robustness of our findings. However, previous HG studies have been conducted with similar sample sizes [26]. Furthermore, one limitation is the variability in hospital discharge criteria, which were based on subjective assessments of patient well-being rather than biomarkers. Nevertheless, HG is a clinical diagnosis and no definitive biomarkers showing recovery are known [27]. In addition, the absence of standardized criteria for hospital admission and discharge likely contributes to variation in clinical practice, including differences in the length of inpatient care. Some women may have been discharged prematurely, potentially increasing the risk of a recurrent hospitalization, whereas others may have remained in the hospital longer than necessary despite clinical improvement. These inconsistencies may have influenced both the duration of hospital stays and number of readmissions to some extent. We considered both the duration of hospitalization and the occurrence of readmissions when determining the severity of HG to reduce bias related to variation in discharge practices. However, differences in clinical routines cannot be fully eliminated. We did not utilize any specific questionnaires, like Pregnancy-Unique Quantification of Emesis (PUQE) or Hyperemesis Level Prediction (HELP) score, to measure the severity of HG in our study. Using any validated questionnaires could have improved comparison of our study results to other studies with similar study designs. However, at the time of our study, no questionnaires were in clinical use in Finland to guide decisions regarding hospital admission or discharge. Furthermore, family circumstances may also have influenced discharge decisions, either shortening or prolonging hospital stays. However, parity and marital status were comparable between the groups, and these factors were included as adjusting factors to minimize such bias. We assessed the occurrence of NVP in relatives but did not specifically evaluate the occurrence of HG. It is important to note that NVP is highly prevalent, whereas HG is considerably less common. This methodological approach may have attenuated the observed association, potentially explaining the absence of a detectable link between family history and HG severity. Smoking, although associated with a reduced risk of HG [28], was extremely rare and therefore could not be included as an adjusting factor in our analysis. Information on weight during hospitalization was not available in our study. Instead, data on pre-pregnancy BMI were available; however, BMI was not identified as a risk factor for the severity of HG. A history of HG in a previous pregnancy has been shown to be associated with an increased risk of recurrence in subsequent pregnancies [29] and may therefore act as a potential confounding factor for prolonged hospitalization and readmissions [12,13]. Unfortunately, information on HG recurrence was not available for the multiparous women in our study, and thus, we were unable to include this variable as a confounder in statistical analyses.

Conclusion

Earlier onset of HG was characterized by a longer and recurrent need for inpatient care. This finding may indicate that earlier-onset HG represents a more severe HG phenotype. However, although a personal history of nausea and a family history of NVP have been identified as important risk factors for developing HG, their associations with prolonged hospitalization or readmissions were less evident.

Ethics statement

All procedures were performed in compliance with relevant laws and institutional guidelines. The study was approved by the Joint Ethics Committees of University of Turku and Turku University Central Hospital, Turku, Finland (60/180/2011) and carried out according to the Declaration of Helsinki. Women received oral and written information of the study and gave a written informed consent. Participation in the study was voluntary.

Data availability

The data that support the findings of this study are available from the corresponding author (VL), upon reasonable request.

CRediT authorship contribution statement

Venla S. Lindström: Writing – review & editing, Writing – original draft, Investigation, Data curation. **Linda M. Laitinen:** Writing – review & editing, Investigation, Conceptualization. **J.Miina A. Nurmi:** . **Mari A. Koivisto:** Data curation. **Päivi Polo-Kantola:** Writing – review & editing, Supervision, Resources, Conceptualization.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejogrb.2026.115072.

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