ORIGINAL RESEARCH

A profile of Gestational Trophoblastic Neoplasia in a tertiary hospital in Surabaya, Indonesia

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ABSTRACT

Objective: Gestational Trophoblastic Neoplasia (GTN) is a pregnancy-related malignancy due to abnormal proliferation of trophoblastic tissue. This study aimed to identify the characteristics of patients with GTN to help diagnose cases of GTN earlier and provide better treatment.

Materials and Methods: This was a descriptive retrospective study on medical records of patients with GTN in Dr. Soetomo General Academic Hospital Surabaya, Indonesia, during the period of January 2018 to December 2020 with a total sampling technique. There were 41 patients with GTN included as study subjects.

Results: Forty-one cases of GTN met the inclusion criteria out of the fifty medical records collected. The majority of patients aged 21 – 30 years old (34%) and had parity status without data (42%). Regarding the clinical profile based on prognostic factors, the predominant patients (71%) also had no data about the time interval between the end of the last pregnancy and the first time diagnosed by GTN, Those with more than 100,000 mIU/ml of beta-hCG levels were 32%, and those without metastases were 41.5%. Most patients belonged to the low-risk group (49%) and received chemotherapy (71%) with the MTX LD regimen (69%).

Conclusion: GTN occurred predominantly in reproductive women that belonged to the low-risk group. Furthermore, chemotherapy is one of the chosen therapy for those patients.

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Highlights:

1. This study aimed to identify the characteristics of Gestational Trophoblastic Neoplasia (GTN).
2. GTN is chemosensitive, but without appropriate therapy and follow-up, GTN will develop into complications and fatalities.

INTRODUCTION

Gestational trophoblastic neoplasia (GTN) is classified as a gestational trophoblastic disease (GTD). GTN is due to the abnormal proliferation of placental trophoblastic tissue and is associated with pregnancy. The features of GTN lesions depend on the genotype and phenotype of the trophoblastic tissue involved, including invasive mole, choriocarcinoma, placental site trophoblastic tumour (PSTT) and epithelioid trophoblastic tumour (ETT).[1] GTN does not have exact statistics because the incidence of events is considered rare. Epidemiologically, according to Lurain,[2] GTN affects more women in Asia than in America or Europe. In Europe and North America, choriocarcinoma affects about 1 in 40,000 pregnancies, while in Southeast Asia and Japan, choriocarcinoma has a higher incidence rate of 9.2 and 3.3 per 40,000 pregnancies.

There are various risk factors for GTN, ie. endogenous estrogen, extreme reproductive age, multiparity, certain gestational age, history of spontaneous abortion, high beta carotene diet, high fat diet, ABO blood type, environmental pollution/toxins, ethnicity, smoking, alcohol consumption, socioeconomic status, and other risk factors.[2] More than 50% of patients with GTN show no clinical manifestations, but currently, stable or even elevated serum levels of human chorionic gonadotropin (hCG) in pregnant women or a history of previous pregnancy can be used as a tumour marker to confirm the diagnosis, monitor the effects of chemotherapy, and evaluate the presence of recurrences.[3] Goldstein and Berkowitz[4] explained that this malignant tumour is highly sensitive to chemotherapy and has a cure rate of more than 90%. The cure rate for GTN is indeed high, but all risk factors must be evaluated immediately after someone is diagnosed or suspected of GTN because GTN can invade, metastasize, and cause death if left untreated.

This study was conducted to identify several risk factors and clinical profiles experienced by GTN patients. The elaboration of these points will show how to handle it properly and also educate society regarding this matter.

MATERIALS AND METHODS

This was a descriptive retrospective study described the characteristics of GTN patients at Dr. Soetomo General Academic Hospital, Surabaya, Indonesia for the period January 2018 – December 2020. This study was conducted at the POSA (*Poli Onkologi Satu Atap*/Integrated Oncology Clinic) with data sources from patients' medical records. The population in this study were all GTN patients at Dr. Soetomo Hospital for the period of January 2018 – December 2020. The sample in this study were patients with a diagnosis of GTN who met the inclusion criteria, ie. those with complete and unduplicated medical record data. The flow of this research was started with planning the theme, preparing proposals, then collecting, processing and analyzing data and preparing research reports. The results of data analysis in the form of GTN patient profiles are in the form of percentages and presented in tables. This research had received Ethical Eligibility Number: 0607/LOE/301.4.2/IX/2021.

RESULTS AND DISCUSSION

From the medical records of GTN patients at POSA Dr. Soetomo General Academic Hospital for the January 2018 – December 2020 period, 41 patients met the inclusion criteria. The results of the 41 sample study (Table 1) showed that most of the patients was in the age group of 21-30 years (34%), followed by ages 31-40 years (32%), >40 years (24%), and ≤20 years (10%). Based on parity status, there were more multiparous patients (34%) than nulliparas (24%). However, 17 (42%) of 41 patients had insufficient data on this subject. Another characteristic was the time interval between the end of the last pregnancy and the time the patient was first diagnosed with GTN. A total of 29 patients (71%) showed no data, 8 patients (19%) had an interval of fewer than 4 months, 2 patients with 4 - 6 months interval and 2 patients with >12 months.

In patients whose beta-hCG levels were known, 13 (32%) patients had the highest beta-hCG levels >100,000 mIU/ml, followed by 12 (29%) patients with beta-hCG levels <1000 mIU/ml, then 8 (24%) patients with beta-hCG levels of 10,000 - 100,000 mIU/ml. For the last, 6 (15%) patients had beta-hCG levels of 1000 - 10,000 mIU/ml. Patients who experienced metastases were 15 (36.5%) patients, then patients who did not experience metastases were more than those who experienced metastases, comprising 17 (41.5%) patients. Meanwhile, 9 (22%) other patients had no data. The most metastases were lung metastases, which were experienced by 10 (66.5%) patients out of all patients with metastases. Regarding single metastases in the vagina or brain, each patient did not have a single metastasis in these locations. Based on WHO and FIGO prognostic factor assessment scores. Most of the patients, consisting of 20 (49%) patients, were low-risk patients, 16 (39%) were high-risk patients, and 5 other patients had no data.

According to the therapy for GTN (Table 2), chemotherapy was the mainstay of management in GTN patients, provided to 29 (71%) cases, while surgery or

hysterectomy was only in 1 (2.5%) patient. In addition, there was no data on combination therapy between chemotherapy and hysterectomy (7%), combination therapy of chemotherapy and external radiation (2.5%) and the remaining 7 (17%) patients. Of the patients receiving chemotherapy, methotrexate (MTX) was the regimen given to most patients (69%). Then the others were MTX–EMACO in 2 patients (7%), MTX–EMACO – EP EMA in 1 patient (3%), EMACO in 4 patients (14%), and finally EMACO – EP EMA in 1 patient (7%).

The age of GTN patients in this study was mostly (34%) in the 21 - 31-year-old group which was also in line with the opinion expressed by Li et al.[5] that GTN is more experienced by reproductive age. The study by Raudina, Hidayat, and Rachmayati[6] showed that 57 (64.8%) of 88 patients aged less than 40 years old. In addition, referring to Katke's[7] study in Mumbai, it was stated that 17 out of 23 (73.4%) GTN patients aged 20-30 years. Then, a study in India showed that patients in the age range of 20-30 years were 89.6%.[8] In Denpasar, Indonesia, Azizi, Mahendra, and Widiyanti[9] conducted a study with the results explaining that 45.5% of GTN patients (5 out of 11 cases) were 21-30 years old. However, there are studies showing that age does not have a significant relationship with the patient's risk of experiencing malignancy in post-molar pregnancies.[10]

Table 1. Distribution of characteristics of GTN patients at Dr. Soetomo General Academic Hospital, Surabaya, Indonesia in 2018 – 2020

No.	Characteristics	Total	(%)
1.	Age		
	≤20	4	10%
	21 – 30	14	34%
	31 – 40	13	32%
	> 40	10	24%
	Total	41	100%
2.	Parity		
	Nuliparous	10	24%
	Multiparous	14	34%
	No data	17	42%
	Total	41	100%
3.	Time interval*		
	< 4 months	8	19%
	4 - 6 months	2	5%
	7 - 12 months	-	-
	> 12 months	2	5%
	No data	29	71%
	Total	41	100%
4.	β-hCG		
	< 1000 mIU/ml	12	29%
	1000 – 10,000 mIU/ml	6	15%
	10,000 – 100,000 mIU/ml	8	24%
	> 100,000 mIU/ml	13	32%
	Total	41	100%
5.	Metastasis		
a.	Metastasis (+)	15	36,5%
	1 site		
	Vagina	-	-
	Liver	1	6,7%
	Lung	10	66,5%
	Brain	-	-
	Vertebrae	1	6,7%
	>1 sites		
	Vagina and lung	1	6,7%
	Liver and lung	1	6,7%
	Lung and brain	1	6,7%
b.	Metastasis (–)	17	41,5%
c.	No data	9	22%
	Total	41	100%
6.	GTN type		
	Low risk GTN (≤ 6)	20	49%
	High risk GTN (≥ 7)	16	39%
	No data	5	12%
	Total	41	100%

Table 2. Distribution of the therapy of GTN patients at Dr. Soetomo General Academic Hospital, Surabaya, Indonesia in 2018 – 2020

No.	Therapy	Total	(%)
1.	Chemotherapy	29	71%
	MTX LD	20	69%
	MTX LD – EMACO	2	7%
	MTX – EMACO – EP EMA	1	3%
	EMACO	4	14%
	EMACO – EP EMA	1	7%
2.	Histerectomy	1	2,5%
3.	Chemotherapy and histerectomy	4	7%
4.	Chemotherapy and external radiation	1	2,5%
5.	No data	7	17%
	Total	41	100%

In one study, the highest cases of GTN patients were from the primigravida or nullipara group, comprising 115 (37.7%) patients out of 235 patients.[11] Meanwhile, Orr et al.[12] considered that parity was not significantly related to GTN risk. Although in this study the parity status of GTN patients did not have enough data, 42% did not have data, other results showed that multiparous women were the dominant group, consisting of 14 (34%) patients compared to 24% nulliparous women. A case-control study of molar pregnancies that develop into a choriocarcinoma, a type of GTN, shows that multiparous women have a relatively greater risk. However, the association was significant only for women with more than 5 births.[13]

This study presented inadequate data regarding the time interval between the end of the patient's last pregnancy and the first diagnosis of GTN and receiving therapy. Of the 41 patients, 29 patients had no data and the other 12 patients showed results that were dominated by intervals <4 months, comprising 8 patients (19%), then 4-6 months, and >12 months. In a study in Bandung, Indonesia, 37 (58.7%) hydatidiform mole patients who had an interval of fewer than 4 months between the end of the last pregnancy and the first time they were diagnosed with GTN and received therapy had a greater risk of developing an invasive mole or GTN.[6]

β-hCG is the most used tumour marker for the diagnosis of GTN because it is more sensitive than other imaging techniques. The amount of beta-hCG produced by the chorionic tissue corresponds to the volume of this tumour. Since histopathology is not mandatory for diagnosing GTN, FIGO has prepared criteria for this diagnosis.[14] Patients with β-hCG levels >100,000 mIU/ml in this study were predominant, consisting of 12 patients (29%). These results were supported by research by Angelina and Hartono[15] that most GTN patients were in the group with β-hCG levels of 100,000 – 1,000,000 mIU/ml, comprising 26 patients (63%) of a total of 41 patients. In addition, a study commensurate with this study was conducted by Azizi, Mahendra, and Widiyanti[9] showing that 4 patients (36.4%) out of 11 patients had β-hCG levels >100,000 mIU/ml. In contrast to this study, Jagtap et al.[8], mentioned most gestational trophoblastic diseases show β-hCG levels between 50,000 – 100,000 mIU/ml. Then, the lowest β-hCG level of 65,340 mIU/ml was observed in PSTT cases.

The results of a total of 41 GTN patients, 17 patients (41.5%) did not experience metastases, then 15 patients (36.5%) had metastases, and 9 patients (22%) had no data. Most patients had lung metastases, covering 10 patients (66.5%) of the total who had metastases. Many studies support this research, such as the study of Hemida et al.[16] in 2020, 71.4% of low-risk patients did not experience metastases, then 16.1% of low-risk patients had metastases, and the remaining 12.5% were high-risk patients. Twenty-five of them had metastases (22.3%), with 20 patients dominated by lung metastases. A previous study conducted by Hemida et al.[17] in 2011 also showed that the most metastatic locations in GTN patients were in the lungs, which was 62.5%. Other cases that did not experience metastases were 33 (71.7%) cases out of a total of 46 cases. Meanwhile, most cases of metastases were in the lungs as many as 10 cases 76.9%.[18]

One study grouped patients diagnosed with GTN according to FIGO prognostic factors and found that 63.6% were categorized as low-risk GTN and 36.4% as high-risk GTN.[6] The study by Sita-Lumsden et al.[19] in London, based on the results of the FIGO prognostic assessment, 579 (94%) patients were in the low-risk category and only 39 (4%) patients were in the high-risk category. Likewise in this study, 49% of GTN had low risk, 39% had high risk, and the remaining 12% had no data. The results of this grouping were in line with the characteristics of metastases that have been discussed earlier in those patients who predominantly did not have metastases so the prognostic score of these patients was lower than those who have metastases.

This study showed the highest results, 29 patients (71%) were given chemotherapy. The results of this study confirmed studies which stated that 72.7% of GTD patients received methotrexate chemotherapy to treat their GTD.[9] Hussain et al.[20] also considered that chemotherapy could be a good option for low-risk GTN patients, especially in developing countries. Li et al.[5] thought that GTN is one of the most curable malignancies with monitoring of serum hCG and effective combination therapy of chemotherapy with other procedures such as surgery so that the cure rate reaches 90% even for extensive metastases.

Due to the limitations of this study, such as very limited medical record data and the inavailability of complete data regarding the studied variables, some dominant characteristics were found as having no data. In addition, the research variables also did not vary so they were not regarded as the risk factors for GTN.

CONCLUSION

This study describes many characteristics about the risk factor of GTN. Predominantly, the patients of GTN aged 21–30 years (34%) and had parity status without data (42%). Regarding the clinical profile based on prognostic factors, the predominant patients (71%) also had no data about the time interval between the end of the last pregnancy and the first time diagnosed by GTN, with more than 100,000 mIU/ml of beta-hCG levels (32%), and had no metastases (41.5%). Most patients belonged to the low-risk group (49%) and received chemotherapy (71%) with the MTX LD regimen (69%). Further studies using various variables and longer time are needed to accurately identify the characteristics of GTN.

DISCLOSURES

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Conflict of interest

The authors declare no conflict of interest.

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Author contribution

All authors have contributed to all processes in this research, including preparation, data gathering and analysis, drafting and approval for publication of this manuscript.

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