Gynecologic Oncology Reports 53 (2024) 101392

Contents lists available at ScienceDirect

Gynecologic Oncology Reports

journal homepage: www.elsevier.com/locate/gynor

Research Report

Mortality factors in high and ultra-high-risk gestational trophoblastic neoplasia at moi teaching & referral hospital: A decade-long observation in kenya

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ARTICLE INFO

Keywords:
Gestational trophoblastic neoplasia
Mortality
Ultrahigh risk
Chemotherapy

1. Background

GTN refers to persistent or malignant disorders originating from the abnormal proliferation of trophoblastic tissue, which may occur subsequent to a hydatidiform mole or a nonmolar pregnancy (Lurain, 2011). An accurate determination of the global prevalence of GTN remains a challenge due to inconsistencies in data reporting across different regions. Analysis of cancer registries in Africa indicated an average incidence of 0.38 cases per 100,000 women of reproductive age (Grimes, 1984) (Singh et al., 2021).

Patients diagnosed with GTN are typically categorized into risk groups according to the prognostic scoring system established by the World Health Organization (WHO): low risk (with a score of 0 to 6), high risk (with a score of 7 to 12), and ultrahigh risk (with a score $\geq$ 13) (Figo Oncology Committee, 2002). This system takes into account eight risk factors that predict the potential for developing resistance to single-agent chemotherapy with methotrexate (MTX) or actinomycin D (Act D). Low-risk patients exhibit an almost 100 % overall survival (OS) rate, whereas high-risk patients experience a survival rate ranging from 80 % to 90 % (Lurain, 2011). A score of $\geq$ 13 is associated with a heightened risk of early mortality, leading to recommendations for managing these patients in highly specialized GTN centers. High-risk GTN cases often originate from a normal pregnancy rather than a hydatidiform mole and are frequently linked to lung metastases and, occasionally, metastases to the brain and liver (Bolze et al., 2016).

Historically, prior to the introduction of effective chemotherapy regimens, GTN was almost invariably fatal. However, advances in chemotherapeutic agents for treatment have dramatically transformed GTN into a highly curable disease.

Despite these advances in the management of GTN, the burden of disease and outcomes from LMICs remain a concern, as mortality data are sparse. The development of strategies for improving GTN care in this setting is therefore a challenge. The inadequacies of healthcare infrastructure and poor accessibility to specialized GTN care could contribute to disparities in treatment outcomes in LMICs compared to those in the Global North.

The objective of this study was to determine the proportion of mortality in GTN patients and identify factors contributing to treatment failure over a 10-year period at the second largest tertiary healthcare facility in Kenya. This analysis seeks to highlight deficiencies in the management of GTN within a low-resource setting and provide valuable insights into areas requiring improvement.

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https://doi.org/10.1016/j.gore.2024.101392
Received 7 January 2024; Received in revised form 1 April 2024; Accepted 8 April 2024
Available online 16 April 2024
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2. Methods

2.1. Study setting

The study was carried out at the Chandaria Cancer and Chronic Diseases Centre (CCCDC) of MTRH in Eldoret, Kenya. The MTRH is the second largest referral hospital in Kenya and serves a population of more than 24 million people from the western parts of Kenya, eastern Uganda, and southern parts of South Sudan. The facility offers comprehensive gynecologic oncology services and serves as the major GTN Center within the region. In terms of treatment, the facility provides chemotherapy, radiotherapy, surgery, and supportive care services. Every week, the CCCDC attends to 50 to 60 patients with gynecologic cancers, approximately 5 % of whom have GTN. At the time of the study, MTRH was staffed with two consultant gynecologic oncologists and four fellows (gynecologic oncologists in training). The Gynecologic Oncology Team is responsible for conducting appropriate assessments, staging, and initiation of treatment.

2.2. Study design and methods

A retrospective review of the GTN database at MTRH was performed. The CCCDC database includes records of women diagnosed with GTN. Data from 1st January 2013 to 31st December 2022 were extracted. The patients' medical records were then traced and comprehensively reviewed for data collection. A data extraction form was used to collect information on demographic characteristics, including age, referral status, and pregnancy history, clinical presentation, treatment protocols/types of regimens, and outcomes (i.e., complications and survival status). These data were then entered into a secure electronic database and anonymized to maintain patient confidentiality. For women who were still undergoing follow-up, recent medical records were reviewed, and their treatment outcomes and survival statuses were updated.

Inclusion and exclusion criteria: Women who were diagnosed with high-risk or ultrahigh-risk GTN based on the WHO criteria were included in the study. Patients diagnosed with low-risk GTN and patients with incomplete data were excluded.

2.3. Data analysis

IBM SPSS Statistics for Windows, Version 28.0. The Armonk, NY: IBM Corp computer program was used for analysis. Descriptive statistics were generated for demographic, clinical, and treatment characteristics. Categorical variables were summarized as frequencies using non-parametric statistics. The association between mortality from GTN and covariates was assessed using the log-rank test. Cox regression modeling was used to assess the factors that were independently associated with mortality. Kaplan-Meier survival curves were used to describe the survival of participants after treatment. The crude and adjusted ratios as well as the corresponding 95 % confidence limits (95 % CL) and p values were reported. Differences were considered statistically significant at a p-value < 0.05.

2.4. Ethical consideration

Ethical approval was obtained from MTRH-MU IREC (approval number FAN: 0004496). The collected data were deidentified, and unique study patient identifiers were created. All electronic databases used in this study were protected by procedures consistent with applicable laws, directives, policies, regulations, and standards in Kenya.

3. Results

Between January 2013 and December 2022, a total of 155 women were diagnosed with GTN at MTRH. Utilizing the WHO prognostic scoring system, 20 of these women were classified as having ultrahigh-risk GTN, 16 resulting in mortality (80 %). Eighty women had high-risk disease, 15 of whom died (18.8 %). Fifty-five women who had low-risk disease were excluded from the study. Moreover, two medical records with incomplete data were excluded. A total of 98 participants were analyzed (Fig. 1).

Among the 98 high-risk and ultrahigh-risk GTN patients analyzed, 31 (31.6 %) died. A high proportion (74.2 %) of patients who died were younger than 40 years of age and were predominantly admitted as referrals from health facilities located outside Uasin-Gishu County, the County where MTRH is located.

The status of employment and health insurance utilization at admission were also notable factors, with 58.1 % of deceased women being unemployed and only a minority (32.3 %) having health insurance **(**Table 1**).**

More than half (54.8 %) of the women who died had a pregnancy interval greater than 5 months, with the antecedent pregnancy being a molar pregnancy or spontaneous abortion (each 38.7 %). The majority (77.4 %) of the deceased had a poor performance status (ECOG > 1). The sites of metastasis were commonly the lungs (61.3 %), liver (29.0 %), and brain (25.8 %). Moreover, 83.9 % of these women had pretreatment human chorionic gonadotropin (HCG) levels exceeding 100,000 mIU/ml and presented with advanced disease (FIGO 3 & 4) **(**Table 2**).**

Etoposide, methotrexate, actinomycin D, cyclophosphamide and vincristine (EMACO) were the predominant (84.7 %) chemotherapy regimens administered.

Induction chemotherapy was given to 31.0 % (9/29) of patients with a heavy disease burden, i.e., women with FIGO stage 3 or 4 disease, as well as those with ultrahigh-risk disease (WHO score ≥ 13).

Treatment delay was observed in 45.9 % of all 98 GTN patients. Also, 54.8 % of the women who died had a delay in diagnosis which was defined as a diagnosis made more than four weeks after the onset of symptoms or an interval months from the end of the index pregnancy of more than 4 months, while treatment delay was defined as treatment initiation more than two weeks after diagnosis or treatment interruption of two weeks or more. Complications were recorded in 61.2 % of GTN patients; bone marrow suppression (35.7 %), electrolyte derangement (32.7 %), and renal function derangement (31.6 %) were the most frequent.

Among the 31 patients who died, almost half (48.4 %) died early, occurring within one month of initiating treatment. The probable causes of mortality were advanced disease resulting in hemorrhage (83.9 %), acute kidney injury (32.3 %), and sepsis (22.6 %) **(**Table 3**).**

Patients residing outside Uasin Gishu County had a greater risk of death than did those residing within the county (AOR 2.75, 95 % CI 0.55–13.64). An ECOG score > 1 was strongly associated with GTN mortality (AOR 5.41, 95 % CI 1.52–19.21). Brain (AOR 2.39, 95 % CI 0.37–15.43), lung (AOR 0.72, 95 % CI 0.19–2.72) and liver metastasis (AOR 2.92, 95 % CI 0.43–19.55) were also associated with an increased risk of death among GTN patients. Additionally, HCG levels $\geq$ 100,000 mIU/ml and the presence of any complication (AOR 5.11, 95 % CI 1.08–24.04) were strong predictors of mortality **(**Table 4**).**

There was a significant difference in the survival rate of patients with β-HCG levels $\leq$ 100,000 compared with those with β-HCG levels $>$ 100,000 mIU/ml [log rank (Mantel Cox); $p < 0.001$]. The risk of death among GTN patients with β-HCG levels $>$ 100,000 mIU/ml was 6.7 times greater than that among those with β-HCG levels $\leq$ 100,000 mIU/ml [HR (95 % CI: 6.713 (2.324–19.393); $p < 0.001$] **(**Fig. 2**).**

There was a significant difference in the survival rate between ultrahigh-risk patients and high-risk patients [log rank (Mantel Cox); $p < 0.001$]. The risk of death among ultrahigh-risk GTN patients was 6.4 times greater than that among high-risk patients [HR (95 % CI: 6.427 (3.114–13.263); $p < 0.001$] **(**Fig. 3**).**

4. Discussion

The mortality rate associated with GTN provides important insight

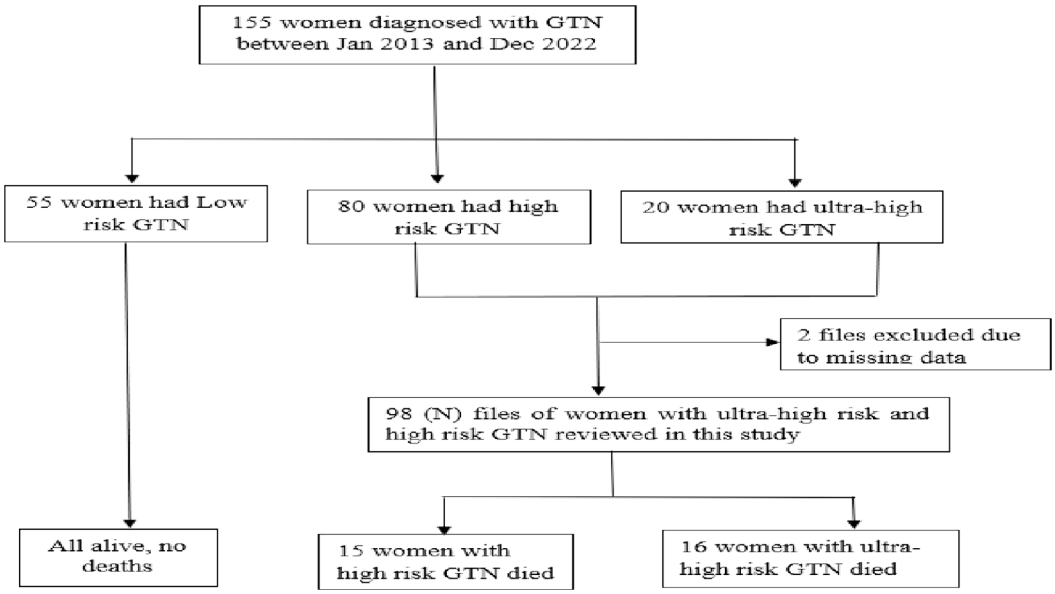

Fig. 1.

Table 1
Sociodemographic characteristics of patients with high and ultrahigh risk GTN.

Variable	Alive (n = 67)	Died (n = 31)	Total (n = 98)
Age (years)			
< 40	54 (80.6 %)	23 (74.2 %)	77 (78.6 %)
≥ 40	13 (19.4 %)	8 (25.8 %)	21 (21.4 %)
Referral status			
Primary admissions at MTRH	22 (32.8 %)	6 (19.4 %)	28 (28.6 %)
Referrals from others facilities	45 (67.2 %)	25 (80.6 %)	70 (71.4 %)
Residence			
Uasin Gishu	22 (32.8 %)	4 (12.9 %)	26 (26.5 %)
Others	45 (67.2 %)	27 (87.1 %)	72 (73.5 %)
Employment status			
Employed	27 (40.3 %)	13 (41.9 %)	40 (40.8 %)
Unemployed	40 (59.7 %)	18 (58.1 %)	58 (59.2 %)
Health insurance at admission			
Yes	30 (44.8 %)	10 (32.3 %)	40 (40.8 %)
No	37 (55.2 %)	21 (67.7 %)	58 (59.2 %)

Percentage calculation based on the total number of patients in each category i.e alive, died, or total.

Table 2
Clinical characteristics of patients with high and ultrahigh risk GTN.

Variable	Alive (n = 67)	Died (n = 31)	Total (n = 98)
Last pregnancy interval (months)			
0–4	52 (77.6 %)	14 (45.2 %)	66 (67.3 %)
5–8	11 (16.4 %)	7 (22.6 %)	18 (18.4 %)
>8	4 (6.0 %)	10 (32.2 %)	14 (14.3 %)
Antecedent pregnancy			
Molar pregnancy	39 (58.2 %)	12 (38.7 %)	51 (52.0 %)
Spontaneous abortion	15 (22.4 %)	12 (38.7 %)	27 (27.6 %)
Term pregnancy	13 (19.4 %)	6 (19.4 %)	19 (19.4 %)
Ectopic pregnancy	0 (0 %)	1 (3.2 %)	1 (1.0 %)
ECOG status			
0–1	53 (79.1 %)	7 (22.6 %)	60 (61.2 %)
2–3	14 (20.9 %)	21 (67.7 %)	35 (35.7 %)
>3	0 (0 %)	3 (9.7 %)	3 (3.1 %)
Sites of metastasis*			
Lungs	20 (29.9 %)	19 (61.3 %)	39 (39.8 %)
Vagina	5 (7.5 %)	7 (22.6 %)	12 (12.2 %)
Liver	2 (3.0 %)	9 (29.0 %)	11 (11.2 %)
Brain	3 (4.5 %)	8 (25.8 %)	11 (11.2 %)
Gastrointestinal tract	3 (4.5 %)	2 (6.5 %)	5 (5.1 %)
Spine	0 (0 %)	1 (3.2 %)	1 (1.0 %)
Pretreatment HCG levels			
1,000—10,000	13 (19.4 %)	3 (9.7 %)	16 (16.3 %)
10,001 ≤ 100,000	26 (38.8 %)	2 (6.5 %)	28 (28.6 %)
>100,000	28 (41.8 %)	26 (83.9 %)	54 (55.1 %)
FIGO stage			
I	39 (58.2 %)	0 (0 %)	39 (39.8 %)
II	8 (11.9 %)	5 (16.1 %)	13 (13.3 %)
III	15 (22.4 %)	13 (41.9 %)	28 (28.6 %)
IV	5 (7.5 %)	13 (41.9 %)	18 (18.4 %)
WHO prognostic score			
High Risk (7–12)	64 (95.5 %)	15 (48.4 %)	79 (80.6 %)
Ultra-High Risk (≥13)	3 (4.5 %)	16 (51.6 %)	19 (19.4 %)

*Multiple sites of metastasis noted in a single patient.
Percentage calculation based on the total number of patients in each category i.e alive, died, or total.

into the challenges experienced by young women during their reproductive peak. The high GTN death rates among women under 40 years old and occurring within a month of treatment initiation at the facility may suggest health system inadequacies. In contrast, developed countries such as China and the United States (US) have reported lower GTN mortality rates of 5.6 % and 3.9 %, respectively (Yang et al., 2006) (Lurain, 2016).

GTN is a highly curable disease when managed promptly and appropriately. In our setup access to specialized care is limited and GTN cases are commonly managed by generalists or lower cadre professionals, who have limited knowledge of GTN. This leads to failure to recognize the disease in its early stages in a timely manner, with most of the women being misdiagnosed and receiving suboptimal treatment typically leading to poor outcomes. Regionalization of GTN care would improve outcomes and is crucial to reducing mortality with ease of access to timely and specialized care. However, in our setup just like the rest of low-middle-income countries, there are no GTN centers, this leads to lack of a multi-disciplinary approach and non-standardized care for our women with GTN. In high-income countries, women with GTN are managed at GTN centers and this has been shown to presumably result in early presentation and diagnosis, consistent treatment, and improved results (Lurain, 2016). Also, the mortality rate was significantly lower for patients treated primarily at a trophoblastic center compared to patients who were referred to a center after failure of initial chemotherapeutic treatment elsewhere (Kohorn, 2014).

Most GTN patients in this review were referred from other healthcare

Table 3
Treatment, complications and outcomes of patients with high and ultra-high risk GTN (N = 98).

Variable	Alive (n = 67)	Died (n = 31)	Total (n = 98)
Patients who received chemotherapy			
Yes	67 (100 %)	28 (90.3 %)	95 (96.9 %)
No	0 (0 %)	3 (9.7 %)	3 (3.1 %)
Types of chemotherapy regimens administered			
Single Agent Methotrexate	4 (6.0 %)	2 (6.5 %)	6 (6.1 %)
Single Agent D-Actinomycin	7 (10.4 %)	2 (6.5 %)	9 (9.2 %)
EMACO	63 (94.0 %)	20 (64.5)	83 (84.7 %)
EMA-EP	3 (4.5 %)	9 (29.0 %)	12 (12.2 %)
TP-PE	1 (1.5 %)	4 (12.9 %)	5 (5.1 %)
Induction chemotherapy*			
Received low dose induction chemotherapy	2 (25 %)	7 (33.3 %)	9 (31.0 %)
Did not receive low dose induction chemotherapy	6 (75 %)	14 (66.7 %)	20 (69.0 %)
Delays / Resistant disease			
Diagnosis delay	15 (22.4 %)	17 (54.8 %)	32 (32.7 %)
Treatment delay	26 (38.8 %)	19 (61.3 %)	45 (45.9 %)
Resistant disease	10 (14.9 %)	6 (19.4 %)	16 (16.3 %)
Granulocyte colony stimulating factor (G-CSF)			
Yes	19 (28.4 %)	15 (48.4 %)	34(34.7 %)
No	48 (71.6 %)	16 (51.6 %)	64(65.3 %)
Complications			
Yes	32 (47.8.6 %)	28 (90.3 %)	60 (61.2 %)
No	35 (52.2 %)	3 (9.7 %)	38 (38.8 %)
***Treatment*-associated complications**			
Bone marrow suppression	13 (19.4 %)	22 (71 %)	35 (35.7 %)
Electrolyte derangement	10 (14.9 %)	22 (71 %)	32 (32.7 %)
Renal function derangement	12 (17.9 %)	19 (61.3 %)	31 (31.6 %)
Mucositis	12 (17.9 %)	12 (38.7 %)	24 (24.5 %)
Liver function derangement	7 (10.4 %)	14 (22.5 %)	21(21.4 %)
Neutropenic sepsis	3 (4.5 %)	8 (25.8 %)	11(11.2 %)
Sepsis	2 (3.0 %)	7 (22.6 %)	9 (9.2 %)
Neuropathy	3 (4.5 %)	0 (0 %)	3 (3.1 %)
Septic shock	0 (0 %)	2 (6.5 %)	2 (2.0 %)
Acute psychosis	1 (1.5 %)	0 (0.0 %)	1 (1.0 %)
Cellulitis	0 (0 %)	1 (3.2 %)	1 (1.0 %)
Disease-related complications			
Seizures	1 (1.5 %)	4 (13.0 %)	5 (5.1 %)
Thromboembolism	1 (1.5 %)	3 (9.7 %)	4 (4.1 %)
Internal bleed	2 (3.0 %)	0 (0.0 %)	2 (2.0 %)
Organ rupture	1 (1.5 %)	0 (0.0 %)	1 (1.0 %)
Paralysis	0 (0 %)	1 (3.2 %)	1 (1.0 %)
Lower gastrointestinal bleed	0 (0 %)	1 (3.2 %)	1 (1.0 %)
Peritonitis	0 (0 %)	1 (3.2 %)	1 (1.0 %))
Duration between initiation of treatment and death#			
Died before treatment commenced		3 (9.7 %)	
Less than 1 month,		15 (48.4 %)	
1–4 months		9 (29.0 %)	
More than 4 months		4 (12.9 %)	
Probable causes of mortality			
Metastatic disease (hemorrhage)		26 (83.9 %)	
Acute kidney injury		10 (32.3 %)	
Sepsis		7 *(22.6 %)*	
Pulmonary embolism		4 *(13.0 %)*	

N*=29, number of women who had heavy burden disease and required induction chemotherapy (21 died and 8 alive).
N# = 31, number of women who died.

facilities, indicating that for a significant proportion of this cohort, specialized care is primarily available and accessible at tertiary facilities such as MTRH that involves long distance travel and attendant higher costs. These women often faced the challenge of having to travel for hundreds of kilometers to reach the main referral hospital with some coming from as far as West Pokot covering 1006 km (22 h' drive).

The majority of GTN patients present to tertiary health facilities with advanced disease, often due to delayed diagnosis and prior suboptimal management (Mburu et al., 2022). The cost of cancer testing and treatment is a significant barrier facing many Kenyan people, with Kenya having the lowest health expenditure (only 3.5 % of its gross domestic product) compared to its neighbors (Makau-Barasa et al., 2018). A distinct feature in this region is the absence of comprehensive health insurance coverage in the majority of households (Maritim et al., 2023)—a fact that is mirrored in our findings. While certain diagnostic tests are subsidized at the referral facility, the financial responsibility for chemotherapy medications falls upon the patients and their families with a cycle of EMACO costing 83 US dollars (about 11,000 Kenyan shillings) for the uninsured. The majority of patients in this GTN cohort were unemployed and uninsured, which could have contributed to inadequate monitoring of HCG levels, causing delays in timely diagnosis of GTN and subsequently worsening disease prognosis.

As much as these appear to be patient-specific factors, the health systems in LMICs could also have a role to play. The lack of universal healthcare coverage that completely takes care of the entire diagnostic and treatment cascade and value chain could also be blamed. This could be attributed to limited healthcare commodities supply, inadequate healthcare professionals who are optimally trained and are competent to manage gynecological oncology conditions across multiple levels of care. This was evidenced by the fact that about three quarters of this study's participants were referred from lower healthcare facilities. This has been witnessed in other African Countries (Makau-Barasa et al., 2018).

More than half of the patients who died of the GTN had a prior pregnancy interval of more than 4 months, underscoring the need for vigilant post pregnancy monitoring to detect GTN early.

While most GTN patients presented with a relatively good performance status, it is noteworthy that all the women who died in this review had a poor ECOG status. In line with other literature, performance status can influence mortality (van der Zee et al., 2021). A poor ECOG status may predict a poor response and tolerability to GTN chemotherapy.

GTN patients in this review predominantly received an EMA/CO chemotherapy treatment regimen. The EMA/CO protocol is recognized as an effective protocol for managing GTN, resulting in a complete remission rate of up to 100 % in patients with high-risk stage 2 disease and as high as 97.3 % in patients with higher-stage disease and metastatic disease (Berkowitz et al., 1998 Jan). Nearly half of the GTN patients experienced treatment delay, which may have had a significant contribution to mortality outcomes, as treatment delays can lead to increased mortality due to disease progression as well as potential drug resistance.

Women with ultrahigh-risk disease (WHO score $\geq$ 13) had a 6.4-fold greater risk of death than women with high-risk disease with 80 % of the women with ultrahigh-risk from this cohort dying. This finding aligns with results from the French Center for Trophoblastic Diseases review by Bolze et al., which showed that the majority (52 %) of deaths in their GTN cohort were in patients with a FIGO score $\geq$ 13 (Bolze et al., 2016). Early identification and treatment of GTN patients at increased risk of death are crucial.

The majority of the women who died had high pretreatment HCG levels, indicating a heavy disease burden. Those with HCG levels greater than 100,000 had more than sixfold increased risk of death. Compared to our review, a study performed by Lurain et al. showed that the pretreatment HCG titer was significantly greater in women who died (Lurain et al., 1982). Furthermore, most of the mortalities occurred in

Table 4
Factors associated with mortality in women with high risk and ultrahigh risk GTN, N = 98.

Variables	Alive n (%)	Died n (%)	COR (95 % CI)	*P value*	AOR (95 % CI)	*P value*
Area of residence						
Uasin Gishu county	22 (84.6)	4 (15.4)	1		1	
Other counties	45 (62.5)	27 (37.5)	3.30 (1.02–10.60)	*0.038*	2.75 (0.55–13.64)	*0.215*
ECOG status						
0–1	53 (88.3)	7 (11.7)	1		1	
>1	14 (36.8)	24 (63.2)	12.98 (4.64–36.26)	*<0.001*	5.41 (1.52–19.21)	*0.009*
Brain Metastasis						
No	64 (73.6)	23 (26.4)	1		1	
Yes	3 (27.3)	8 (72.7)	7.42 (1.81–30.39)	*0.004*	2.39 (0.37–15.43)	*0.357*
Liver Metastasis						
No	65 (74.7)	22 (25.3)	1		1	
Yes	2(18.2)	9 (81.8)	13.29 (2.66–66.29)	*<0.001*	2.92 (0.43–19.55)	*0.269*
Lungs Metastasis						
No	47 (79.7)	12 (20.3)	1		1	
Yes	20 (51.3)	19 (48.7)	3.72 (1.52–9.08)	*0.003*	0.72 (0.19–2.72)	*0.628*
HCG levels						
≤100,000	39 (88.6)	5 (11.4)	1		1	
>100,000	28 (51.9)	26 (48.1)	7.24 (2.47–21.18)	*<0.001*	4.73 (1.27–17.52)	*0.020*
Complications						
Absent	35 (92.1)	3 (7.9)	1		1	
Present	32 (53.3)	28 (46.1)	10.20 (2.82–36.84)	*<0.001*	5.11 (1.08–24.04)	*0.039*

COR – crude odd ratio, AOR – adjusted odd ratio.

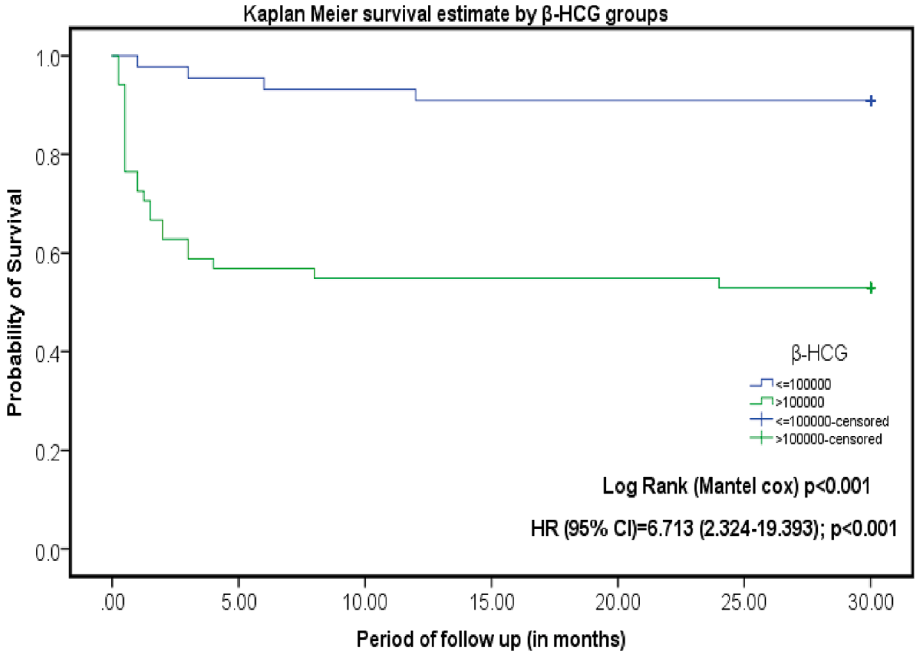

Fig. 2. Kaplan–Meier survival rate of patients with β-HCG levels ≤ 100,000 compared with those with β-HCG levels > 100,000 mIU/ml.

women with FIGO stages 3 and 4, underscoring the influence of tumor burden on GTN treatment outcomes.

Early mortality is prevalent among women with ultrahigh-risk disease, usually due to sudden hemorrhage and tumor lysis, indicating a high burden of disease. This can be averted with appropriate and early initiation of chemotherapy as well as low-dose induction chemotherapy (Braga et al., 2023 Feb). According to a Dutch central registry, the number of deaths, especially early deaths, associated with the management of women with GTN over four decades has decreased substantially following the introduction of low-dose etoposide and cisplatin (EP) for women with high-risk and heavy disease burdens (Lybol et al., 2012). In this review, unfortunately, only 9 women received low-dose EP, while the majority of the women with a heavy disease burden (70 % of the women who died) who required low-dose EP did not receive it.

Most GTN patients who died had complications related to metastatic disease resulting from chemotherapy treatment, leading to 58.1 % of early deaths. Studies indicate that patients who previously succumbed to metastatic disease now have a better prognosis with multiagent chemotherapy and single-site disease (Raffin et al., 2023). Managing the GTN is a challenge in our study, as most patients present with multiple-site metastasis and experience treatment delays.

In our study, frequent chemotherapy-associated complications among women who died included hemorrhage, which was a major cause of early death in 83.9 % of the patients. Bone marrow suppression, often leading to neutropenic sepsis and eventual septic shock, was also prevalent. Moreover, renal, electrolyte and liver function imbalances were observed. Challenges in obtaining blood and blood products, as well as appropriate supportive treatment, lack of ICU space for these women, may be worsened by poor infrastructural and under-developed cancer care in Kenya. The careful monitoring of renal, hepatic, and complete

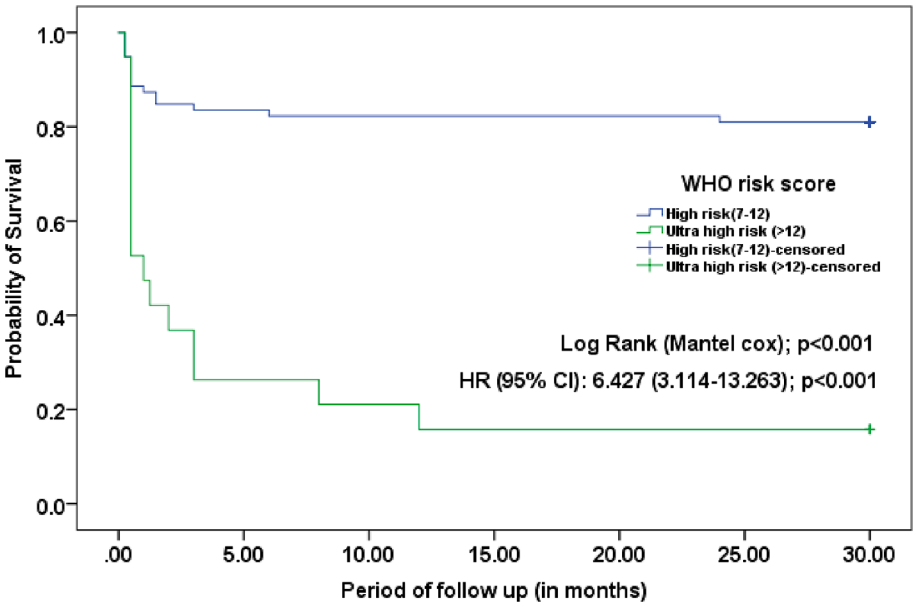

Fig. 3. Kaplan–Meier survival rate of high-risk versus ultrahigh-risk patients.

blood counts; transfusion; and granulocyte colony-stimulating factor to support neutrophil production has been shown to avert toxicity and morbidity (Lu et al., 2008) (Escobar et al., 2003) (Turan et al., 2006).

This study's main limitation was its retrospective nature, resulting in some missing information in the medical files. We addressed this by sourcing information from multiple records and omitting two patient files. We also analyzed survival curves over three years instead of five years.

5. Conclusion

Mortality associated with GTN is significantly high in LMICs, and women with WHO scores ≥ 13 have an increased risk of death and particularly early death. Delayed diagnosis, late presentation at advanced stages of disease, delayed treatment, healthcare constraints and social and economic barriers are thought to be predictors of mortality.

An excellent prognosis can be achieved by early referral and appropriate, timely and free treatment of women with GTN.

6. Recommendations

With respect to the regionalization of care and the creation of GTN centers in LMICs, there is a dire need to educate healthcare workers on the need for and importance of early referral, early diagnosis, and prompt treatment.

CRediT authorship contribution statement

Amina R. Hassan: . **Peter M. Itsura:** Supervision. **Barry P. Rosen:** Supervision. **Allan L. Covens:** Supervision. **Afrin F. Shaffi:** Writing – review & editing, Supervision, Resources. **Elly B. Odongo:** Supervision. **Anisa W. Mburu:** Writing – review & editing, Supervision. **Wilmot L. Smith:** Data curation. **Sharon K. Moturi:** Resources, Data curation. **Ronald K. Too:** Resources, Data curation. **Chia M. Ayeah:** Methodology, Formal analysis, Data curation. **Philiph K. Tonui:** Writing – review & editing, Supervision, Resources, Conceptualization.

Declaration of Competing Interest

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

Acknowledgments

The authors would like to thank the records office at MTRH and Chandaria Cancer and Chronic Diseases Center.

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