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# Prevalence of menopausal symptoms among young gestational trophoblastic neoplasia survivors and its relationship to their health-related quality of life

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**Abstract:**

**BACKGROUND:** Since the advent of chemotherapy, cure rates for gestational trophoblastic neoplasia (GTN) have improved significantly. With increased survival, patients must cope with long-term sequelae of their treatment, including early menopause. Unlike natural menopause, treatment-induced menopause may cause a sudden and dramatic decline in estrogen, which can lead to more severe symptoms.

**OBJECTIVES:** This study aimed to evaluate the prevalence of menopausal symptoms among young GTN survivors and to determine the impact of these symptoms on their health-related quality of life (QoL).

**METHODOLOGY:** Ninety GTN survivors (<45 years old) treated from 2012 to 2022 were asked to answer the modified Menopause Rating Scale and the European Organization for Research and Treatment of Cancer QoL Questionnaire Core 30 questionnaires. Treatment records were reviewed for the chemotherapy regimen and the presence of adjunctive procedures. A series of Chi-square tests were performed to compare characteristics between those with symptoms and those without. Logistic regression models were generated to estimate odds ratios of reporting menopausal symptoms.

**RESULTS:** A total of 90 patients were enrolled in the study with a mean age of 33.06 years. Majority (81.1%) reported at least one menopausal symptom. The most prevalent symptoms were psychological symptoms, followed by somatic, then urogenital problems. Among those with an intact uterus, 8.2% reported permanent amenorrhea. Only Stage III/IV and the presence of total hysterectomy were significantly associated with menopausal symptoms. The presence of menopausal symptoms was significantly associated with poorer health-related QoL among the respondents.

**CONCLUSION:** Menopausal symptoms are prevalent among young GTN survivors, and these negatively affect their health-related QoL. Emphasis should be placed on recognizing and addressing these symptoms. Adjunctive procedures, especially hysterectomy, should be carefully considered because these are significantly associated with menopausal symptoms.

**Keywords:**

Chemotherapy, gestational trophoblastic neoplasia, menopause

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## Introduction

Gestational trophoblastic neoplasia (GTN) encompasses a heterogeneous group of malignant neoplasms that arise from abnormal trophoblastic proliferation.[1] The cornerstone of the management of GTN is chemotherapy – single-agent chemotherapy for nonmetastatic and low-risk metastatic patients and combination chemotherapy for metastatic high-risk cases.[2]



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Since the advent of chemotherapy, cure rates for GTN have improved significantly, with 78.4% of patients treated in Philippine General Hospital (PGH) from 2014 to 2018 achieving complete remission.[3] With increased survival rates, cancer survivors must cope with long-term sequelae of their cancer and its treatment, including the possibility of early menopause. A cross-sectional study in the United Kingdom found that compared to controls, menopause occurred 3 years earlier in GTN patients who received chemotherapy.[4] In another survey of 1903 GTN patients given chemotherapy in Charing Cross Hospital, the incidence of menopause occurring before 40 years old and 45 years old was found to be 13% and 36%, respectively, in those given multiagent chemotherapy.[5] Unlike in natural menopause wherein estrogen and androgen decline gradually, treatment-induced menopause causes a sudden and dramatic decline in hormonal levels. This may cause more frequent and more severe symptoms of menopause, such as hot flashes, insomnia, vaginal atrophy, depression, mood swings, cardiac symptoms, and osteoporosis.[6]

### Objectives

In spite of the growing evidence that chemotherapy hastens menopause in GTN survivors, data on the frequency of menopausal symptoms, as well as its effects on the quality of life (QoL) of GTN survivors, are sparse. The general objective of this study was to determine the prevalence of menopausal symptoms among young GTN patients who underwent chemotherapy in a tertiary government hospital and to determine the relationship of these symptoms to their health-related QoL. The specific objectives include: (1) to determine the prevalence of menopausal symptoms in GTN survivors, (2) to describe the clinicopathologic profile of the GTN survivors, (3) to identify clinical factors that may affect the incidence of menopausal symptoms, and (4) to determine the health-related QoL of GTN survivors.

## Methodology

A cross-sectional study was conducted among young (<45 years old) GTN patients in remission who were treated in a tertiary government hospital from January 2012 to December 2021. Those who were currently pregnant, were taking menopausal hormone therapy, or who underwent bilateral salpingo-oophorectomy were excluded from the study. The sample size was calculated at 90 respondents based on a level of significance of 5%, a power of 80%, and an assumed small effect size (0.2). The institution's patient registry was reviewed for eligible respondents. Patients were invited to answer two questionnaires either via Google Forms or in person. The details of each respondent's clinical course, such as stage, prognostic score, age at diagnosis, chemotherapeutic agents used, number of cycles, dose and date of remission, and presence of any adjunctive procedure were obtained from the division's records.

### Study tools

The respondents were asked to answer two structured questionnaires. The first one, the Modified Menopause Rating Scale, was composed of 11 questions which were divided into three categories – somatic, psychological, and urogenital. Each question was graded according to the absence or presence of the symptom.[7] This modified version was previously translated to Tagalog and validated in a local study which assessed the prevalence of climacteric symptoms in Filipino women aged 40 years old and above in Metro Manila.[8] The second questionnaire, the European Organization for Research and Treatment of Cancer Core Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) (version 3), consists of 30 questions: 15 questions covering five functional domains (physical, social, role, cognitive, and emotional); 13 items devoted to cancer-related symptoms (fatigue, nausea/vomiting, pain, dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial difficulties); 1 global health status question; and 1 overall QoL question. Responses to the items under the five functional domains and cancer-related symptoms were rated on a 4-point scale, whereas responses to the two global health and QoL questions were rated on a 7-point scale. For each scale, the responses to the questions under this particular scale were averaged to get a raw score. All raw scores then underwent linear transformation to produce the score, which ranged from 0 to 100. A higher score in the functional domains and global health scales meant a higher level of functioning, while a higher score for the symptomatology scale translated to a higher level of problems.[9] A Tagalog version of this questionnaire, which has been validated in a sample of Filipino patients with various cancer diagnoses, was used.[10]

### Data analysis

The sample population was dichotomized into those who reported at least one menopausal symptom, and otherwise. The clinicodemographic characteristics were presented using the median and interquartile range (IR) for the scales, while frequency and percentage were used for the remaining categorical variables such as disease stage, risk, or time in remission. A series of Chi-square tests were performed to compare clinicodemographic characteristics between those who did or did not report any menopausal symptoms. Independent *t*-test and median test were used to compare the age at diagnosis between those who underwent total hysterectomy. For the EORTC scales, Kruskal–Wallis and Wilcoxon rank-sum procedures were performed to compare the ratings in the scale ratings between similar groups.

Unadjusted and adjusted logistic regression models were generated to estimate the odds ratios, and its 95% confidence intervals, of reporting menopausal symptoms. The adjusted model also controlled for the effects of predetermined variables, specifically age at diagnosis, disease stage, risk score, chemotherapy regimen, and other EORTC scales. The level of significance for all sets of analysis was set at $P < 0.05$ using two-tailed comparisons.

### Ethics approval

This study was approved by the institutional ethics review board. Informed consent was obtained from the respondents.

## Results

A total of 90 patients were recruited and enrolled in the study. The mean age of the respondents was 33.06 ± 6.19 years, and their mean age at diagnosis was 27.91 ± 6.54 years. The majority had Stage III disease (62.22%) and were considered high risk (53.33%). The most common chemotherapy regimen given was methotrexate (65.56%), followed by etoposide, methotrexate, actinomycin D, cyclophosphamide, and vincristine (EMACO) (53.33%), and then actinomycin (12.22%). Thirty-two respondents (35.6%) received more than one chemotherapy regimen. Twenty-three respondents (25.6%) received 5-day methotrexate chemoprophylaxis before developing GTN, which was considered in this study as one cycle of chemotherapy. Thirty-four respondents (37.8%) underwent an adjunctive procedure, the most common of which was total hysterectomy (18.89%). Majority underwent at least 5 cycles of chemotherapy (94.44%) and had been in remission for less than 5 years (53.33%). Table 1 summarizes the characteristics data of the respondents.

Majority of the respondents reported at least one menopausal symptom (81.11%). The most frequently reported symptoms were psychological symptoms, such as physical and mental exhaustion (62.22%) and irritability (53.33%) [Table 2]. Almost half of the respondents reported somatic symptoms – namely joint and muscular discomfort (46.67%), difficulty sleeping (37.78%), and chest discomfort (37.78%). The least frequently reported symptoms were urogenital problems, with only 32.22% reporting sexual problems, 15.6% reporting vaginal dryness, and only 14.44% reporting urinary difficulties. Among those with an intact uterus ($n = 73$), only 6 respondents reported cessation of menstruation for at least 1 year (8.2%). The current age of those with amenorrhea ranged from 24 to 38 years old, with a mean age of 29.6 years.

All respondents who underwent total hysterectomy reported menopausal symptoms ($n = 17$). Among the respondents without any menopausal symptoms ($n = 17$), none underwent hysterectomy. The presence of hysterectomy was significantly higher among those who reported menopausal symptoms than those who did not (23.9% vs. 0, $P < 0.05$). There were also significantly more respondents with Stage III and IV disease among those who reported menopausal symptoms ($P < 0.05$).

There was a higher proportion of respondents with menopausal symptoms among those given methotrexate and EMACO. All respondents who were given Etoposide-Actinomycin (EA) and Methotrexate-Etoposide-Actinomycin (MEA) also exhibited menopausal symptoms. Furthermore, a higher proportion of symptomatic respondents received >5 cycles of chemotherapy. However, these observations were not statistically significant [Table 1].

Based on adjusted logistic regression analysis, only disease stage was associated with the presence of menopausal symptoms [Table 3]. The likelihood of reporting menopausal symptoms was approximately eight times more likely among women with Stage III and Stage IV disease compared to those with Stage I and Stage II disease (odds ratio: 7.86, confidence interval: 1.13–54.37, $P < 0.05$). The wide confidence interval estimate can be attributed to the sparse distribution of menopausal symptoms across specific disease stages and the limited number of observations. The presence of total hysterectomy, which was highly correlated with the presence of menopausal symptoms, was not included in the adjusted analysis because it would introduce threats to validity in the findings. To a certain extent, the odds of reporting menopausal symptoms also increased approximately three-fold as the number of actinomycin cycles increased by one. However, this association was not statistically significant due to the limited number of observations.

The median global health status/QoL score of the respondents was 83.33 (IR 66.67–100). In general, the respondents had high scores in the functional scales. The highest score was for social functioning (median 100; IR 100–100) and role functioning (median 100; IR 83.33–100). The lowest score was for emotional functioning, with a median score of 83.33 and IR score of 58.33–100. In terms of symptom scale, high overall median scores (i.e., more bothersome symptoms) were observed for fatigue (22.22) and pain (16.67). Except for social functioning, which had a high median score for all respondents, respondents with menopausal symptoms had significantly lower functional scale scores than those without symptoms. For the symptoms scale, respondents with menopausal symptoms had higher median scores in the scales of pain, fatigue, and insomnia, compared

**Table 1: Characteristics of the study population stratified across menopausal symptoms**

| Characteristics | Overall, *n* (%) | Menopausal symptoms | | *P* |
|---|---|---|---|---|
| | | Absent, *n* (%) | Present, *n* (%) | |
| *n* (%) | 90 (100) | 17 (18.89) | 73 (81.11) | - |
| Current age (years) | | | | |
| 20–29 | 29 (32.22) | 2 (11.76) | 27 (36.99) | 0.07 |
| 30–39 | 47 (52.22) | 13 (76.47) | 34 (46.58) | |
| 40–44 | 12 (16.44) | 2 (11.76) | 12 (16.44) | |
| Age at diagnosis (years) | | | | |
| 20–29 | 51 (56.67) | 7 (41.18) | 44 (60.27) | 0.14 |
| 30–39 | 35 (38.89) | 10 (58.82) | 25 (34.25) | |
| 40–44 | 4 (4.44) | - | 4 (5.48) | |
| Disease stage | | | | |
| I | 22 (24.44) | 7 (41.18) | 15 (20.55) | 0.03* |
| II | 1 (1.11) | 1 (5.88) | - | |
| III | 56 (62.22) | 9 (52.94) | 47 (64.38) | |
| IV | 11 (12.22) | - | 11 (15.07) | |
| Risk score | | | | |
| <7 | 42 (46.67) | 8 (47.06) | 34 (46.58) | 0.59 |
| ≥7 | 48 (53.33) | 9 (52.94) | 39 (53.42) | |
| Chemotherapy regimen | | | | |
| Methotrexate | 59 (65.56) | 12 (70.59) | 47 (64.38) | 0.63 |
| Actinomycin | 11 (12.22) | 1 (5.88) | 10 (13.70) | 0.38 |
| EMACO | 48 (53.33) | 9 (52.94) | 39 (53.42) | 0.97 |
| EP-EMA | 4 (4.44) | 2 (11.76) | 2 (2.74) | 0.10 |
| EP | 5 (5.56) | 1 (5.88) | 4 (5.48) | 0.95 |
| EA | 7 (7.78) | - | 7 (9.59) | 0.34 |
| MEA | 1 (1.11) | - | 1 (1.37) | 0.63 |
| Number of chemotherapy cycles | | | | |
| <5 | 5 (5.56) | 2 (11.76) | 3 (4.11) | 0.22 |
| ≥5 | 85 (94.44) | 15 (88.24) | 70 (95.89) | |
| Initial β-hCG value | | | | |
| <1000 | 10 (11.11) | 1 (5.88) | 9 (12.33) | 0.71 |
| 1000–<10,000 | 11 (12.22) | 3 (17.65) | 8 (10.96) | |
| 10,000–<100,000 | 32 (35.56) | 7 (41.18) | 25 (34.25) | |
| ≥100,000 | 37 (41.11) | 6 (35.29) | 31 (42.47) | |
| Presence of adjunctive procedure | | | | |
| Total hysterectomy | 17 (18.89) | - | 17 (23.29) | 0.03* |
| Bilateral internal iliac artery | 5 (5.56) | - | 5 (6.85) | 0.27 |
| Embolization | 3 (3.33) | - | 3 (4.11) | 0.40 |
| Intrathecal methotrexate | 1 (1.11) | - | 1 (1.37) | 0.63 |
| Whole brain radiation | 5 (5.56) | - | 5 (6.85) | 0.27 |
| Wedge resection | 2 (2.22) | - | 2 (2.74) | 0.49 |
| Oophorocystectomy | 1 (1.11) | - | 1 (1.37) | 0.63 |
| Time in remission | | | | |
| <5 | 48 (53.33) | 8 (47.06) | 40 (54.79) | 0.57 |
| ≥5 | 42 (46.67) | 9 (52.94) | 33 (45.21) | |

*A *P* value < 0.05 is considered statistically significant. EMACO: Etoposide, methotrexate, actinomycin D, cyclophosphamide, and vincristine, EA: Etoposide-Actinomycin, MEA: Methotrexate-Etoposide-Actinomycin, EP-EMA: Etoposide – Cisplatin - Methotrexate – Actinomycin

to those without symptoms ($P < 0.01$). To a certain extent, the median score for dyspnea was also higher in those with menopausal symptoms, though lacking in statistical significance. Finally, respondents with menopausal symptoms had significantly lower global health status/QoL median scores than those without symptoms (83.33 vs. 100, $P < 0.01$). Table 4 summarizes the EORTC QLQ-C30 scores of the respondents.

## Discussion

GTN is a rare but highly curable malignancy, with an overall cure rate of over 98%. Chemotherapy, which is the cornerstone of the treatment of GTN, is gonadotoxic and may affect ovarian function, potentially leading to infertility and early menopause.[11] Existing literature on early menopause in GTN has focused on investigating

**Table 2: Menopausal symptoms assessed by the modified Menopause Rating Scale stratified according to presence of hysterectomy**

| Characteristics | Overall (*n*=90), *n* (%) | Total hysterectomy | | *P* |
|---|---|---|---|---|
| | | Not done (*n*=73), *n* (%) | Done (*n*=17), *n* (%) | |
| Somatic | | | | |
| Hot flushes and sweating | 17 (18.89) | 10 (13.70) | 7 (41.18) | 0.01* |
| Heart discomfort | 34 (37.78) | 23 (31.51) | 11 (64.71) | 0.01* |
| Sleeping problems | 34 (37.78) | 26 (35.62) | 8 (47.06) | 0.38 |
| Joint and muscular discomfort | 42 (46.67) | 30 (41.10) | 12 (70.59) | 0.03* |
| Psychological | | | | |
| Depressive mood | 41 (45.56) | 32 (43.84) | 9 (52.94) | 0.50 |
| Irritability | 48 (53.33) | 37 (50.68) | 11 (64.71) | 0.30 |
| Anxiety | 17 (18.89) | 13 (17.81) | 4 (23.53) | 0.59 |
| Physical and mental exhaustion | 56 (62.22) | 43 (58.90) | 13 (76.47) | 0.18 |
| Urogenital | | | | |
| Sexual problems | 29 (32.22) | 21 (28.77) | 8 (47.06) | 0.15 |
| Bladder problems | 13 (14.44) | 9 (12.33) | 4 (23.53) | 0.24 |
| Dryness of vagina | 14 (15.56) | 9 (12.33) | 5 (29.41) | 0.08 |
| Amenorrhea >1 year | 6 | 6 | - | - |

*A *P* value < 0.05 is considered statistically significant

**Table 3: Factors associated with reported menopausal symptoms**

| Characteristics | Unadjusted OR | *P* | Adjusted OR | *P* |
|---|---|---|---|---|
| Age at diagnosis | 0.96 (0.89–1.04) | 0.35 | 1.00 (0.90–1.11) | 0.95 |
| Disease stage | | | | |
| Stage I/II | 1.00 | 0.03* | 1.00 | 0.04* |
| Stage III/IV | 3.44 (1.13–10.42) | | 7.86 (1.13–54.37) | |
| Risk score | | | | |
| <7 | 1.00 | 0.97 | 1.00 | 0.22 |
| ≥7 | 1.02 (0.35–2.94) | | 0.19 (0.01–2.67) | |
| Number of chemotherapy cycles | | | | |
| Methotrexate | 0.91 (0.78–1.05) | 0.19 | 0.74 (0.53–1.04) | 0.08 |
| Actinomycin | 1.21 (0.71–2.06) | 0.49 | 2.50 (0.90–6.89) | 0.08 |
| EMACO | 1.00 (0.89–1.12) | 0.97 | 0.95 (0.79–1.13) | 0.56 |

*A *P* value < 0.05 is considered statistically significant. OR: Odds ratio, EMACO: Etoposide, methotrexate, actinomycin D, cyclophosphamide, and vincristine

**Table 4: Median and interquartile range score on European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30, with stratification based on menopausal symptoms**

| Characteristics | Overall | Menopausal symptoms | | *P* |
|---|---|---|---|---|
| | | Absent | Present | |
| Global health status/QoL | 83.33 (66.67–100) | 100 (83.33–100) | 83.33 (66.67–100) | <0.01** |
| Functional scales | | | | |
| Physical | 93.33 (73.33–100) | 100 (93.33–100) | 86.67 (73.33–100) | <0.01** |
| Role | 100 (83.33–100) | 100 (100–100) | 100 (66.67–100) | <0.01** |
| Emotional | 83.33 (58.33–100) | 100 (100–100) | 75 (50–100) | <0.01** |
| Cognitive | 91.67 (66.67–100) | 100 (100–100) | 83.33 (66.67–100) | <0.01** |
| Social | 100 (100–100) | 100 (100–100) | 100 (83.33–100) | 0.06 |
| Symptom scales | | | | |
| Fatigue | 22.22 (0–44.44) | 0 (0–22.22) | 22.22 (11.11–44.44) | <0.01** |
| Nausea and vomiting | 0 | 0 | 0 | 0.46 |
| Pain | 16.67 (0–33.33) | 0 | 16.67 (0–33.33) | <0.01** |
| Dyspnea | 0 (0–33.33) | 0 | 0 (0–33.33) | 0.09 |
| Insomnia | 0 (0–33.33) | 0 | 0 (0–33.33) | <0.01** |
| Appetite loss | 0 | 0 | 0 (0–33.33) | 0.20 |
| Constipation | 0 | 0 | 0 | 0.47 |
| Diarrhea | 0 | 0 | 0 | 0.25 |
| Financial difficulties | 0 (0–33.33) | 0 | 0 (0–33.33) | 0.18 |

**A *P* value < 0.05 is considered statistically significant. QoL: Quality of life

the timing of menopause, which is defined as permanent cessation of menses for 12 consecutive months.[12] Few studies have evaluated the incidence and burden of menopausal symptoms among young GTN patients.

Our results showed that even though the mean age of our respondents was only 33 years, majority (81.1%) were already exhibiting at least one menopausal symptom. This suggests that these respondents could already be entering menopausal transition, or perimenopause, which has a median duration of 4 years.[13] GTN survivors should be counseled regarding the possibility and sequelae of early menopause. They should also be informed that it is possible to experience menopausal symptoms even without amenorrhea, as only 8.2% of respondents with an intact uterus reported amenorrhea.

In a survey of 360 Filipino women aged ≥40 years old, it was found that the most prevalent symptom among perimenopausal and menopausal women was joint and muscular discomfort.[8] Similarly, a survey of perimenopausal/menopausal breast cancer survivors in Korea found that somatic symptoms (e.g., joint and muscular discomfort and hot flushes) were the most significant symptoms.[14] In contrast, psychological symptoms (physical and mental exhaustion and irritability) were the most common symptoms among our respondents. Jewell *et al*. (2018) have shown that cancer-specific distress continues to have an effect on patients even after going into remission. Preoccupation with tumor marker (ß-hCG) surveillance, anxiety about tumor recurrence, and reproductive concerns have been shown to contribute to the perceived distress of GTN survivors. In addition, the trauma from having a possible pregnancy turn into a diagnosis of cancer could have a lasting psychological impact on them.[15] All GTN patients should be offered counseling upon diagnosis, and this should be continued until survivorship, if needed. These patients should also be regularly screened for signs of depression.

Multiagent chemotherapy with EMACO has been shown to increase the risk of early menopause in GTN patients.[5] In particular, increasing doses of etoposide and vincristine have been associated with a significant decrease in serum anti-Müllerian hormone (AMH) levels in GTN patients.[11] In contrast, our results showed that the type of chemotherapy regimen was not significantly associated with the frequency of menopausal symptoms. Even though menopausal symptoms were more frequent in our respondents who were given methotrexate and EMACO, our findings failed to reach statistical significance. This lack of significant association could perhaps be attributed to our limited sample size. The fact that 35.6% of the respondents were given more than one chemotherapy regimen could have also served as a confounder.

In our study, only Stage III/IV disease and total hysterectomy were found to be significantly associated with menopausal symptoms. Patients with more advanced disease have a higher tumor burden and thus require more chemotherapeutic drugs and more cycles of chemotherapy. Hysterectomy and irradiation, which are both potential contributors to early menopause, are also performed more frequently for these patients. Despite the lack of statistical significance in our study, the practice of giving multiagent chemotherapy to patients with more widespread disease still could have contributed to the association of Stage III/IV disease with menopausal symptoms.

We found that total hysterectomy was also significantly associated with menopausal symptoms. The indications for hysterectomy in the treatment of GTN are as follows: (1) decrease tumor burden and the number of chemotherapy cycles needed, (2) remove a chemo-resistant focus, (3) control life-threatening hemorrhage, (4) relieve obstruction, and (5) remove a focus of infection.[2] Total hysterectomy, even with ovarian preservation, has been associated with increased risk of premature ovarian failure, especially when performed at a younger age. It has also been linked to increased risk of cardiovascular events, lower urinary tract problems, osteoporosis, vasomotor symptoms, depression, and decline in cognitive function, which are all known sequelae of estrogen decline.[16] Hysterectomy has also been shown to result in a significant decrease in AMH, which is a marker for ovarian reserve. It is thought that hysterectomy diminishes ovarian blood flow and removes endocrine/paracrine signals from the uterus, leading to accelerated follicular depletion and early menopause.[17]

The median scores of our respondents in all the EORTC QLQ-C30 functional scales were above the published thresholds for clinical importance, indicating a high level of functioning.[18] For the symptoms scale, the highest median scores (more bothersome symptoms) were observed for fatigue and pain. However, these scores were still below the threshold for clinical importance. Overall, the median global health status/QoL score of our respondents (83.33) indicates that they have good health-related QoL. Despite this, it appears that the QoL of respondents with menopausal symptoms was significantly poorer than those without symptoms. Given the apparent impact of menopausal symptoms on the QoL of patients, physicians should give more importance to recognizing and treating these symptoms. It should also be made known to patients that pharmacologic interventions and lifestyle modifications exist to alleviate these menopausal symptoms.

## Conclusion

Menopausal symptoms are prevalent among young GTN survivors, suggesting that they may already be entering

the menopausal transition. These patients should thus be educated in the recognition of early menopause, and they should be encouraged to report these symptoms. Physicians should also prioritize the mental health concerns of these patients since the most common symptoms were psychological. Hysterectomy should be carefully considered, especially in young patients, since it is significantly associated with menopausal symptoms. Finally, recognition and treatment of menopausal symptoms should be foremost in these patients' survivorship care, as the presence of these symptoms negatively affects their health-related QoL.

## Limitations

The hormonal status of the respondents (e.g. AMH and follicle-stimulating hormone) were not assessed. The incidence of premature ovarian failure could not be determined due to the lack of biochemical markers needed to clinch the diagnosis. The results were obtained during a single point in time and could not be compared to pretreatment values. The results were also limited by the small sample size.

## Recommendations

Further studies may look into the hormonal status of respondents with menopausal symptoms. The prevalence of depression among GTN survivors should also be explored. The knowledge and attitude of GTN survivors toward menopausal hormone therapy should also be determined. It would also be beneficial to explore the reproductive outcomes of these patients, as our results showed that only 41% of those with an intact uterus were able to have additional children.

## Authorship contributions

Victoria May Velasco-Redondo - Involved in conceptualization, methodology, resources, data curation, writing of the original draft, review and editing.

Ma. Stephanie Fay S. Cagayan - Involved in supervision, review and editing of the draft.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

## Data availability statement

The data that support the findings of this study are available on request from the corresponding author VVR.

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