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# Prospective cohort study of vitamin D deficiency in pregnancy: Prevalence and limited effectiveness of 1000 IU vitamin D supplementation

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## Abstract

**Background:** Vitamin D deficiency is highly prevalent worldwide among pregnant women. Although vitamin D supplementation is effective in improving vitamin D status, the safety and optimal dosing of vitamin D supplementation during pregnancy remain less well understood.

**Objective:** This study aimed to investigate the prevalence of vitamin D deficiency among pregnant women and evaluate the effectiveness of vitamin D supplementation in improving vitamin D status during pregnancy.

**Design:** This prospective cohort study assessed the impact of a 16-week daily vitamin D supplementation 1000 IU regimen on vitamin D status among pregnant women.

**Methods:** A total of 365 pregnant women were recruited, and their baseline total circulating 25-hydroxy vitamin D concentrations were measured. Of these, 249 participants completed the study, which involved oral daily supplementation with 1000 IU of vitamin D and a repeat of total circulating 25-hydroxy vitamin D concentrations after 16 weeks.

**Results:** The study found that 57.7% of the participants had vitamin D deficiency, consistent with the rates reported in other studies. However, vitamin D supplementation at a dose of 1000 IU had a small effect size and was not clinically significant. However, 67% of participants with vitamin D deficiency remained deficient; among participants initially with vitamin D insufficiency, 30% became deficient. Moreover, 26.5% of individuals with sufficient vitamin D status at 12 weeks showed insufficient levels by 28 weeks.

**Conclusion:** Vitamin D deficiency is widespread among pregnant women, and vitamin D supplementation at a daily dose of 1000 IU may not adequately address this problem. Although the study has limitations, its results align with previous research and may apply to other populations with a high prevalence of vitamin D deficiency during pregnancy. Further research is necessary to determine the most effective approach for addressing prenatal vitamin D deficiency.

## Plain Language Summary

### Prevalence and effectiveness of vitamin D supplementation during pregnancy

Vitamin D deficiency is common among pregnant women and can lead to various health issues. This study aimed to investigate the effectiveness of vitamin D supplementation in improving vitamin D levels during pregnancy. A total of 365 pregnant women were recruited, and their vitamin D levels were measured at the beginning of the study. The participants were given a daily vitamin D supplement of 1000 IU, and their vitamin D levels were measured at 3-month intervals. The study found that more than half of the participants had vitamin D deficiency, which is consistent with the rates reported in other studies. However, vitamin D supplementation at the given dosage had a small effect and

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did not significantly increase vitamin D levels in pregnant women. Moreover, vitamin D-rich diets had no significant impact on vitamin D levels. The study emphasizes the importance of identifying effective strategies for preventing and treating vitamin D deficiency during pregnancy. The findings suggest that current strategies advised by international and national guidelines may not be sufficient to address the problem. Further research is needed to identify more effective approaches, including screening, higher safe dosages, and monitoring responses after 3 months of treatment. In summary, vitamin D deficiency is common among pregnant women, and current strategies may not be enough to address the issue. The study highlights the need for effective approaches to prevent and treat vitamin D deficiency during pregnancy, and further research is needed to find these strategies.

**Keywords**
pregnant women, vitamin D deficiency, vitamin D status, vitamin D supplementation

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## Introduction

Vitamin D is a fat-soluble vitamin that plays a crucial role in bone health, immune function and regulating calcium and phosphate levels in the body.[1,2] The majority of international endocrine guidance defines vitamin D sufficiency as serum levels of 25(OH)D of more than 50 nmol/L (20 ng/mL), although it should be noted that there are differing opinions on the desirable levels. For instance, the Institute of Medicine (IOF) recommends a desired level greater than 50 nmol/L (20 ng/mL). In comparison, the Endocrine Society and other prominent researchers advocate for a minimum level of at least 75 nmol/L (30 ng/mL).[3–5] Vitamin D is produced in the skin in response to sunlight exposure, diet and supplements.[6]

Vitamin D deficiency during pregnancy has been a subject of increasing interest in the scientific literature in recent years, given the vital role vitamin D plays in supporting health and the high prevalence of vitamin D deficiency in pregnant women.

### *Global research supports a high prevalence of vitamin D deficiency and more so in pregnancy*

Global research indicates high prevalence rates of vitamin D deficiency. In Europe, Deficiency varied from 6.6% to 60%, as reported in the European position statement published in 2019.[3] A recent systematic review reported that the overall prevalence of low vitamin D status in Africa was 34.2%. The Asian population is not much luckier, with a systematic review specific to the Indian population suggesting a lower pooled estimate of 32.4%. Studies from the Middle East are scarcer but report higher prevalence, with the most recent studies in Qatar reporting vitamin D deficiency in more than 70% of adults.[3,7–9]

Higher deficiency rates are more likely in specific populations, such as those with darker skin, those living in northern latitudes, and those with limited sun exposure. It was found that there were several countries (Afghanistan, Pakistan, India, Tunisia, Syria, the West Bank and Gaza and Mongolia) classified as 'hot spots' for exceptionally low vitamin D status.[10]

Studies show that mean serum 25(OH)D concentrations were lower in women than men and higher rates of deficiency in pregnant women.[11] A global systematic review conducted in 2016 found that the prevalence of 25(OH) $D \leqslant 50$ nmol/L in pregnant women by WHO region was Americas (64%), Europe (57%), Eastern Mediterranean (46%), South-East Asia (87%) and Western Pacific (83%).[12] In South Asian countries, another systematic review of literature considered original research on pregnant women reported an overall prevalence of deficiency of 76% among females.[13,14]

Vitamin D deficiency during pregnancy has been linked to several adverse outcomes for the mother and the developing foetus. Vitamin D deficiency in pregnancy has been associated with an increased risk of gestational diabetes, preeclampsia and preterm birth.[15–18] In addition, vitamin D deficiency in pregnant women has been linked to a higher risk of low birth weight, which can have long-term health consequences for the infant.[19,20]

### *Vitamin D screening and supplementation recommendations in pregnancy vary significantly across international guidelines*

Vitamin D screening and supplementation recommendations in pregnancy vary significantly across international guidelines. All international guidelines agree that there is a clear knowledge gap and a need for unambiguous evidence on the effectiveness, dosing and best timing of initiating vitamin D supplements in the pregnant population.

The WHO 2020 guidelines recommend that no vitamin D supplements are needed in the population with normal levels. WHO recommends administering 200 IU vitamin D

supplements to pregnant women with suspected vitamin D deficiency.[21]

The American College of Obstetrics and Gynaecology does not recommend screening in a normal population. They report that 1000–2000 IU is safe.[22]

The National Health Service (NHS) England employs a pragmatic approach with no clear guidance on screening or testing. The guidelines recommend 400 IU units per day for pregnant women if they are not getting enough sun exposure, especially between September and March. They advise against doses of more than 4000 IU per day as it may be harmful.[23]

British Columbia guidelines, Canada, recommend 400–600 IU for pregnant women and higher doses for women at higher risk of deficiency. They did not specify the maximum safe dose.[24]

All international guidelines agree that there is a clear knowledge gap and a need for unambiguous evidence on the effectiveness, dosing and best timing of initiating vitamin D supplements in the pregnant population. Concerns about maximum safe dose drive a conservative approach to dose, but it may equally be driving untherapeutic dosing, which does not address the problem.

Note: All the above international guidelines are deployed in nations with low vitamin D deficiency prevalence and different public health interventions, including fortified food and milk products.

### *LOCAL context*

Despite the abundant sunlight in countries such as Qatar, Vitamin D deficiency is highly prevalent across the Middle East.[25–29] A 2012 systematic review found that deficiency rates were over 90%, but the reviews used $< 75$ (nmol/L) levels rather than $< 50$ (nmol/L) levels, which is the current approved level.[30] More recent reports specific to Qatar, which use the approved level by the Endocrine Society, suggest a deficiency rate of 71% in the population.[9]

Only one study reports on vitamin D status among postpartum women in Qatar, which found a prevalence of 78%.[31]

In Qatar, pregnant women are routinely screened for vitamin deficiency at 12 weeks, and local guidelines recommend a daily dose of 1000 IU of vitamin D throughout the pregnancy. However, there is a lack of research evaluating the effectiveness of vitamin D supplementation during pregnancy, and no studies have reported on the prevalence of vitamin D deficiency in pregnant women attending primary health care in Qatar.

Due to the limited research conducted in the Middle East, there is a need for a study that specifically examines the response to a daily dose of 1000 IU of vitamin D. The primary objective of this study is to evaluate how pregnant women respond to the standard dose of 1000 IU of vitamin D, which is routinely prescribed during the initial antenatal visit at 12 weeks, by retesting their total circulating 25(OH) D concentrations at the last antenatal visit at 28 weeks.

As a result, this research can provide valuable insights at both a national and global level. By analysing the effectiveness of the current vitamin D supplementation protocol and the prevalence of vitamin D deficiency among pregnant women, this study may contribute to enhancing prenatal care in Qatar and other regions worldwide.

The study aims to accomplish the following:

1. Determines the vitamin D status among the pregnant population during the initial antenatal visit at 12 weeks, which is included in the antenatal care package (routine care).
2. Measures the total circulating 25(OH)D concentrations at 28 weeks of pregnancy as part of the follow-up care, which will be added to routine care.
3. Estimates the effectiveness of the routine vitamin D supplement (1000 IU) per day administered from 12 weeks of pregnancy until 28 weeks.
4. Examines the associations between the second vitamin D measurement and various dietary intake components that may impact total circulating 25(OH)D concentrations during the antenatal period. To accomplish this, a survey tool will be employed at the time of the second measurement.

## Methods

This prospective cohort study aims to observe vitamin D status during the first 12 weeks of pregnancy as part of routine care. All participants were offered a reassessment of vitamin D status 16 weeks after starting vitamin D tablets, and serum 25-hydroxy vitamin D concentration was measured quantitatively. The recruitment of cases and the follow-up period spanned from 28 February 2021 to 28 February 2022. We included all pregnant women in the first trimester (up to 12 weeks of pregnancy) who attended the booking visit in primary health care settings in Qatar. Conversely, pregnant women in the high-risk group, such as those with chronic diseases or advanced maternal age, were excluded from the study.

To determine the sample size, the previous year's number of pregnancies in the study population was considered. This population consisted of approximately 1500 pregnant women who received care at primary care health centres over 1 year (2019–2020). A simple random sampling technique was employed to select participants who met the inclusion criteria.[32] The sample size was calculated using the 'Sample Size for Frequency in a Population' formula. Based on a 90% confidence interval, the study required a sample size of 230 patients.

As the biomarker of vitamin D status, total circulating 25(OH)D concentration as a measure of vitamin D status was measured using Abbott Architect 25-OH-D vitamin D

immunoassay. Vitamin D deficiency was defined as a concentration less than 50 nmol/L, and vitamin D insufficiency as a concentration less than 75 nmol/L. All women received routine care, including a prescription for vitamin D (1000 IU) in the form of ergocalciferol (vitamin D3) dispensed from PHCC pharmacy.

Information on ethnicity, history of vitamin D deficiency, vitamin D intake and dietary habits was obtained through face-to-face interviews after the second visit. A semi-quantitative food frequency questionnaire was used to assess vitamin D dietary intake. Participants were queried regarding their adherence to a high vitamin D diet as part of their daily routine. Those who answered affirmatively were asked to provide information on the frequency of their consumption. The questionnaire employed in this study underwent piloting and pre-testing to ensure the relevance and clarity of the questions. However, it is essential to note that the questionnaire was not formally validated. The study received ethical approval from the Primary Health Care Corporation ethics committee. The STROBE reporting guideline was employed for this observational study.[33]

The study population consisted of 365 patients, of whom 249 completed the study. The power of the results was calculated given the sample size, observed effect and a 5% error margin. The study outcomes measured vitamin D levels (25-hydroxyvitamin D) in ng/mL at 12 and 28 weeks of pregnancy. Dietary vitamin D intake was assessed using a validated questionnaire that included four foods: oily fish, milk, yoghurt and margarine.[34]

The Primary Health Care Corporation IRB approved the study with the reference number PHCC/DCR/2020/09/104. All study participants consented to participate and were informed of their right to withdraw at any time.

### *Statistical analysis*

Descriptive analyses of all variables, including continuous and categorical variables, were conducted for all study participants. Mean, range and standard deviations were reported for continuous variables, while numbers and percentages were reported for categorical variables. A Wilcoxon test was used to examine for statistical and clinical differences before and after vitamin D intervention for patients with two measures at 12 and 28 weeks. A contingency table was used to show variations in different vitamin D categories before and after the intervention. The Mann–Whitney U test was used to evaluate whether consumption of distinct types of diet had an impact on vitamin D status at 28 weeks.

## Results

We recruited a total of 365 pregnant females during the spring of 2022. The mean age was $30 \pm 4.1$ years. The mean of population weight was $68.4 \pm 12.9$ kg. The vast majority were from the Middle East (48%) and Asia and Pacific (47.1%). However, 60% of study participants had PMH of vitamin D deficiency. In addition, 249 cases had two total circulating 25(OH)D concentrations done at 12 and 28 weeks and filled the final survey. Reasons for dropouts varied between miscarriage, abortion and follow-up in other health care facilities.

Total circulating 25(OH)D concentrations at 12 weeks had a mean of $19 \pm 10.5$ ng/mL. Vitamin D categories were 58% for vitamin D deficiency, 28% vitamin D insufficiency and only 14% of study participants had sufficient levels.

At 28 weeks visit, the mean of total circulating 25(OH)D concentrations post-treatment was $21 \pm 9.9$ ng/mL. However, 47% of participants continued to have vitamin D deficiency, and only 21% achieved sufficient levels.

Overall, 90% reported taking their prescribed vitamin D 1000 IU more than three times per week. Only 18% were considered to have adequate sun exposure, and more than 80% to have a diet rich in vitamin D (Table 1).

For the 249 cases that had two samples done, the data were not normally distributed. The Wilcoxon rank t-test

**Table 1.** Descriptive analysis of study participants and outcomes.

| Characteristics | Overall (N = 365) |
|---|---|
| Age | |
| N-Miss | 86 |
| Mean (SD) | 30.0 (4.1) |
| Range | 20.0–40.0 |
| Region | |
| Africa | 11 (3.0%) |
| Asia and Pacific | 172 (47.1%) |
| Europe | 6 (1.6%) |
| Middle East | 175 (47.9%) |
| South/Latin America | 1 (0.3%) |
| PMH f Vit D | |
| N-Miss | 130 |
| No | 94 (40.0%) |
| Yes | 141 (60.0%) |
| Malabsorption problems, e.g. coeliac disease, inflammatory bowel | |
| N-Miss | 41 |
| No | 319 (98.5%) |
| Do not know | 4 (1.2%) |
| Yes | 1 (0.3%) |
| Descriptive of total circulating 25(OH)D concentrations at 12 and 28 weeks' levels and categories | |
| Vit D first visit | |
| N-Miss | 32 |
| Mean (SD) | 19.0 (10.5) |
| Range | 4.0–73.0 |
| First category | |
| N-Miss | 32 |
| Deficiency | 192 (57.7%) |
| Insufficiency | 93 (27.9%) |
| Sufficiency | 48 (14.4%) |

*(Continued)*

**Table 1.** (Continued)

| Characteristics | Overall (N = 365) |
|---|---|
| Taken Vitamin D 1000 IU daily as recommended by physician | |
| N-Miss | 132 |
| Always (everyday) | 184 (79.0%) |
| Often (more than three times /day) | 25 (10.7%) |
| Sometimes (three times /week) | 6 (2.6%) |
| Occasionally (once to twice /week) | 3 (1.3%) |
| Not at all | 15 (6.4%) |
| Vit D at 28 weeks | |
| N-Miss | 108 |
| Mean (SD) | 21.0 (9.9) |
| Range | 3.0–54.0 |
| Second vit D def categories | |
| N-Miss | 108 |
| Sufficiency | 56 (21.8%) |
| Deficiency | 119 (46.3%) |
| Insufficiency | 82 (31.9%) |
| Diet | |
| Fish | |
| N-Miss | 139 |
| Yes | 184 (81.4%) |
| No | 42 (18.6%) |
| Fish frequency | |
| N-Miss | 169 |
| At least twice a week | 28 (14.3%) |
| 3–4 times per month | 69 (35.2%) |
| 1–2 times per month | 72 (36.7%) |
| Seldom | 27 (13.8%) |
| Milk | |
| N-Miss | 138 |
| Yes | 193 (85.0%) |
| No | 34 (15.0%) |
| Milk frequency | |
| N-Miss | 164 |
| More than (400 mL) two cups per day | 67 (33.3%) |
| (200 mL) One cup per day | 92 (45.8%) |
| Less than one cup per day | 42 (20.9%) |
| Yogurt | |
| N-Miss | 131 |
| Yes | 184 (78.6%) |
| No | 50 (21.4%) |
| Yogurt frequency | |
| N-Miss | 179 |
| Less than one cup per day | 75 (40.3%) |
| One cup per day | 76 (40.9%) |
| More than two cups per day | 35 (18.8%) |
| Margarine | |
| N-Miss | 132 |
| Yes | 188 (80.7%) |
| No | 45 (19.3%) |
| Margarine frequency | |
| N-Miss | 176 |
| 4–7/week | 87 (46.0%) |
| 1–3/week | 65 (34.4%) |
| At least 4 /day | 2 (1.1%) |
| 2–3 /day | 8 (4.2%) |
| Fewer | 27 (14.3%) |

SD: standard deviation.

was used to compare the means. The comparison of both levels showed a statistically significant $p < 0.05$ change in vitamin D status but with an effect size 0.235 and a mean difference of 2.00 suggesting non-clinically significant impact (Table 2).

Following the intervention period, it was observed that a significant proportion of patients who initially presented with vitamin D deficiency (67%) did not show improvement in their total circulating 25(OH)D concentrations. In addition, among the participants who had vitamin D insufficiency at the start, a notable percentage (30%) experienced a decline in their total circulating 25(OH)D concentrations, transitioning into a state of deficiency, despite receiving a daily supplement of 1000 IU for 16 weeks. Moreover, concerning individuals with sufficient vitamin D status at 12 weeks, a substantial proportion (26.5%) exhibited a decrease in their levels, falling into the insufficient range by the 28-week mark (Table 3).

The associations of consuming a vitamin D-rich diet, including butter, fish, eggs, and margarine, with vitamin D status at 28 weeks were examined using the Mann–Whitney U test. The results suggested a non-significant statistical association

## Discussion

### *Key results*

Our study's results support previous research indicating that vitamin D deficiency is common among pregnant women. Specifically, 60% of the study participants had a history of vitamin D deficiency, similar to the rates reported in other studies.[9,12,27,35] Our findings also indicate that vitamin D supplementation at a 1000 IU dose increases total circulating 25(OH)D concentrations in pregnant women, although the effect size is small and not clinically significant. This aligns with previous studies reporting mixed results regarding the effectiveness of vitamin D supplementation at that dose during pregnancy.[36–38]

Vitamin D metabolism undergoes significant changes during pregnancy compared to when a woman is not pregnant. A daily regimen of 1000 IU of vitamin D is likely to be insufficient, especially if it is the only source of the vitamin and not augmented by sunlight exposure. In contrast, a 4000 IU/day regimen is predicted to achieve better sufficiency levels safely. This point is underscored when considering that neonates and infants are often prescribed a 400 IU/day dose, which, on a per-kilogram basis, far exceeds what a 60-kg woman would receive with a 1000 IU/day regimen. Moreover, dietary sources of vitamin D offer limited benefits compared to sunlight or higher-dose supplementation.

### *Limitations*

Our study has some limitations that should be considered when interpreting the results. First, our study was conducted

**Table 2.** Wilcoxon W test for total circulating 25(OH)D concentrations at 12 and 28 weeks.

| All study participants | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Statistic | p | Mean difference | SE difference | 95% confidence interval | | | Effect size |
| | | | | | | Lower | Upper | | |
| Vit D 12 weeks | Vit D 28 weeks | 8881[a] | 0.003 | −2.00 | 0.563 | −3.00 | −0.50 | Rank-biserial correlation | 0.235 |

SE: standard error.
[a]34 pair(s) of values were tied.

**Table 3.** Contingency table.

| First category | | Second vit D def categories | | | Total |
|---|---|---|---|---|---|
| | | Sufficiency | Deficiency | Insufficiency | |
| Deficiency | Count | 19 | 95 | 28 | 142 |
| | % Within row | 13.4% | 66.9% | 19.7% | |
| Insufficiency | Count | 9 | 22 | 42 | 73 |
| | % Within row | 12.3% | 30.1% | 57.5% | |
| Sufficiency | Count | 25 | 0 | 9 | 34 |
| | % Within row | 73.5% | 0.0% | 26.5% | |
| Total | Count | 53 | 117 | 79 | 249 |
| | % Within row | 21.3% | 47.0% | 31.7% | |

in a single geographic region, which may limit the generalizability of our findings. Second, we relied on self-reported data for compliance and food diaries, which may be subject to recall bias. Also, one limitation of this study is that the questionnaire used was not validated or pre-tested. Finally, we did not control for potential confounding variables, such as sun exposure or skin pigmentation, which may have influenced our results.

### *Interpretation and implications*

Our study adds to the growing evidence that vitamin D deficiency is a common issue among pregnant women. However, our findings suggest that the current strategy recommended by international and national guidelines, which includes vitamin D supplementation at a dose of 1000 IU or less, may not be sufficient to address the problem.

Many randomized controlled trials have shown that vitamin D3 supplementation at 4000 IU per day during pregnancy is effective and safe.[39–41] This dosage has been linked to reduced risks of preeclampsia and caesarean sections without adverse effects on women's health. Recent reviews, such as the one by Mansur et al.,[42] have further emphasized the significance of maintaining sufficient vitamin D status during pregnancy, given the associated risks and complications. These findings underscore the importance of considering vitamin D status for promoting maternal and neonatal health.

More research is needed to identify the most effective strategies for preventing and treating vitamin D deficiency during pregnancy. This may include screening for deficiency, using higher safe dosages of supplementation, and monitoring responses after 3 months of treatment.

### *Generalizability*

Although our study was conducted in a specific geographic region, our results are consistent with previous research on this topic, suggesting that our findings may apply to other populations, especially those where vitamin D deficiency during pregnancy is prevalent. Nevertheless, further research is necessary to confirm our results in larger, more diverse samples.

## Conclusion

In this prospective cohort study conducted in Qatar, we aimed to observe the 25-hydroxy vitamin D status in early pregnancy. Out of the initial 365 pregnant females, 249 completed the study. Following a 16-week intervention with a daily supplement of 1000 IU of vitamin D, it was found that 47% of participants remained deficient, and only 21% achieved sufficient levels. Interestingly, even individuals who initially had sufficient levels experienced a decline, with 26.5% becoming insufficient by 28 weeks.

The study highlights the challenges in improving vitamin D status during pregnancy, as many participants did not experience improvement or even showed a decline in levels. The current intervention strategies, including

supplementation of daily 1000 IU of vitamin D and dietary intake, need to be revised. Further research is required to explore alternative intervention strategies, higher dosage supplements and the underlying factors contributing to persistent deficiency. Addressing vitamin D deficiency during pregnancy is crucial for improving maternal and foetal health outcomes.

## Declarations

### *Ethics approval and consent to participate*

The Primary Health Care Corporation IRB approved the study with the PHCC/DCR/2020/09/104 reference number. All study participants signed a written consent to participate and to publish their anonymous data. All participants were informed of their right to withdraw at any time.

### *Consent for publication*

All participants provided consent to publish their anonymous data collected during the study.

### *Author contribution(s)*

**Rasha Mohammed Abdelmageed:** Conceptualization; Methodology; Project administration; Writing – original draft; Writing – review & editing.
**Suha Majeed Mohammed Hussein:** Conceptualization; Data curation; Methodology; Writing – review & editing.
**Shamil Mohamed Anamangadan:** Conceptualization; Data curation; Formal analysis; Investigation; Writing – review & editing.
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**Lubna Rauf:** Conceptualization; Data curation; Formal analysis; Methodology; Writing – review & editing.
**AlAnoud Saleh AlFehaidi:** Conceptualization; Data curation; Formal analysis; Methodology; Writing – review & editing.
**Ehab Hamed:** Conceptualization; Formal analysis; Methodology; Supervision; Validation; Writing – original draft; Writing – review & editing.

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### *Competing interests*

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### *Availability of data and materials*

All data included in the study are property of Primary Health Care Corporation, Qatar and are available following organizational approval as per institutional policies.

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## Supplemental material

Supplemental material for this article is available online.

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