

# BMJ Open Usability of Pregnancy-Unique Quantification of Emesis questionnaire in women hospitalised for hyperemesis gravidarum: a prospective cohort study

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## ABSTRACT

**Objectives** Pregnancy-Unique Quantification of Emesis (PUQE) questionnaire is mainly used in outpatient care to assess the severity of nausea and vomiting of pregnancy (NVP). Our aim was to evaluate the usability of the Finnish-translated PUQE in hospitalised women with hyperemesis gravidarum (HG).

**Design** Prospective cohort study.

**Setting** University hospital in Finland.

**Participants** Ninety-five women admitted due to HG for at least overnight.

**Primary and secondary outcome measures** Categorised and continuous PUQE scores, physical and mental quality of life (QoL) and urine ketones at admission and at discharge, analysing the first admission and readmissions separately.

**Results** The most common PUQE categories at admission were 'moderate' and 'severe', whereas at discharge they were 'mild' and 'moderate'. Likewise, continuous PUQE scores improved between admission and discharge ( $p < 0.0001$ ). At admission, women rating worse physical QoL (first admission adjusted OR (AOR) 1.09; 95% CI 1.03 to 1.16; readmissions AOR 1.13; 95% CI 1.02 to 1.25) and women with ketonuria of +++ (first admission AOR 16.00; 95% CI 1.44 to 177.82) fell into higher PUQE score category. On discharge day, women with better physical QoL had lower PUQE score category (first admission AOR 0.94; 95% CI 0.91 to 0.98; readmissions AOR 0.93; 95% CI 0.90 to 0.97). The results between physical QoL and continuous PUQE scores were similar. Concerning readmissions, better mental QoL was associated with lower PUQE score category at discharge (AOR 0.93; 95% CI 0.89 to 0.97). As for continuous PUQE score, worse mental QoL was associated with higher score at admission (readmissions,  $p = 0.007$ ) and better mental QoL with lower score at discharge (readmissions,  $p = 0.007$ ).

**Conclusions** PUQE scores reflected alleviation of NVP severity in women hospitalised due to HG. Further, the decrease in PUQE score was associated with improved physical QoL and partly also with improved mental QoL. We therefore suggest PUQE as a complementary instrument for inpatient setting.

## INTRODUCTION

Hyperemesis gravidarum (HG) represents the extremity of symptoms of nausea and

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This study applied Pregnancy-Unique Quantification of Emesis (PUQE) questionnaire in patients with hyperemesis gravidarum in inpatient setting comparing PUQE scores at admission and at discharge and distinguishing the first admission period and readmissions.
- ⇒ Both categorised PUQE scores according to the original validation studies of the questionnaire as well as continuous PUQE scores were analysed, and the scores were compared with the estimations of physical and mental quality of life and urine ketones.
- ⇒ Admission and discharge criteria were not strictly defined, and the treatment protocol was not standardised.
- ⇒ Selection bias was possible since the women were enrolled from a single unit and information of women who refused to participate was lacking.

vomiting of pregnancy (NVP).<sup>1 2</sup> Most pregnant women have some degree of NVP.<sup>2</sup> Hence, NVP is often considered as a normal part of pregnancy,<sup>3</sup> whereas HG is rare, with an estimated prevalence of only 0.3%–3.6%.<sup>1</sup> However, the distinction between severe NVP and HG is often overlapping. In addition, even mild NVP may decrease women's quality of life (QoL).<sup>3 4</sup> Consequently, it is evident that HG causes extreme physical impairment and substantial mental distress, leading even to suicidal ideation, depressive symptoms continuing post partum and affecting future family planning.<sup>5–8</sup>

Usually in clinical practice, HG is diagnosed when severe NVP symptoms lead to weight loss, dehydration and electrolyte imbalances.<sup>2</sup> No usable biomarker has been established,<sup>9</sup> although urine ketones are often used despite controversial evidence.<sup>9–12</sup> All in all, need of hospitalisation is assessed individually and due to the lack of standardised diagnostic criteria of HG or generally applied



questionnaire to evaluate the severity of HG symptoms, admittance to hospital and length of admission easily varies according to the physician's assessment. Repeated hospital admissions are often needed.<sup>13 14</sup>

Pregnancy-Unique Quantification of Emesis (PUQE) questionnaire<sup>15</sup> is a simple tool for measuring the severity of NVP. PUQE score, ranging from 3 to 15 points, is the sum of the replies to three questions concerning duration of nausea in hours and the quantity of both vomiting and retching episodes. According to the total PUQE points, NVP is categorised into 'no', 'mild', 'moderate' and 'severe'. PUQE has been validated to cover symptoms from previous 12 hours<sup>16</sup> and 24 hours<sup>17</sup> (PUQE-24) as well as from the entire first trimester.<sup>18</sup> PUQE is mostly used in outpatient setting to screen patients with NVP and accordingly the need of hospitalisation.<sup>2 10</sup> The PUQE questionnaire has previously been translated into Finnish by a professional translator with the permission of the PUQE owners and back translated by another professional translator and used in general Finnish pregnant outpatient population.<sup>19</sup> In hospital settings of patients with HG, PUQE has been used in few studies mainly comparing the effectiveness of different therapeutic interventions.<sup>20–22</sup>

To the best of our knowledge, only two previous studies, a Norwegian PUQE validation study<sup>23</sup> and another study from Nepal,<sup>24</sup> applied the PUQE questionnaire during hospitalisation due to HG, both showing an improvement in PUQE score after treatment. In the Norwegian study, also a connection between higher PUQE score and both lower general well-being and insufficient nutritional intake was shown. While in the Norwegian study both categorised PUQE scores as validated in the original studies<sup>15 16</sup> and continuous PUQE scores were analysed, the Nepalese study considered PUQE scores only as continuous scores.

Given the sparsity of previous research, further studies were needed regarding the usability of the PUQE questionnaire in clinical settings, including evaluation of the tool in both the first admission period and in readmissions, reflecting milder HG (first admission) and prolonged HG (readmissions). Thus, our aim was to evaluate the clinical usability of the Finnish PUQE questionnaire in terms of the improvement of the PUQE scores between admission and discharge among women hospitalised for HG. The PUQE scores were considered both as categorised and continuous values and compared with both physical and mental QoL scores and to urine ketones, measures which in clinical practice are typically used as markers of hospital admittance and discharge of patients with HG.

## MATERIALS AND METHODS

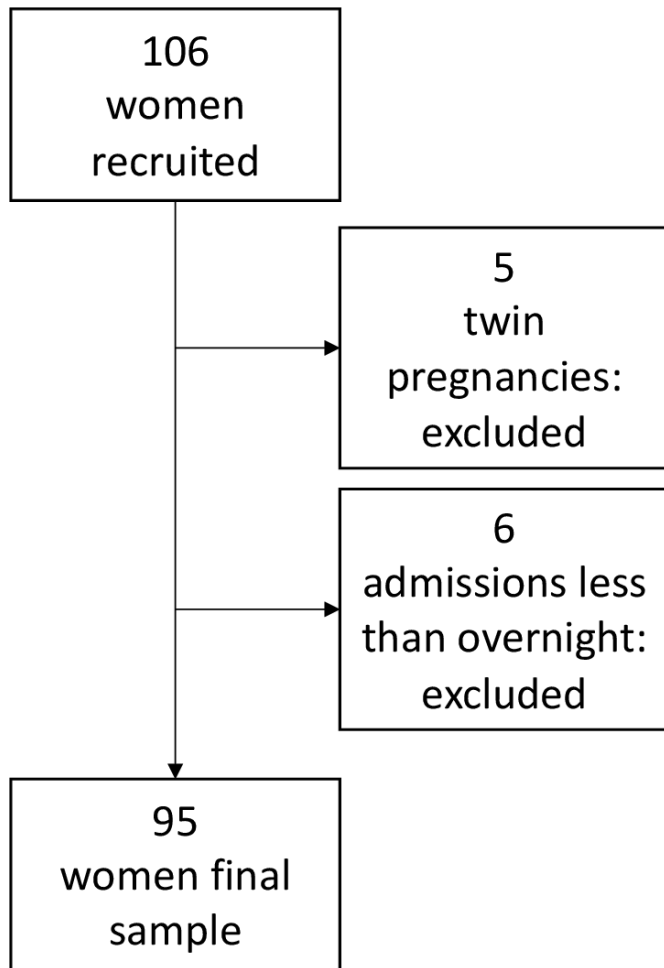
Women hospitalised for HG in antenatal ward of Turku University Hospital, Turku, Finland during 2011–2019 were enrolled after oral and written information about the study. Volunteers were eligible to participate and gave

**Table 1** Basic characteristics of women.

	n	Mean±SD or n (%)	Range
Age (years)	95	29.5±5.0	18.9–42.7
gwk	95	9.8±2.5	6.3–20.3
Parity	93		
Nulliparous		35 (37.6)	
Multiparous		58 (62.4)	
Pre-pregnancy BMI (kg/m <sup>2</sup> )	91	25.2±5.4	18.0–40.6
Smoking	90		
Non-smokers		87 (96.7)	
Smokers		3 (3.3)	
Marital status	92		
Cohabited		85 (92.4)	
Single		7 (7.6)	
Admissions (n)	95		
1		60 (63.2)	
≥2		35 (36.8)	2–14
Length of admissions (days)	160*	3.1±2.2	1–12
HG treatment	93		
Intravenous fluids		93 (100.0)	
Antiemetic medication		75 (80.6)	
Metoclopramide		32 (42.7)	
Ondansetron		12 (16.0)	
Both		31 (41.3)	
Parenteral nutrition		5 (5.4)	
Total n=95.			
*Total number of all admission periods with available data.			
BMI, body mass index; gwk, gestational week; HG, hyperemesis gravidarum.			

written informed consent. Capability to read and understand Finnish language was required, and thus most of the participants were Finnish.

HG was diagnosed according to the International Statistical Classification of Diseases and Related Health Problems 10th Revision (O21.0, O21.1, O21.9). Decision of admission for HG was based on current practice<sup>25</sup> and clinician's assessment concerning general sickness of the women, as well as clinical signs or laboratory findings of dehydration or presence of urine ketones. HG treatment for all women consisted of intravenous fluids and most women received antiemetic medication (metoclopramide and/or ondansetron). Only a minority of women needed parenteral nutrition (table 1). Decision to discharge was made according to cessation or alleviation of vomitus and nausea, signs of improved hydration and self-judgement of the woman of her own well-being.



**Figure 1** Flow chart of the study.

Altogether 106 women participated. Only data of women with singleton pregnancies and admissions lasting at least overnight were included, and thus data of 95 women were eligible for analysis (figure 1). In Turku University Hospital, during the recruitment period, there were annually 32–68 admissions for HG (including readmissions of the same women), resulting in 433 admission periods, which gave estimation of the participation rate of 37% (162 periods/433 periods). Furthermore, the number of deliveries varied from 3708 to 4214 annually,<sup>26</sup> giving the admission rate due to HG of 0.8%–1.7%.

NVP was assessed with PUQE score concerning the previous 12 hours.<sup>15</sup> In accordance with the original version,<sup>15</sup> four NVP categories of ‘no’ (3 points), ‘mild’ (4–6 points), ‘moderate’ (7–12 points) and ‘severe’ (13–15 points) were formed. In addition, PUQE score was used as a continuous variable. PUQE scores were recorded only for study purposes, and thus the scores did not guide the decisions of treatment, admittance, discharge or readmission of the women.

Physical and mental QoL were estimated with two visual analogue scales (VAS). Urine ketones were measured by urinalysis reagent strips (Mission, Acon Laboratories, San Diego, USA), with detection levels of – (no detectable

ketones), + (15 mg/dL=1.5 mmol/L), ++ (40 mg/dL=4.0 mmol/L) and +++ (80 mg/dL=8.0 mmol/L).

Basic demographic data of the women were obtained from hospital medical records including gestational weeks (gwk) at admission, parity (nulliparous/multiparous), body mass index (BMI, kg/m<sup>2</sup>, calculated from pre-pregnancy weight and height), smoking (no/yes), marital status (cohabited/single), the total length of all admissions (days), the number of readmissions and urine ketone results. Age was calculated by comparing the date of reply to the date of birth.

### Statistical analyses

Power calculation estimated minimum sample size of 58 (difference of three PUQE points between admission and discharge, alpha=5% and power of 80%, nQuery Advisor V.4.0: paired t-test). The distribution of values was evaluated before statistical analyses both visually and statistically and the variables followed approximately normal distribution, enabling the use of parametric tests. Continuous variables were characterised using means, SDs and ranges, and categorical variables using frequencies and per cent. The severity of NVP was categorised according to PUQE total score (‘no’/‘mild’/‘moderate’/‘severe’) on both admission and discharge days. Because of low number of values in category ‘mild NVP’ (n=2) on admission day and ‘severe NVP’ (n=1) on discharge day, these values were excluded from the analyses on admission and discharge days, respectively. In addition, when analysing the change of PUQE categories (delta, Δ) between admission and discharge, due to the low number of values in the change of three PUQE categories (n=3), the change of three PUQE categories and the change of two PUQE categories were combined.

Concerning physical or mental QoL measured by VAS, the probability to belong to a higher (admission day) PUQE category or lower (discharge day) PUQE category was calculated with multinomial logistic regression on both admission and discharge days. Two separate analyses were performed: (1) analysis of the first admission period and (2) analysis of readmission periods. Generalised estimating equation estimation was used when readmissions were included in analyses. The same analyses were performed for urine ketone categories (–/+/++/+++), but concerning the analyses of readmissions, the number of variables in different categories was too low for calculating the estimates and CIs and thus only the first admission was eligible for analysis. In analysis of urine ketones, p values were adjusted using Tukey-Kramer method because of multiple comparisons. Further, similar analyses on admission and discharge days using PUQE score as a continuous score were also performed. Comparisons both with physical and mental QoL VAS, urine ketones and continuous PUQE scores were calculated with linear mixed model for the first admission and linear mixed model with random intercept for patient for readmissions. All these results were adjusted for age, BMI and parity. In addition, continuous PUQE scores and VAS

**Table 2** Continuous PUQE scores and VAS scores.

	First admission				Readmissions			
	n*	Mean±SD	Range	P value	n*	Mean±SD	Range	P value
PUQE score				<0.0001				<0.0001
Admission day	68	11.6±2.3	5–15		54	12.3±2.7	4–15	
Discharge day	65	6.5±2.4	3–12		57	6.1±2.8	3–13	
Physical QoL VAS				<0.0001				<0.0001
Admission day	68	84.2±11.7	50–100		54	83.4±13.7	30–100	
Discharge day	65	45.4±19.3	4–90		57	47.4±21.4	0–88	
Mental QoL VAS				<0.0001				<0.0001
Admission day	68	65.4±17.9	15–100		54	75.1±19.7	12–100	
Discharge day	65	38.2±20.3	0–90		57	48.0±26.0	0–90	

Analysis of variance (ANOVA).

\*Total number of women=95. Total number of available data for the first admission period=93 and for readmission periods=69.

PUQE, Pregnancy-Unique Quantification of Emesis; QoL, quality of life; VAS, visual analogue scale (0–100, higher number indicates worse QoL).

scores on admission and discharge days were compared using analysis of variance. The results are presented with ORs and beta with 95% CI. Both unadjusted and adjusted results are shown in the tables, but only adjusted results are presented in the Results main text. Statistical significance was set at p values <0.05. Analyses were carried out using SAS V.9.4 (SAS Institute) for Windows.

### Patient and public involvement

Patients and the public were not involved in the design or reporting of this study.

## RESULTS

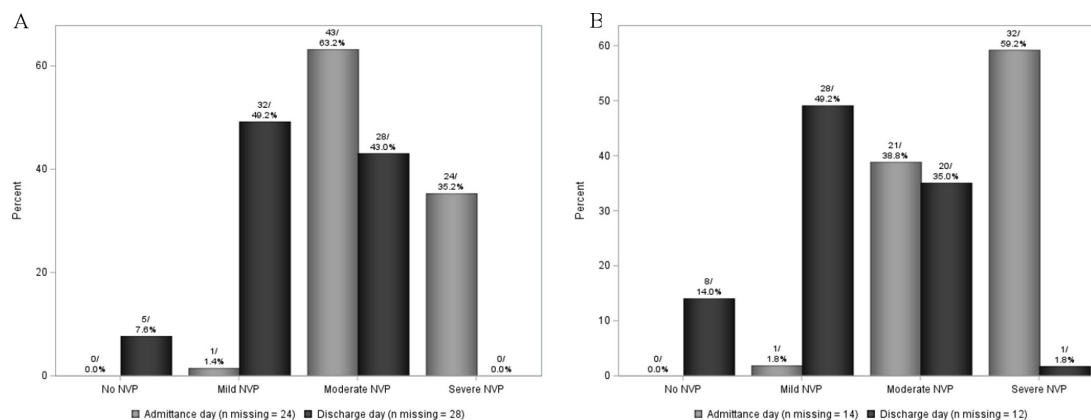
### Basic characteristics

Basic characteristics of the women and the questionnaire data are presented in tables 1 and 2. On admission day, according to categorised PUQE scores, most of the women suffered from 'moderate' or 'severe NVP'. On the contrary, on discharge day, most of the women had 'mild' or 'moderate NVP' (figure 2). Likewise, the mean continuous PUQE scores were higher on admission day

compared with discharge day (table 2). Further, on admission day, physical and mental QoL scores were higher indicating worse QoL than on discharge day (table 2). On admission day, over half of the women had urine ketones, whereas most of the women had no urine ketones on discharge day (figure 3).

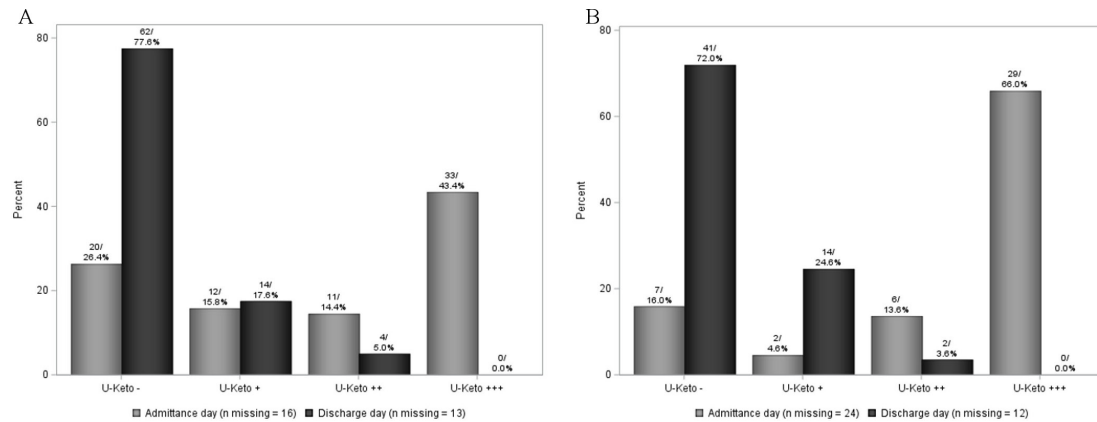
### PUQE score category and the first admission period

When evaluating only the first admission period, on admission day women with worse physical QoL fell into a higher PUQE score category. Instead, worse mental QoL was not associated with PUQE score category. In addition, women with severe ketonuria (+++ vs no urine ketones) fell into higher PUQE score category (p=0.016). On discharge day of the first admission period, the women with better physical QoL fell into lower PUQE score category. Instead, mental QoL and the presence of urine ketones were not associated with PUQE score categories (table 3 and online supplemental table 1).



**Figure 2** Pregnancy-Unique Quantification of Emesis (PUQE) categories on admission and discharge days including (A) the first admission and (B) readmissions. NVP, nausea and vomiting of pregnancy.





**Figure 3** Urine ketone categories on admission and discharge days including (A) the first admission and (B) readmissions.

### PUQE score category and readmission periods

When including readmission periods, the results between physical QoL and PUQE score categories on admission day and on discharge day were similar to those including only the first admission period: worse physical QoL was associated with higher PUQE category on admission day and better physical QoL with lower PUQE category on discharge day. As for mental QoL, on admission day of readmission periods, mental QoL was not associated with categorised PUQE score. On discharge day of readmission periods, women with better mental QoL fell into lower PUQE score category (table 3).

During both the first and readmission periods, the decrease (indicating better QoL) in both physical and mental QoL VAS scores was associated with a decrease in the PUQE category (table 3).

### Continuous PUQE score, QoL scores and urine ketones

When PUQE scores were considered as continuous value, on admission day, worse physical QoL was associated with high continuous PUQE score both during the first admission period and when readmission periods were included. Worse mental QoL was associated with high continuous PUQE score only when including readmissions. On admission day, severe ketonuria (+++ vs no urine ketones) was associated with high continuous PUQE score at first admission ( $p=0.026$  first admission,  $p=0.270$  readmissions). On discharge day, both better physical QoL and better mental QoL were associated with low continuous PUQE scores during the first admission period and when including readmissions. On the contrary, urine ketones showed no association ( $p=0.224$  first admission,  $p=0.990$  readmissions) (figures 4 and 5).

The improvement (the mean difference in VAS values between admission and discharge days) in both physical QoL and mental QoL was associated with the change in continuous PUQE scores during the first admission period and when including readmissions. Instead, no association emerged between the change in continuous PUQE score and urine ketones ( $p=0.620$  first admission,  $p=0.746$  readmissions) (figures 4 and 5).

### DISCUSSION

We were the first to use PUQE questionnaire in hospitalised HG women in Finland. PUQE showed to be a feasible clinical tool for assessing recovery; a marked improvement in PUQE score was found when comparing scores between admission and discharge using PUQE both as categorised and as continuous scores. In addition, high PUQE scores were associated with worse physical QoL at admission and low PUQE scores with better physical QoL at discharge, both in the first admission and in readmissions, indicating that PUQE scores were well concurrent with the measurement of physical QoL. As for the associations between mental QoL and PUQE scores, the association was found at both admission and discharge when PUQE scores were taken as continuous scores in readmissions. Concerning mental QoL and categorised PUQE scores, the association was found only in the adjusted results at discharge. These findings could be explained by that even though PUQE questionnaire is measuring physical events of NVP, it may also reflect mental QoL, especially in prolonged NVP: the overall misery of illness at admission and on readmissions and, on the other hand, the relief of improved condition at discharge. As for ketonuria, only severe ketonuria at admission was associated with higher PUQE score category, but otherwise ketonuria showed no connection with PUQE.

Our study has limitations. First, admission and discharge criteria were not strictly and uniformly defined, being based on common current practice concerning the well-being of the women and clinical signs or laboratory findings of dehydration. In Finland, the primary healthcare system is based on national health coverage and practically all pregnant women visit free-of-cost public maternity healthcare clinics. From there, women with HG are referred to hospitals to specialised obstetric clinics which are part of public services provided to all citizens by several hospital districts. These clinics in hospitals are led by specialists in obstetrics and women can be admitted to hospital or the treatment can continue in outpatient care. Therefore, hospital admittance and discharge decisions were not dependent, for instance,


**Table 3** Physical and mental QoL in VAS on admission and discharge days and the probability to fall into a higher or lower PUQE score category.\*

	PUQE admission day					PUQE discharge day					Δ							
	OR	95% CI	P value	AOR	95% CI	P value	OR	95% CI	P value	AOR	95% CI	P value	OR	95% CI	P value	AOR	95% CI	P value
<b>First admission</b>																		
Physical QoL	1.10	1.04 to 1.16	0.001	1.09	1.03 to 1.16	0.003	0.95	0.92 to 0.98	0.001	0.94	0.91 to 0.98	0.003	0.95	0.93 to 0.98	0.0008	0.93	0.90 to 0.97	0.0002
Mental QoL	1.00	0.97 to 1.03	0.983	1.01	0.97 to 1.04	0.765	0.98	0.95 to 1.00	0.071	0.97	0.94 to 1.00	0.062	0.97	0.95 to 1.00	0.045	0.97	0.94 to 0.99	0.011
<b>Readmissions</b>																		
Physical QoL	1.12	1.05 to 1.21	0.001	1.13	1.02 to 1.25	0.016	0.95	0.92 to 0.98	0.0007	0.93	0.90 to 0.97	0.0003	0.96	0.93 to 1.00	0.025	0.96	0.93 to 0.99	0.013
Mental QoL	1.06	0.99 to 1.14	0.113	1.04	0.99 to 1.09	0.166	0.96	0.93 to 0.99	0.018	0.93	0.89 to 0.97	0.002	0.97	0.94 to 1.00	0.046	0.95	0.92 to 0.98	0.001

Multinomial logistic regression.

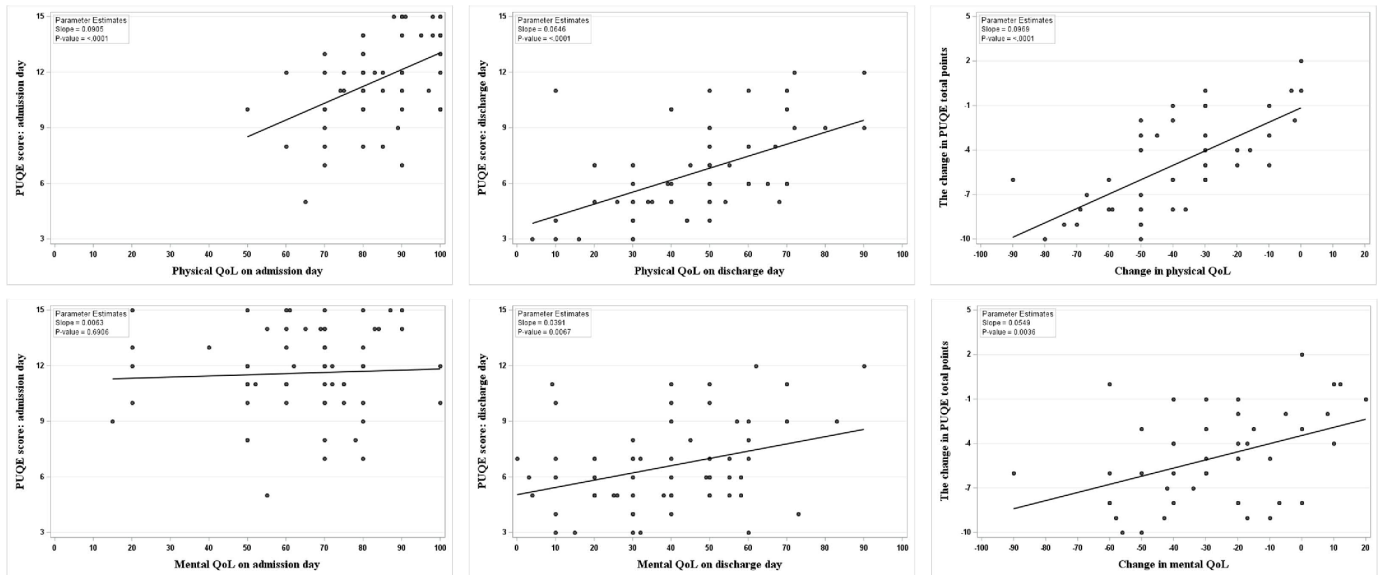
\*Higher PUQE category on admission day and lower PUQE category on discharge day.

AOR, adjusted OR (adjusted for age, body mass index and parity); PUQE, Pregnancy-Unique Quantification of Emesis; QoL, quality of life; VAS, visual analogue scale.

on women having a healthcare insurance or adequate wealth. Second, management between the patients was not totally similar, but standardised clinical practice and the treatment protocols were followed. However, since there were no strict admission or discharge criteria, no reliable biomarker to assess or predict the disease severity of HG or the probability of readmission, the treatment decisions were clinically individually assessed and possibly additionally affected by other determinants than physical parameters, for instance, factors related to women's housing situation or to family responsibilities. Hence, these factors may have influenced our results. In addition, all women were enrolled in the same unit, which further ensured that the treatment was uniform. Third, the number and reasons of refusal to participate were not recorded and thus dropout analyses were not possible to perform. Therefore, we cannot rule out selection bias that only women who felt better participated and those too sick did not, or vice versa. Moreover, the recruitment process took several years and was dependent on the activity of the nurses in the ward who recruited the women according to researchers' instructions on the top of their other duties without any extra compensation. In addition, we lack the information of previous HG, although almost half of the participants were nulliparas. The weight change during admission periods was not recorded although it could have reflected the nutritional status of the women better than urine ketones. Due to low number of values in urine ketone categories in readmissions, only analyses concerning the first admission period with categorised PUQE scores were possible. Further, we used the original 12-hour PUQE, but PUQE-24 could have recorded the previous day more accurately.

The merits of our study included a prospective study design with a large sample size based on power calculations. As the study questionnaire was available only in Finnish it practically ruled out foreign participants and thus our sample was quite homogenous and representative of the Finnish population. Compared with existing literature, we were the first to analyse the first admission period and readmissions separately, which roughly reflected milder HG (first admission) and prolonged HG (readmissions). This procedure also considered the possibility of learning effect since the women who were repeatedly hospitalised filled in the PUQE several times. Also, PUQE and exact VAS scores were available and analysed only by the researchers, not by clinicians treating the women, and thus the discharge or readmittance was not dependent on the research data.

Similar to our study, only two previous studies, one Scandinavian three-centre study from Norway<sup>23</sup> and another study from Nepal,<sup>24</sup> applied PUQE questionnaire to evaluate the severity of NVP in hospitalised patients with HG. In the Norwegian PUQE validation study, Birke-land *et al*<sup>23</sup> compared 38 hospitalised patients with HG to 31 healthy pregnant outpatient controls. PUQE-24 scores of patients with HG were recorded at admission (median 13) and discharge (median 6). In addition to

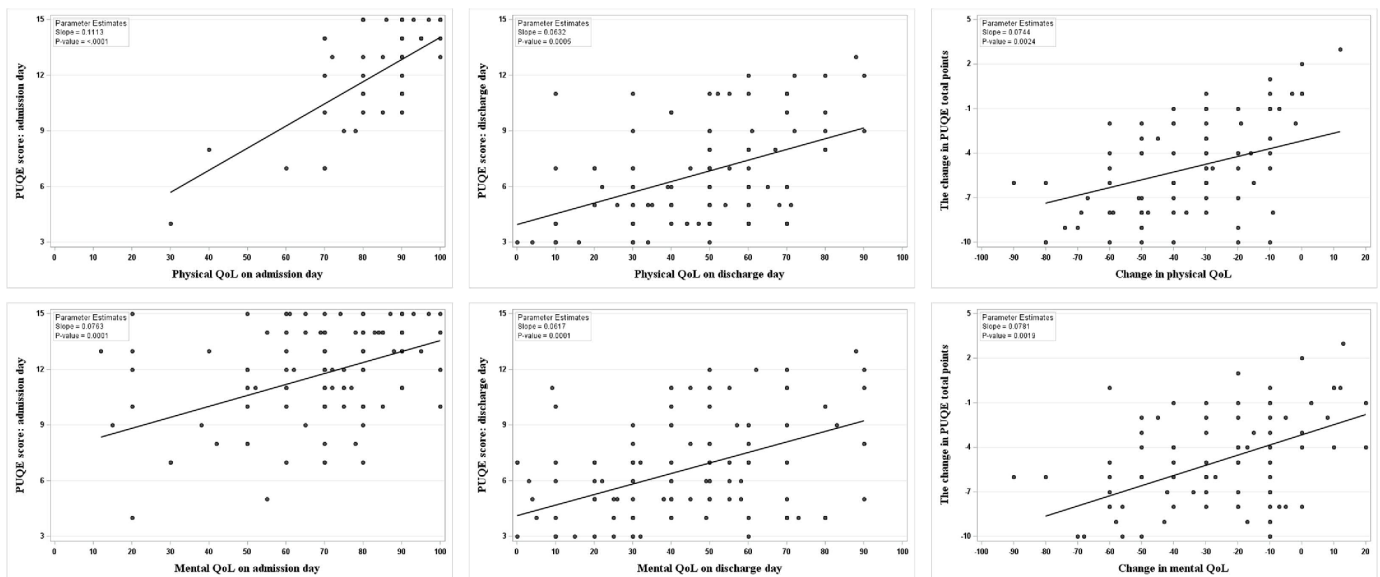


**Figure 4** Associations between continuous Pregnancy-Unique Quantification of Emesis (PUQE) score, physical quality of life (QoL) and mental QoL including the first admission.

the significant improvement in the continuous PUQE scores, also shifting to the lower PUQE categories was found between admission and discharge days. Furthermore, the PUQE scores correlated with the general well-being score. Although using PUQE-12, which evaluates NVP in the past 12 hours as originally validated by Koren *et al*,<sup>16</sup> we ended up with similar results as Birkeland *et al*'s study. Comparative results were obtained also in the Nepalese study;<sup>24</sup> all patients with HG (n=81) admitted in B P Koirala Institute of Health Sciences during 1 year were selected and studied for different maternal characteristics. NVP symptoms were evaluated with modified PUQE daily, but information of whether they used PUQE-12 or PUQE-24 was not available in the publication. The mean PUQE score at admission was 12.4, whereas after 2 days it

had decreased to mean 5.5 (mean hospital stay 3.2 days); however, no analyses of categorised PUQE scores were performed. In addition, the authors in the Nepalese study did not analyse the usability of the PUQE score, mainly concentrating on describing the basic characteristics of the HG women.

As the diagnostic criteria of HG are currently not firmly established despite of very recent consensus definition,<sup>27</sup> and no reliable biomarker has been found,<sup>9</sup> the use of validated questionnaires would bring an important addition for diagnosis and treatment follow-up care. Owing to its shortness and simplicity, PUQE is practical, including both quality (vomitus and retching), quantity (frequency) and duration of NVP.<sup>15</sup> However, HG may manifest with other discomforts as well, and therefore, not all women



**Figure 5** Associations between continuous Pregnancy-Unique Quantification of Emesis (PUQE) score, physical quality of life (QoL) and mental QoL including readmissions.



hospitalised for HG fulfil the criteria of severe NVP rated by the highest PUQE scores, as was seen in our study, too. In addition to physical symptoms, other reasons such as emotional needs or social challenges can contribute to the need of hospitalisation. To cover even better most of the HG symptoms, MacGibbon *et al*<sup>28</sup> have invented and validated a new HyperEmesis Level Prediction (HELP) Score, which, besides including the severity of nausea, vomiting and retching, encompasses estimations of intake, psychosocial functioning, hydration, treatment effectiveness and overall progress. The superiority of a longer and detailed questionnaire which certainly gives a more comprehensive estimation of the illness than the considerably shorter PUQE questionnaire may be, however, lost by being too time consuming in daily use in hospital setting.

PUQE questionnaire concentrates on physical symptoms. Adjacent to the original PUQE, Koren *et al*<sup>15</sup> used a single rating scale (0–10) of overall well-being. In their PUQE validation study,<sup>16</sup> lower value in the well-being score indicating lower QoL correlated with higher PUQE score. We used two VAS questions separately for both physical and mental QoL to assess QoL comprehensively. Predictably, the physical QoL was associated rather with PUQE than the mental QoL. However, women suffering especially from prolonged and severe NVP report marked negative psychosocial effects to everyday life and even psychiatric symptoms continuing to post partum.<sup>5–7</sup> Accordingly in our study, the mean mental QoL VAS score in readmissions was higher indicating worse mental QoL than the mean score in the first admission, and the associations between mental QoL and PUQE score emerged in women with readmissions, thus emphasising the mental consequences of prolonged HG. To estimate QoL in women with NVP in more detail, Lacasse and Bérard<sup>29</sup> have validated a Health-Related Quality of Life for Nausea and Vomiting during Pregnancy (NVPQOL) questionnaire. It evaluates QoL during the past week and consists of questions of four different domains: physical symptoms/aggravating factors, fatigue, emotions and limitations. All in all, as mental well-being consists of wide spectrum of traits, comprehensive estimation with a single question is a challenge.

Ketones are produced when the body lacks carbohydrates, for example, in fasting and in prolonged starvation.<sup>30</sup> Ketones can be easily measured from urine, and they are often detected in patients with HG. Thus, the existence of urine ketones has been used in guidelines as a sign of HG.<sup>10 11</sup> However, recent studies have questioned the importance of urine ketones in diagnosing HG since urine ketones are not present in all HG women.<sup>9 12</sup> In our study, the women had different categories of urine ketones both at admission and at discharge, although in most of the women they resolved during treatment and at discharge severe ketonuria (+++) was not detected. Thus, the clinical value of urine ketones in HG should be interpreted with caution, although severe ketonuria (+++) at admission was associated with higher PUQE score in our study, reflecting more severe NVP.

## CONCLUSION

In our study, the PUQE questionnaire showed to be a usable tool to measure the severity of NVP symptoms in a hospital setting. Distinct alleviation of the scores was found between admission and discharge when using the PUQE score both as categorised according to the original version and as continuous PUQE score which supports the assessment of individual PUQE points instead of focusing only on the change of PUQE categories. Utilisation of PUQE could thus bring feasible complement to the evaluation of the women hospitalised for HG, in addition to the simple question of physical well-being and measurement of urine ketones typically assessed in clinical care. Further challenge would be to develop a tool for estimating the optimal length of hospital admission for sufficient recovery and to avoid rapid readmission.

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Supplementary table 1. Urine ketones categories on admission and discharge days and the probability to fall into higher or lower PUQE score category\*.

First admission Urine ketones	PUQE admission day						PUQE discharge day					
	OR	95%CI	<i>P</i>	AOR	95%CI	<i>P</i>	OR	95%CI	<i>P</i>	AOR	95%CI	<i>P</i>
+ vs -	1.56	0.11– 22.22	0.974	5.11	0.22– 118.15	0.542	0.68	0.23– 1.99	0.676	2.07	0.24– 17.80	0.709
++ vs -	1.33	0.10– 18.49	0.992	1.69	0.10– 29.43	0.965	0.38	0.02– 8.21	0.740	NA		
+++ vs -	7.00	1.00– 48.81	0.049	16.00	1.44– 177.82	0.016	NA			NA		

Urine ketones categories: -/+ /++ /+++

Multinomial logistic regression

AOR = Adjusted odds ratio: adjusted for age, body mass index and parity

PUQE = Pregnancy-Unique Quantification of Emesis Questionnaire

NA = Not applicable

\*Higher PUQE category on admission day and lower PUQE category on discharge day