Med (Zenica) Glas

Medicinski Glasnik

ISSN 1840-2445 (Online); ISSN 1840-0132 (Print)

Medical Association of Zenica-Doboj Canton

Included by: PubMed (MEDLINE), SCOPUS, EMBASE, CNKI and DOAJ.

Med Glas (Zenica) publishes a "First Online" version as a free service to authors to accelerate the dissemination of scientific findings as soon as possible after acceptance, following peer review and any necessary revisions. The "First Online" manuscript appears online prior to copyediting, formatting/typesetting, and author proofreading, but it is fully citable via its Digital Object Identifier (DOI). However, this "Ahead of Print" version is NOT the final version of the manuscript. Once the final, copyedited and fully paginated version is published in a journal issue, it will be accessible through the same DOI and the "Ahead of Print" version will be replaced.

Type of the paper:	ORIGINAL ARTICLE
Running title:	**Namlı et al.** Guideline use in hyperemesis gravidarum
Title:	**Guideline use and factors associated with guideline-discordant management of hyperemesis gravidarum among first-contact physicians**
Authors:	Mehmet Efe Namlı*, Hande Kurt Güven, Elif Yılmaz
Affiliations:	Department of Obstetrics and Gynaecology, Ankara Atatürk Sanatorium Research and Training Hospital, Ankara, Türkiye
Corresponding author:	Mehmet Efe Namlı Department of Obstetrics and Gynaecology, Ankara Atatürk Sanatorium Research and Training Hospital, Kuşcağız Mah., Sanatoryum Cad. No. 271, 06290 Keçiören, Ankara, Türkiye Phone: +90 539 328 01 67; Fax: +90 312 567 70 00; E-mail: drmefenamli@gmail.com
DOI:	https://doi.org/10.17392/medglas24835

Received: 25 June 2026
Revised: 24 August 2026
Accepted: 25 August 2026

ORIGINAL ARTICLE

Guideline use and factors associated with guideline-discordant management of hyperemesis gravidarum among first-contact physicians

Mehmet Efe Namlı*, Hande Kurt Güven, Elif Yılmaz

Department of Obstetrics and Gynaecology, Ankara Atatürk Sanatorium Research and Training Hospital, Ankara, Türkiye

Running title: Namlı et al. Guideline use in hyperemesis gravidarum

***Correspondence:**

Mehmet Efe Namlı

Department of Obstetrics and Gynaecology, Ankara Atatürk Sanatorium Research and Training Hospital, Kuşcağız Mah.,

Sanatoryum Cad. No. 271, 06290 Keçiören, Ankara, Türkiye

Phone: +90 539 328 01 67; Fax: +90 312 567 70 00;

E-mail: drmefenamli@gmail.com

ORCID ID: 0000-0001-7352-8373

Pre-proof (Clinica)

ABSTRACT

Aim: To assess guideline awareness and use and identify factors associated with inadequate hyperemesis gravidarum (HG)-related knowledge and guideline-discordant management among first-contact physicians.

Methods: In this multicentre cross-sectional survey, 1,025 of 1,540 invited physicians from 28 institutions in Türkiye were analysed (analytic participation proportion, 66.6%). Knowledge was scored using 10 dichotomous items (Kuder–Richardson 20 = 0.71); inadequate knowledge was defined as ≤ 6, with alternative descriptive classifications at ≤ 5 and ≤ 7. Guideline-discordant management was defined as at least two of four components, with guideline use analysed only as an explanatory variable. Modified Poisson regression with robust variance estimated adjusted prevalence ratios (aPRs).

Results: Guideline awareness was 83.0%, whereas moderate-or-higher use was 54.7%. Inadequate knowledge affected 35.1% and guideline-discordant management 44.4%. Low use was most strongly associated with inadequate knowledge (aPR = 1.98, 95% CI 1.69–2.32) and guideline-discordant management (aPR = 1.77, 95% CI 1.54–2.04). Absence of guideline awareness, low annual case exposure, and absence of postgraduate specialist training were also associated with both outcomes after adjustment.

Conclusion: Guideline awareness did not consistently translate into routine use, and low use was the factor most strongly associated with inadequate knowledge and guideline-discordant management.

Keywords: guideline adherence; health knowledge; attitudes. practice; hyperemesis gravidarum; physicians, primary care; practice guidelines as topic

Pre-proof Med Clas (Zenica)

INTRODUCTION

Nausea and vomiting are among the most common problems of early pregnancy, but at the severe end of the spectrum they become hyperemesis gravidarum (HG), a condition that is more than an exaggerated form of morning sickness. Recent international consensus has defined HG by its clinical features rather than by counts of vomiting episodes: symptoms beginning in early pregnancy, at least one severe component, an inability to eat or drink normally, and a marked effect on daily functioning (1). Contemporary guidance stresses that HG must be recognised and managed across every level of care, from the community and outpatient clinic to the hospital ward (2).

HG complicates approximately 0.3–3% of pregnancies and is a leading cause of hospital admission in the first trimester (3). Dehydration, electrolyte disturbance, weight loss, and nutritional depletion can progress to severe maternal morbidity (4), and unrecognised thiamine deficiency may result in Wernicke encephalopathy (5). More severe or prolonged disease has been associated with adverse perinatal outcomes (6) and longer-term offspring morbidity (7), while psychological effects, including anxiety, depression, and impaired maternal-infant bonding, are increasingly recognised (8). Early recognition and timely treatment therefore matter for symptom control and maternal-foetal prognosis.

Physicians providing first-contact care occupy a decisive position in this pathway because pregnant women may initially present outside specialist obstetric care (2). The first-contact physician often assesses symptom severity, oral intolerance, the need for differential diagnosis, and whether early treatment is warranted. Current guidance notes that early treatment may reduce severe complications and hospital admissions (2). However, knowledge, confidence, and perceptions of medicine safety in primary care are not uniformly adequate, and available guidance is not consistently reflected in practice (9).

Pre-proof Med Clas (Zenica)

HG is also frequently assessed by subjective impression rather than a standard measure. Brief instruments such as the 24-hour Pregnancy-Unique Quantification of Emesis and Nausea (PUQE-24) scale can structure that assessment, and a validated Turkish version is available (10). Nevertheless, such tools are used inconsistently in routine practice.

The aim of this study was to distinguish guideline awareness from routine use, assess HG-related knowledge and guideline-discordant management using study-specific scores, and identify physician- and practice-related factors associated with inadequate knowledge and discordant management among first-contact physicians in Türkiye.

MATERIAL AND METHODS

Study design and setting

This multicentre cross-sectional survey was conducted between September 2025 and February 2026 among physicians providing first-contact assessment for pregnancy-related symptoms in Türkiye. Eligibility required active clinical practice and involvement in pregnancy follow-up or the initial assessment and management of nausea and vomiting in pregnancy (NVP) or HG. The study population was therefore defined by the participants' first-contact clinical role rather than by a specific specialty designation or practice setting. Physicians who did not provide electronic informed consent, were not in active clinical practice, submitted duplicate questionnaires, or left the principal outcome items incomplete were excluded.

Participants were recruited using a non-probability convenience/voluntary sampling approach through institutional mailing lists and professional communication networks across 28 healthcare institutions representing all seven geographical regions of Türkiye. A total of 1,540 physicians considered potentially eligible were invited. Because eligibility could be formally verified only among respondents, the eligibility status of non-respondents could not be established individually. Therefore, the proportion of analysed participants among all

Pre-proof Med Clas (Zenica)

invitees is reported as an analytic participation proportion rather than an eligible response rate. Study size was determined pragmatically by including all eligible completed questionnaires obtained during the study period. The first questionnaire page was accessed by 1,186 physicians, 1,129 provided electronic informed consent and initiated the survey, and 1,068 questionnaires were submitted. After exclusion of 11 duplicate submissions, nine responses from physicians who did not meet the eligibility criteria, and 23 questionnaires with incomplete principal-outcome data, 1,025 participants entered the final analysis. The final analytic sample represented 1,025/1,540 (66.6%) of invited physicians, and the completion rate among consenting physicians was 1,068/1,129 (94.6%) (Figure 1). Institutions contributed a median of 31 respondents (IQR 20–47); the largest single centre contributed 79 participants (7.7% of the analytic sample). Regional distribution was Central Anatolia, 312 (30.4%); Marmara, 201 (19.6%); Aegean, 128 (12.5%); Mediterranean, 110 (10.7%); Black Sea, 104 (10.1%); Eastern Anatolia, 92 (9.0%); and Southeastern Anatolia, 78 (7.6%).

The study was approved by the Ethics Committee of Ankara Atatürk Sanatorium Training and Research Hospital (approval number E-53610172-799-310990957). Electronic informed consent was obtained from all participants. The study was conducted in accordance with the Declaration of Helsinki and reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement (**11**).

Methods

The questionnaire was developed by the investigators to capture clinically relevant aspects of HG recognition and management reflected in contemporary guidance. Because no validated Turkish instrument existed for assessing first-contact physicians' HG knowledge and management, the knowledge and management scores were treated as study-specific measures rather than validated diagnostic instruments. The draft was reviewed for content, clarity, and

Pre-proof Med Clas (Zenica)

clinical relevance by two obstetricians, one family-medicine specialist, and one epidemiologist, and was pilot-tested in 25 physicians who were not part of the final study population. Minor wording changes followed piloting, but no items were added or removed. The final questionnaire contained six sections: participant characteristics; clinical experience and annual NVP/HG exposure; awareness and use of clinical guidelines; diagnostic assessment and symptom-severity evaluation; treatment and supportive-care practices; and referral, hospitalisation, and guideline-development needs. Participant characteristics included age, sex, duration of professional experience, self-reported postgraduate specialist training, institution type, and geographical region. Clinical-practice items assessed annual patient volume, follow-up practices, use of structured symptom-assessment tools, assessment of hydration and nutritional status, treatment preferences, and referral or hospitalisation criteria. Postgraduate specialist training was recorded as a binary professional characteristic and was not an eligibility criterion.

Guideline awareness was defined by an affirmative answer to whether the participant was aware of any national or international clinical guideline concerning NVP or HG. The frequency of guideline use was assessed using six categories: never, rarely, occasionally, moderately, frequently, and very frequently. Never, rarely, or occasionally was classified as low guideline use; moderately, frequently, or very frequently was classified as moderate-or-higher use. Guideline awareness and use were treated as distinct constructs, as physicians may follow recommendations acquired through clinical training, local protocols, or other professional sources without recognising or being aware of a specific national or international guideline. Frequent and very frequent use were additionally combined as high-frequency use. HG-related knowledge was assessed using 10 dichotomously scored items grouped into seven clinically relevant domains: recognition of disease severity, impaired oral intake, functional limitation, maternal clinical deterioration, standardised symptom assessment, treatment

Pre-proof Med Clas (Zenica)

safety, and referral-related decision-making. The items assessed whether the physician recognised (1) severe nausea and vomiting beginning in early pregnancy as a possible presentation of HG; (2) inability to maintain normal oral intake as a central diagnostic feature; (3) marked restriction of daily activities as an indicator of clinically important disease; (4) dehydration and clinically significant weight loss as signs of deterioration; (5) electrolyte abnormalities and nutritional compromise as potential complications; (6) the role of a structured severity tool such as the PUQE score; (7) that ketonuria alone should not determine disease severity; (8) the availability of guideline-supported antiemetic treatment in pregnancy; (9) the need for thiamine before dextrose-containing fluids in prolonged vomiting; and (10) the principal indications for referral, hospital assessment, or treatment escalation.

Each guideline-concordant response scored 1 point; incorrect, non-concordant, or “do not know” answers scored 0. The total ranged from 0 to 10. Inadequate knowledge was primarily defined as a score below 70% of the maximum (≤ 6). Because this threshold was pragmatic and not previously validated, sensitivity analyses used scores below 60% (≤ 5) and below 80% (≤ 7). Internal consistency of the dichotomous items was evaluated with the Kuder–Richardson 20 (KR-20) coefficient, together with corrected item-total correlations and the coefficient after deletion of each item.

Guideline-discordant management was evaluated using four clinical-practice components: (1) absence of a structured or standardised method for assessing symptom severity; (2) absence of routine objective assessment of hydration, nutritional status, or clinically relevant laboratory abnormalities; (3) reliance on a non-standardised treatment strategy inconsistent with a stepwise guideline-based approach; and (4) absence of predefined referral, hospitalisation, or treatment-escalation criteria. Each discordant component scored 1 point

Pre-proof Med Clas (Zenica)

(range 0–4). The primary outcome was the presence of at least two discordant components; participants with zero or one component were classified as relatively guideline-concordant. Guideline use was deliberately excluded from the management outcome and analysed only as an explanatory variable, so that the outcome and one of its principal associated factors did not overlap. Because the four components represent distinct clinical behaviours rather than interchangeable indicators of a single latent construct, the management score was treated as a formative composite. Sensitivity analyses redefined the outcome using at least one and at least three discordant components.

The following physician- and practice-related variables were examined as factors potentially associated with inadequate knowledge and guideline-discordant management: age group, sex, postgraduate specialist training, institution type, duration of professional experience, annual NVP/HG exposure, guideline awareness, and guideline use. Annual exposure was categorised as fewer than 5 versus 5 or more cases per year. Institution type was categorised as state hospital, private clinic or private hospital outpatient service, university hospital, or other, with university hospitals as the reference. Guideline awareness and guideline use were kept as separate variables because awareness of a guideline's existence does not imply its routine use; their correlation and potential multicollinearity were examined before entry into the multivariable models.

Statistical analysis

Categorical variables were summarised as numbers and percentages, and knowledge and management scores as mean ± standard deviation (SD), median (IQR), and range. Group comparisons used the chi-square or Fisher exact test for categorical variables and the Mann–Whitney U test for scores. Because both outcomes were common, modified Poisson regression with a log link and robust variance estimated crude and adjusted prevalence ratios (PRs and aPRs) with 95% confidence intervals (CIs) (12). Multivariable models included age,

Pre-proof Med Clas (Zenica)

sex, postgraduate specialist training, institution type, annual NVP/HG exposure, guideline awareness, and guideline use, selected a priori on clinical grounds; professional experience was excluded because of its strong correlation with age. Robust standard errors were clustered by institution, and multicollinearity was assessed using variance inflation factors (VIFs) and tolerance, with VIF > 5 or tolerance < 0.20 considered potentially problematic. Companion logistic models assessed discrimination by area under the receiver operating characteristic curve (AUC) and calibration by intercept, slope, calibration plot, and Brier score, with internal validation using 1,000 bootstrap resamples. Alternative outcome thresholds were examined descriptively. Missing values were not imputed and multivariable analyses used complete cases. All tests were two-sided with $p < 0.05$ considered statistically significant. Analyses were performed using IBM SPSS Statistics version 25.0 (IBM Corp., Armonk, NY, USA) and R version 4.3.2 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Of 1,540 invited physicians, 1,129 consented and initiated the questionnaire and 1,068 submitted a completed questionnaire; after exclusion of 43 responses, 1,025 physicians were analysed (analytic participation proportion 66.6%) (Figure 1). Most participants were male, 703 (68.6%). The most frequent age categories were 30–39 years, 362 (35.3%), and 40–49 years, 340 (33.2%); 91 (8.9%) were younger than 30 years, 190 (18.5%) were 50–59 years, and 42 (4.1%) were aged 60 years or older. Postgraduate specialist training was reported by 301 (29.4%). Most worked in state hospitals, 722 (70.4%); private clinics or private hospital outpatient services accounted for 175 (17.1%), university hospitals for 85 (8.3%), and other or incompletely reported institutions for 43 (4.2%). Annual NVP/HG exposure was limited: 749 (73.1%) evaluated fewer than five cases per year and 260 (25.4%) evaluated five or more; exposure was unavailable for 16 (1.6%) (Table 1).

Pre-proof Med Clas (Zenica)

Guideline awareness was reported by 851 physicians (83.0%), while 174 (17.0%) were unaware of any relevant guideline. Moderate-or-higher use was reported by 561 (54.7%), whereas 464 (45.3%) reported no, rare, or occasional use, and only 180 (17.6%) reported frequent or very frequent use. The distance between awareness and moderate-or-higher routine use was 28.3 percentage points. Awareness and use were moderately associated: 61.1% of aware physicians reported moderate-or-higher use, versus 23.6% of unaware physicians ($p<0.001$).

The mean knowledge score was 7.24 ± 1.72 (median 7; IQR 6-9; range 0–10). Guideline-concordant responses were most frequent for recognition of severe early-pregnancy nausea and vomiting, impaired oral intake, and marked functional limitation. Concordance was lower for dehydration and weight loss, electrolyte or nutritional complications, guideline-supported antiemetics, and referral or escalation criteria. It was lowest for thiamine before dextrose-containing fluids, the role of a structured severity tool, and recognition that ketonuria alone should not define severity (Figure 2). The KR-20 coefficient was 0.71 (95% CI 0.68–0.74); corrected item-total correlations ranged from 0.24 to 0.52, and deletion of any single item did not materially improve internal consistency. Using the primary threshold (≤ 6), 360 physicians (35.1%) had inadequate knowledge; corresponding values were 145 (14.1%) at the ≤ 5 threshold and 553 (54.0%) at the ≤ 7 threshold (Table 2).

Inadequate knowledge was more frequent among physicians without postgraduate specialist training (290/724, 40.1%) than with it (70/301, 23.3%; $p < 0.001$), and among those evaluating fewer than 5 cases annually (290/749, 38.7%) than 5 or more (60/260, 23.1%; $p < 0.001$). It was present in 240/464 physicians with low use (51.7%) versus 120/561 with moderate-or-higher use (21.4%; $p < 0.001$), and in 100/174 unaware physicians (57.5%) versus 260/851 aware physicians (30.6%; $p<0.001$). Prevalence was 39.7% below 40 years and 31.5% at 40 or older ($p = 0.006$), with no significant difference by sex.

Pre-proof Med Clas (Zenica)

In the primary modified Poisson model (n = 1,009 complete cases), low guideline use was most strongly associated with inadequate knowledge, aPR = 1.98 (95% CI 1.69–2.32; p < 0.001). Absence of guideline awareness, aPR = 1.31 (95% CI 1.13–1.52; p < 0.001); annual exposure below five cases, aPR = 1.29 (95% CI 1.10–1.51; p = 0.002); and absence of postgraduate specialist training, aPR = 1.32 (95% CI 1.13–1.54; p < 0.001), also remained associated with the outcome after adjustment. Age below 40 years and male sex were not associated, and neither state- nor private-setting practice differed significantly from university practice (Table 3). The maximum VIF was 1.82 and the minimum tolerance was 0.55; awareness and use had VIFs of 1.74 and 1.79, respectively.

Alternative knowledge thresholds classified 145/1,025 participants (14.1%) as having inadequate knowledge at the ≤ 5 threshold and 553/1,025 (54.0%) at the ≤ 7 threshold (Table 2). These thresholds are reported descriptively because complete inferential estimates were not available for all alternative-threshold models. For the primary modified Poisson model, Pearson χ^2/df was 1.04 and no observation had a Cook distance > 0.03. The companion logistic model had an apparent AUC = 0.77 (95% CI 0.74–0.80), a calibration intercept of -0.01, a slope of 0.96, and a Brier score of 0.194; after 1,000 bootstrap resamples, the optimism-corrected AUC was 0.76 and the calibration slope was 0.93.

Absence of a structured symptom-severity method was reported by 587 physicians (57.3%), absence of a predefined referral or hospitalisation framework by 469 (45.8%), absence of routine objective hydration, nutritional, or laboratory assessment by 424 (41.4%), and reliance on a non-standardised treatment strategy by 338 (33.0%). Using the primary definition (≥ 2 components), guideline-discordant management was identified in 455 physicians (44.4%); 570 (55.6%) had zero or one component. Alternative definitions classified 702 physicians (68.5%) as discordant at the ≥ 1-component threshold and 223 (21.8%) at the ≥ 3-component threshold (Table 2).

Pre-proof Med Clas (Zenica)

Guideline-discordant management was present in 300/464 physicians with low use (64.7%) versus 155/561 with moderate-or-higher use (27.6%; $p < 0.001$); in 115/174 unaware physicians (66.1%) versus 340/851 aware physicians (40.0%; $p < 0.001$); in 365/749 low-exposure physicians (48.7%) versus 80/260 higher-exposure physicians (30.8%; $p < 0.001$); and in 360/724 physicians without postgraduate specialist training (49.7%) versus 95/301 with postgraduate specialist training (31.6%; $p < 0.001$). By institution type it occurred in 340/722 state-hospital physicians (47.1%), 75/175 private-setting physicians (42.9%), 22/85 university-hospital physicians (25.9%), and 18/43 physicians in other institutions (41.9%).

In the adjusted modified Poisson model, low guideline use remained most strongly associated with guideline-discordant management, aPR = 1.77 (95% CI 1.54–2.04; $p < 0.001$). Absence of guideline awareness, aPR=1.23 (95% CI 1.08–1.40; $p = 0.001$); annual exposure below five cases, aPR = 1.25 (95% CI 1.09–1.43; $p = 0.003$); and absence of postgraduate specialist training, aPR = 1.27 (95% CI 1.11–1.45; $p = 0.001$), remained associated with the outcome after adjustment. State-hospital practice had a higher prevalence than university-hospital practice, aPR = 1.38 (95% CI 1.05–1.81; $p = 0.020$), whereas private practice did not differ significantly, aPR = 1.22 (95% CI 0.91–1.64; $p = 0.174$). Neither age below 40 years nor male sex was associated with the outcome (Table 3). The maximum VIF was 1.86 (minimum tolerance 0.54).

For the primary modified Poisson model, Pearson χ^2/df was 1.05, with no evidence of overdispersion. The companion logistic model for guideline-discordant management had an apparent AUC = 0.79 (95% CI 0.76–0.82), a calibration intercept of -0.02, a slope of 0.95, and a Brier score of 0.181; bootstrap correction gave an AUC = 0.78 and a slope of 0.92. In sensitivity analyses, low guideline use remained associated with guideline-discordant management at the ≥ 1-component threshold, aPR = 1.42 (95% CI 1.31–1.54; $p < 0.001$), and at the ≥ 3-component threshold, aPR = 2.03 (95% CI 1.65–2.49; $p < 0.001$) (Table 2).

Pre-proof Med Clas (Zenica)

DISCUSSION

This multicentre survey identified a substantial gap between awareness of HG guidance and its routine use. Low guideline use showed the strongest association with both inadequate HG-related knowledge and guideline-discordant management, while postgraduate specialist training and greater case exposure were also associated with lower outcome prevalence. Similar primary-care research has identified uneven confidence and medicine-safety knowledge and a relationship with clinical training and obstetric experience (9).

The cross-sectional design precludes temporal or causal inference; physicians with stronger knowledge may be more likely to consult guidelines, just as routine consultation may reinforce knowledge. Guideline use was analysed separately from the management composite to avoid direct overlap between an explanatory variable and the outcome. Modified Poisson regression was used because both outcomes were common and prevalence ratios are directly interpretable for common binary outcomes (12).

The item-level findings indicate where education may be most useful. Recognition of the core clinical presentation was generally strong, whereas knowledge of thiamine administration, structured severity assessment, and the limited role of ketonuria was weaker. Failure to administer thiamine before dextrose-containing fluids in prolonged vomiting has clinically important consequences because it may precipitate Wernicke encephalopathy (5). Current consensus also indicates that ketonuria alone should not define HG severity (1). These gaps correspond to concrete clinical decisions rather than isolated factual knowledge.

Our findings add to the limited primary care literature on HG. In a cross-sectional study of general practitioners in Wales, confidence and medicine-safety knowledge were uneven, while additional training and obstetric experience were associated with greater confidence (9). We observed a similar relationship with exposure and training, but in a larger sample and with guideline awareness distinguished from routine use. Although differences between

Pre-proof Mea Glas (Zenica)

settings limit direct comparison, the similar pattern warrants further investigation of barriers to guideline implementation in first-contact care.

Recent evidence offers both reassurance and practical challenges. Comparative evidence remains limited, with no clear efficacy advantage between commonly used agents such as ondansetron and metoclopramide (13). First-line doxylamine-pyridoxine has support from a randomised trial (14), and a defined inpatient pathway is available for refractory disease (3). The challenge in primary care is therefore to use a safe medicine at the appropriate step, recognise clinical deterioration, and identify when outpatient management is no longer suitable.

Inability to maintain oral intake, marked dehydration, electrolyte disturbance, intolerance of oral antiemetics, and clinical deterioration are accepted indications for escalation (2). The frequent absence of a predefined referral or hospitalisation framework in this sample may contribute to inconsistent referral decisions.

These findings support evaluation of implementation-focused interventions. Awareness campaigns alone may be insufficient when awareness is already high. A brief structured severity instrument such as PUQE-24 is available in Turkish (10). Current guidance also provides practical recommendations for treatment, thiamine administration, and referral or hospitalisation thresholds (2). Non-specialists, clinicians with low case exposure, and those who rarely consult guidelines may be priority groups for implementation-focused education.

Several limitations should be considered. The cross-sectional design precludes temporal and causal inference, and self-reported responses may overestimate guideline-concordant behaviour because of social desirability. The knowledge and management scores were study-specific and were not externally validated; the thresholds were pragmatic, and misclassification remains possible. The management score was a formative composite of distinct clinical behaviours and was therefore not treated as a unidimensional latent scale.

Pre-proof Med Clas (Zenica)

Voluntary participation may have selected physicians with greater interest in HG, potentially underestimating the observed gaps. Residual confounding is possible, and findings from one country may not be generalisable to other healthcare systems. These constraints should be considered when comparing the findings with previous survey-based primary-care research on HG (9).

CONCLUSION

In this multicentre survey, a gap between guideline awareness and routine use was evident. Low guideline use, limited case exposure, and absence of postgraduate specialist training were associated with inadequate knowledge and guideline-discordant management. Practical tools for objective severity assessment, safe stepwise treatment, thiamine administration, and referral decisions may support first-contact care. Prospective and intervention studies are needed to determine whether these strategies improve practice.

Pre-proof Med Clas (Zenica)

ACKNOWLEDGEMENTS

The authors thank all physicians who participated in the survey for their time and contributions.

FUNDING

No external funding was received for this study.

CONFLICTS OF INTEREST

None to declare.

ETHICS STATEMENT

The study was approved by the Ethics Committee of Ankara Atatürk Sanatorium Training and Research Hospital (approval number E-53610172-799-310990957). Electronic informed consent was obtained from all participants, and the study was conducted in accordance with the Declaration of Helsinki.

AUTHOR CONTRIBUTIONS

Conceptualization, M.E.N., H.K.G. and E.Y.; Methodology, M.E.N. and H.K.G.; Formal Analysis, M.E.N. and H.K.G.; Writing – Original Draft Preparation, M.E.N.; Writing – Review & Editing, M.E.N., H.K.G. and E.Y.; Supervision, E.Y. All authors read and approved the final version of the manuscript.

DATA AVAILABILITY STATEMENT

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Pre-proof Med Glas (Zenica)

REFERENCES

1. Jansen LAW, Koot MH, Van 't Hooft J, Dean CR, Bossuyt PMM, Ganzevoort W, et al. The Windsor definition for hyperemesis gravidarum: a multistakeholder international consensus definition. Eur J Obstet Gynecol Reprod Biol 2021;266:15–22. doi: 10.1016/j.ejogrb.2021.09.004.
2. Nelson-Piercy C, Dean C, Shehmar M, Gadsby R, O'Hara M, Hodson K, et al. The management of nausea and vomiting in pregnancy and hyperemesis gravidarum (Green-top Guideline No. 69). BJOG 2024;131:e1–30. doi: 10.1111/1471-0528.17739.
3. Clark SM, Zhang X, Goncharov DA. Inpatient management of hyperemesis gravidarum. Obstet Gynecol 2024;143:745–58. doi: 10.1097/AOG.0000000000005518.
4. Zerbo A, Kang-Auger S, Jutras G, Brousseau É, Healy-Profitós J, Auger N. Hyperemesis gravidarum and risk of severe maternal morbidity: a retrospective cohort study. Am J Obstet Gynecol MFM 2024;6:101392. doi: 10.1016/j.ajogmf.2024.101392.
5. Fiorentini M, Nedu B, Dapoto F, Brunelli E, Pilu G, Youssef A. When time is brain: a systematic review about Wernicke encephalopathy as a dramatic consequence of thiamin deficiency in hyperemesis gravidarum. J Matern Fetal Neonatal Med 2023;36:2223678. doi: 10.1080/14767058.2023.2223678.
6. Jansen LAW, Nijsten K, Limpens J, van Eekelen R, Koot MH, Grooten IJ, et al. Perinatal outcomes of infants born to mothers with hyperemesis gravidarum: a systematic review and meta-analysis. Eur J Obstet Gynecol Reprod Biol 2023;284:30–51. doi: 10.1016/j.ejogrb.2023.03.004.

Pre-proof Med Glas (Zenica)

7. Auger N, Padda B, Bégin P, Brousseau É, Côté-Corriveau G. Hyperemesis gravidarum and the risk of offspring morbidity: a longitudinal cohort study. Eur J Pediatr 2024;183:3843–51. doi: 10.1007/s00431-024-05647-8.
8. Yang G, Hisada A, Yamamoto M, Kawanami A, Mori C, Sakurai K, et al. Effect of nausea and vomiting during pregnancy on mother-to-infant bonding and the mediation effect of postpartum depression: the Japan Environment and Children's Study. BMC Pregnancy Childbirth 2023;23:704. doi: 10.1186/s12884-023-06014-5.
9. Nana M, Morgan H, Ahmed H, Williamson C. Hyperemesis gravidarum in the primary care setting: cross-sectional study of GPs. BJGP Open 2022;6:BJGPO.2021.0119. doi: 10.3399/BJGPO.2021.0119.
10. Yilmaz T, Dinç Kaya H, Günaydin S, Güdücü N, Dişsiz M. Psychometric properties of the Pregnancy-Unique Quantification of Emesis (PUQE-24) Scale. J Obstet Gynaecol 2022;42:1739–45. doi: 10.1080/01443615.2022.2036961.
11. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. Lancet 2007;370:1453–7. doi: 10.1016/S0140-6736(07)61602-X.
12. Zou G. A modified Poisson regression approach to prospective studies with binary data. Am J Epidemiol 2004;159:702–6. doi: 10.1093/aje/kwh090.
13. Vinnars MT, Forslund M, Claesson IM, Hedman A, Peira N, Olofsson H, et al. Treatments for hyperemesis gravidarum: a systematic review. Acta Obstet Gynecol Scand 2024;103:13–29. doi: 10.1111/aogs.14706.
14. Wu XK, Gao JS, Ma HL, Wang Y, Zhang B, Liu ZL, et al. Acupuncture and doxylamine-pyridoxine for nausea and vomiting in pregnancy: a randomised,

Pre-proof Med Clas (Zenica)

controlled, 2 × 2 factorial trial. Ann Intern Med 2023;176:922–33. doi: 10.7326/M22-2974.

Pre-proof Med Glas (Zenica)

TABLES AND FIGURES

Table 1. Participant and practice characteristics (N = 1,025)

Characteristic	n (%)
Sex	
Male	703 (68.6)
Female	322 (31.4)
Age group, years	
< 30	91 (8.9)
30–39	362 (35.3)
40–49	340 (33.2)
50–59	190 (18.5)
≥ 60	42 (4.1)
Postgraduate specialist training	
Yes	301 (29.4)
No	724 (70.6)
Institution type	
State hospital	722 (70.4)
Private clinic/private hospital outpatient service	175 (17.1)
University hospital	85 (8.3)
Other/incompletely reported	43 (4.2)
Geographical region	
Central Anatolia	312 (30.4)
Marmara	201 (19.6)
Aegean	128 (12.5)
Mediterranean	110 (10.7)
Black Sea	104 (10.1)
Eastern Anatolia	92 (9.0)
Southeastern Anatolia	78 (7.6)
Annual NVP/HG exposure	
< 5 cases/year	749 (73.1)
≥ 5 cases/year	260 (25.4)
Not reported	16 (1.6)
Guideline awareness	
Aware	851 (83.0)
Not aware	174 (17.0)
Guideline use	
Low (never/rarely/occasionally)	464 (45.3)
Moderate-or-higher	561 (54.7)
Of whom frequent/very frequent	180 (17.6)

HG, hyperemesis gravidarum; NVP, nausea and vomiting in pregnancy.

Pre-proof Med Glas (Lenica)

Table 2. Internal consistency, sensitivity analyses, and model diagnostics

Parameter	Value
Inadequate HG-related knowledge model	
Internal consistency, KR-20	0.71 (0.68–0.74)
Corrected item-total correlations	0.24–0.52
Prevalence, threshold ≤ 6 (primary)	360/1,025 (35.1%)
Prevalence, threshold ≤ 5	145/1,025 (14.1%)
Prevalence, threshold ≤ 7	553/1,025 (54.0%)
Maximum VIF (awareness 1.74; use 1.79)	1.82 (tolerance ≥ 0.55)
Companion logistic AUC	0.77 (0.74–0.80)
Calibration intercept/slope/Brier score	-0.01/0.96/0.194
Bootstrap-corrected AUC/slope (1,000 resamples)	0.76/0.93
Pearson χ^2/df	1.04
Guideline-discordant management model	
Prevalence, ≥ 2 components (primary)	455/1,025 (44.4%)
Prevalence, ≥ 1 component	702/1,025 (68.5%)
Prevalence, ≥ 3 components	223/1,025 (21.8%)
Low use aPR, ≥ 1-component definition	1.42 (1.31–1.54); p < 0.001
Low use aPR, ≥ 3-component definition	2.03 (1.65–2.49); p < 0.001
Maximum VIF	1.86 (tolerance ≥ 0.54)
Companion logistic AUC	0.79 (0.76–0.82)
Calibration intercept/slope/Brier score	-0.02/0.95/0.181
Bootstrap-corrected AUC/slope	0.78/0.92
Pearson χ^2/df	1.05

Alternative knowledge thresholds are presented descriptively because complete inferential estimates were unavailable for all alternative-threshold models. For alternative management definitions, only low-use estimates with complete 95% CIs and p values are shown.

Table 3. Principal factors associated with inadequate HG-related knowledge and guideline-discordant management

Inadequate HG-related knowledge				
Factor	**Inadequate, n/N (%)**	**Crude PR (95% CI)**	**aPR (95% CI)**	**p**
Low guideline use	240/464 (51.7)	2.42 (2.02–2.90)	1.98 (1.69–2.32)	< 0.001
Absence of guideline awareness	100/174 (57.5)	1.88 (1.60–2.21)	1.31 (1.13–1.52)	< 0.001
Annual exposure < 5 cases/year	290/749 (38.7)	1.68 (1.32–2.13)	1.29 (1.10–1.51)	0.002
Absence of postgraduate specialist training	290/724 (40.1)	1.72 (1.38–2.15)	1.32 (1.13–1.54)	< 0.001
Guideline-discordant management				
Factor	**Discordant, n/N (%)**	**Crude PR (95% CI)**	**aPR (95% CI)**	**p**
Low guideline use	300/464 (64.7)	2.34 (2.01–2.72)	1.77 (1.54–2.04)	<0.001
Absence of guideline awareness	115/174 (66.1)	1.65 (1.45–1.89)	1.23 (1.08–1.40)	0.001
Annual exposure < 5 cases/year	365/749 (48.7)	1.58 (1.30–1.93)	1.25 (1.09–1.43)	0.003
Absence of postgraduate specialist training	360/724 (49.7)	1.58 (1.31–1.89)	1.27 (1.11–1.45)	0.001

Both multivariable models additionally included age, sex, and institution type as adjustment covariates and used 1,009 complete cases. University hospital, age ≥ 40 years, and female sex were the reference categories for the corresponding adjustment covariates.

PR, prevalence ratio; aPR, adjusted prevalence ratio; CI, confidence interval.

Pre-proof Med Gras (Zambia)

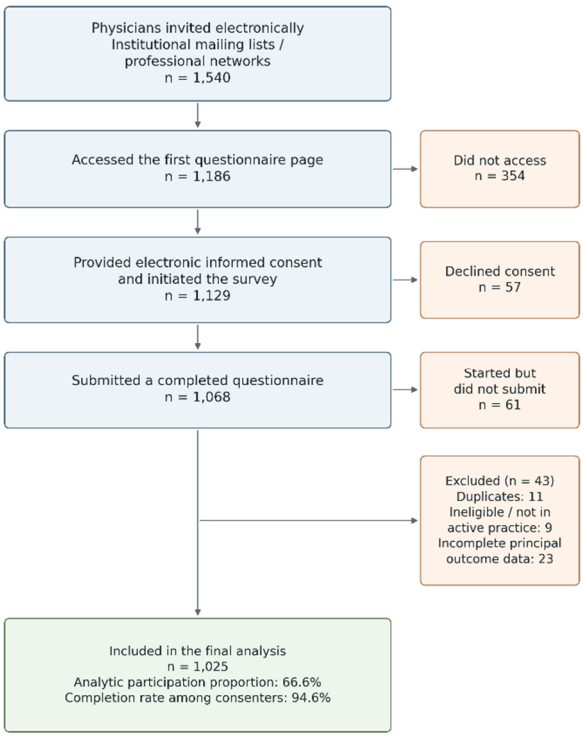


Figure 1. Participant recruitment and flow.

Glas (Zenica)

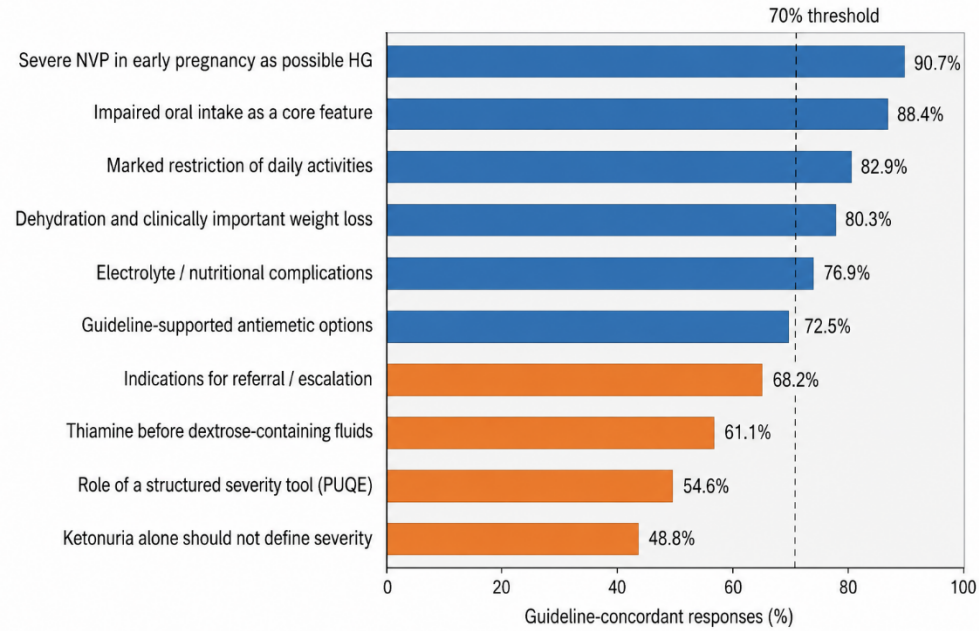


Figure 2. Item-level guideline-concordant knowledge across the 10-item score (n = 1,025). Bars below the 70% threshold (dashed line) indicate the weakest items.