

Characteristics of Gestational Trophoblastic Disease at Indonesian National Referral Hospitals: A Literature Review

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Abstract

Gestational trophoblastic disease (GTD) is a pregnancy disorder due to an abnormality of the placenta, such as enlargement of the chorionic villi. The spectrum of GTD may range from benign to malignant. Characteristics of the gestational trophoblastic disease have been discussed in the literature. This study discussed the characteristics that resulted from previous studies and the relationship of those characteristics and gestational trophoblastic disease. The results of this study revealed that there were five national referral hospitals in Indonesia which discussed the clinical characteristics in their report on gestational trophoblastic disease, namely age, marital age, gestational age, number of parity, patient's educational level, patient's and husband job, haemoglobin levels, region of origin, ethnicity, referral cases, complaints, pregnancy intervals, β -hCG levels, pregnancy history, length of stay, treatment duration, histopathology finding, staging/scoring, metastases, treatment, complications, and contraceptives. Out of the 25 characteristics that has been analyzed, 16 were studied to determine their relationships to gestational trophoblastic disease, while the other 9 were only analyzed descriptively.

Keywords: pregnancy, pregnancy disorder, gestational trophoblastic disease

1. Introduction

Gestational trophoblastic disease (GTD) occurs in the development of pregnancy characterized by abnormal proliferation of trophoblastic tissue [1]. GTD is divided into benign and malignant lesions. The benign lesion may form a hydatidiform mole resulting from an abnormality of chorionic villi. Malignant forms of GTD may emerge as choriocarcinoma, placental site trophoblastic tumor, and epithelioid trophoblastic tumor [2].

GTD, such as hydatidiform moles, are premalignant due to their ability to metastasize and invade by too deep penetration that may destruct the myometrium [3]. One of the factors contributing to an increase in maternal mortality is the early detection of high-risk pregnancies by staff and the management of obstetric complications through the health service sector to manage risks optimally, especially when mothers are indicated to be at high risk and having some complications [4].

Some risk factors may lead to the development of GTD: age, parity, obstetric-gynaecological history, β -hCG levels, therapy and management [5]. Several studies had found other risk factors such as sociodemographics, the invasion process, and rare studies, such as on the use of contraception [6].

Some studies revealed that the incidence of GTD was higher in Asian countries, such as Thailand, which reached 1.67 to 4.27 per 1,000 pregnancies; and Taiwan, with 1 per 125 pregnancies. The incidence of GTD in Indonesia reached 9.9 to 25 per 1,000 pregnancies, which was higher compared to other Asian countries. This increased number was affected by hospital-based epidemiological data on GTD obtained [7].

Kemenkes HK.02.02/MENKES/390/2014 assigns 14 hospitals as national referral hospitals, which are H. Adam Malik Central General Hospital Medan, Dr. M. Djamil Central General Hospital Padang, Dr. Mohammad Hoesin Central General Hospital Palembang, Dr. Cipto Mangunkusumo National Central Hospital Jakarta, Dr. Hasan Sadikin Central General Hospital Bandung, Dr. Kariadi Central General Hospital

Semarang, Dr. Sardjito Central General Hospital Yogyakarta, Dr. Soetomo Regional General Hospital Surabaya, Sanglah Central General Hospital Denpasar, Dr. Soedarso Regional General Hospital Pontianak, Abdul Wahab Sjahranie Regional General Hospital Samarinda, Prof. Dr. R. D. Kandou Central General Hospital Manado, Dr. Wahidin Sudirohusodo Central General Hospital Makassar, and Jayapura General Hospital. The hospitals mentioned above are the main referral hospital in Indonesia that serve for various diseases treatment, such as gestational trophoblastic disease (GTD).

2. General Characteristics Description of Gestational Trophoblastic Disease as Study Analysis

Five studies related to the gestational trophoblastic disease topic that met the inclusion criteria were involving five national referral hospitals, which were Dr Soetomo Regional General Hospital Surabaya, Sanglah Central General Hospital Denpasar, Dr Hasan Sadikin Central General Hospital Bandung, Dr Kariadi Central General Hospital Semarang, and Prof. Dr R.D. Kandou Central General Hospital Manado.

The characteristics analyzed in the study performed at the national referral hospital were different, but they had similar characteristics in general as those studied in the analysis of gestational trophoblastic disease (GTD) cases. Age, parity, educational level, complaints, history of pregnancy, β -hCG levels, contraception, metastases, and management were the more common characteristics analyzed in the study on GTD. The different characteristics of GTD stated in the study at those five national referral hospitals were marriage age, gestational interval, haemoglobin (Hb) level, occupation of the patient and husband, ethnicity, region of origin, histopathology finding, staging, scoring, and complications.

Table 1. General Characteristics Description of Gestational Trophoblastic Disease as Study Analysis Results at the National Referral Hospital

Characteristics	Results of analysis
Age	20-35 years old
Parity	Primiparous and multiparous
Educational Level	Senior High School
Complaints	Vaginal bleeding
Pregnancy History	Hydatidiform mole
Level of β -hCG	<10.000 mIU/ml
Contraception	Not an acceptor of the family planning program
Treatment	Curettage
Metastases	None

Characteristics shown in Table 1 are the characteristics studied by five national referral hospitals in Indonesia. These studies from the five hospitals mentioned above showed that GTD was mostly suffered by women aged 20-35 years or at sexually productive ages. The description of parity characteristics showed that primiparous and multiparous women are the largest group of women who suffer from GTD. Characteristics of the educational level indicated that mothers with an educational level of senior high school were more frequent compared to other women with an educational level of not in school, elementary school, junior high school, diploma, and bachelor degree. Based on the study at five national referral hospitals above, the most common manifestation complained by the mothers that caused them to decide to undergo a follow-up examination was vaginal bleeding; while nausea, vomiting, amenorrhea, lower abdominal pain, and enlarged uterus did not become the main complaints. The hydatidiform mole was the most common history of previous maternal pregnancies characteristic found in the GTD study at those five Indonesian national referral hospitals.

The most frequent β -hCG level measured in the national referral hospital of Indonesia was <10,000 mIU/ml and most commonly found in non-contraceptive mothers. The treatment that was mostly provided by

the five national referral hospitals found in the study was suction curettage, while most GTD patients showed no metastases, although some showed metastases to the lungs and vagina with a lower number of cases.

Table 2. Characteristics Differences of Gestational Trophoblastic Disease Research at 5 Indonesian National Referral Hospitals

Characteristics	Number of hospitals	Results
Marriage age	1	16-25 years old
Gestational age	2	9-16 weeks
Level of Hb	2	10-11 gr/dL
Referral cases	1	95,7%
Length of stay	1	≥3 days
Treatment duration	1	16-20 weeks
Patient occupation	2	Housewife
Husband occupation	1	Private employee
Ethnicity	1	Sundanese
Region of origin	2	Out of area
Histopathology finding	1	Complete hydatidiform mole
Pregnancy intervals	2	< 4 months and >12 months
Stadium	2	I
Scoring	2	< 7
Complications	1	Hyperemesis Gravidarum (HG)+ thyrotoxicosis.

Characteristics of the marriage age (first marriage) were studied by one hospital with the results that out of 11 cases of hydatidiform mole, the most frequent range of marriage age was 16-25 years (54.6%). For the gestational age at two hospitals, it showed that GTD was found mostly at 9-16 weeks gestation and gestation > 20 weeks according to fundal height.

The Hb level which was characteristic in the study at two hospitals was found to be highest at levels of 10-11 gr%. The characteristics of GTD as a reference were found by a study in a hospital with the result that 95.7% of GTD were referral cases. The length of stay was analyzed by two hospitals with the most frequent length of stay being 3 days with a treatment duration of 16-20 weeks.

The patient and husband's occupation were included in the GTD characteristics by two studies at the national referral hospital. The results showed that GTD was most commonly found in patients who were housewives or unemployed. According to a study at the national referral hospital GTD was most commonly found in patients whose husbands worked as private employees.

Ethnicity characteristic was analyzed in a study at a national referral hospital. It showed that GTD was most frequent in Sundanese ethnicity. Meanwhile, there were two studies at two national referral hospitals that analyzed the area of origin with the result that many cases were referred from outside the hospital area or the province.

A study in one national referral hospital revealed that most of the histopathology findings of GTD were collected from complete hydatidiform moles cases. Pregnancy intervals were proposed by two studies at national referral hospitals with the results of intervals <4 months and >12 months as the most common intervals of pregnancy. GTD was mostly found in stage I based on the analysis of two studies of national referral hospitals with the most frequent score being <7. A study conducted in a national referral hospital revealed that the most common complication experienced in a patient with GTD was hyperemesis gravidarum (HG), along with thyrotoxicosis.

3. Discussion

3.1 Age and Parity

Age and parity were the most frequently used characteristics of GTD study subjects. This is supported by a previous study conducted at Syech Yusuf Gowa Hospital which analyzed the relationship between age and parity with hydatidiform mole. The results of the analysis showed that mothers aged $<20 - > 35$ years old were considered to be at high risk to be suffered from hydatidiform moles. However, the results of the analysis showed that there was no relationship between age and hydatidiform moles. Similar to the results of the parity analysis in this study, it showed that there was no relationship between parity and hydatidiform mole, even though the highest risk in this study belonged to the group with >2 parities [8].

A study at Dr Hi. Abdoel Moeloek Regional General Hospital Lampung showed that there was a significant relationship between age and hydatidiform moles, while for parity analysis, A study at Syech Yusuf Regional General Hospital showed that there was no relationship between parity and hydatidiform moles statistically [9].

Age was the most common characteristic used as a study subject for GTD. According to the theory, women aged <19 years or >35 years are in a high-risk pregnancy that may cause obstetric complications [10]. Based on the theory of the pregnancy risk index proposed by Fortney J et al. (1983), the higher the index, the higher the risk of complications for the mother. Based on the two theories above, further study on age and parity in analyzing the risk factors for complications of pregnant women, including GTD [11].

3.2 Marriage age, level of education, and patient occupation

Mothers with a senior high school educational level and not working were more prone to suffer from GTD. Meanwhile, marriage age was one of the difficult characteristics to be studied. Marriage age, level of education, and occupation of women are influenced by the culture in Indonesia. According to Rokhmansyah (2016) in his book titled 'Introduction to Gender and Feminism', the patriarchal culture that is still inherent in Indonesian society places men in the highest, single, and dominating position in the social, economic, political, and even psychological environment. Women are given some limitations, including in education [12]. This is in line with the rate of early marriage in Indonesia according to a study in 2015, which is the second largest in Southeast Asia [13].

The level of education affects someone's insight and views. This is based on the theory that the higher the level of education of a person, the wider the insight and view of a matter. Mothers with a higher education level would easily access knowledge related to health, such as gestational trophoblastic disease for example [14].

Mubarak (2011) suggested that extensive experience and knowledge may be obtained from the work environment. Therefore, it was assumed that mothers with higher education and opportunities to work would find it easier to obtain additional information based on experiences from individuals who interact with each other in the work environment, compared to mothers who had low levels of education and were not working. Theory that increasing age affected changes in psychological aspects to become much more mature. Therefore, it was assumed that mothers at an early marriage age would have limited knowledge due the immature psychological and lower curiosity about things, such as health science, especially about GTD. The more information a person received, the wider the knowledge they owned and the wider their view on various fields as their curiosity increases [15].

The previous discussion proves that there was no relationship between age and the incidence of GTD. However, many women married at an early age. According to the results of the 2012 IDHS report, birth rates in the 15–19-year-old age group reached 48 per 1000 women, which meant that women at an early age were more prone to GTD. According to Martini (2008), women aged <20 years were prone to experience hydatidiform mole pregnancies or molar pregnancies because the reproductive organs were not ready to be

fertilized, and the incidence reached 4-10 times compared to women aged 20-35 years [16].

According to the Ministry of Health (2017) marriage or pregnancy at age <20 years makes a major contribution to high maternal, neonatal, infant, and toddler mortalities [17].

A study on educational level by Lakra (2017) showed that the educational level of mothers with GTD is most obtained from high school with a distribution of 45.5%. The relationship between education level and the incidence of GTD was a characteristic of studied for, but there is no further study analyzing the relationship between education level and the incidence of GTD, so this characteristic was only being analyzed to explore the subject's knowledge about GTD [18]. A study related to previous work was also conducted by Masrina (2019), showing GTD were found more frequently in women who were housewives or did not work as much as 33.3% [14].

3.3 Husband's occupation, Hb levels, and complaints of vaginal bleeding

Occupation is a characteristic related closely to the incidence of GTD. This results from the direct impact of family income. A study showed that families with low incomes would choose a high intake of glucose and fat with quite low nutritional value [19]. This is supported by a previous study which stated that individuals with low economic levels might have lower health status than individuals with high economic levels due to differences in consumption regarding maintaining health [20]. The results of the study revealed that although the highest distribution of GTD was in mothers who did not work, GTD was more commonly found in the patient whose husbands' occupation was private employees, triggering the opinion that the level of health in fulfilling a woman's nutrition, both before pregnancy and during pregnancy, was influenced by support from husband, both in terms of education and occupation.

Persagi (2014) explained that the factors affecting the nutritional status of pregnant women were divided into direct factors and indirect factors. The direct factors consisted of daily consumption intake and infection. Low daily consumption intake might affect the mother's health and cause various diseases. Family income was an indirect factor that determines the quantity and quality of a mother's nutritional intake. Therefore, the husband's occupation had an influence on the well-being of the family, including the mother [21].

A Previous study conducted by Sarah Damongilala (2015) revealed that the number of patients with Hb < 10 gr% suffered from hydatidiform mole was 53.8%. Hb levels in GTD sufferers were also caused by vaginal bleeding which was the main complaint of GTD sufferers. Vaginal bleeding was complained of by 97% of patients with hydatidiform mole [22,23].

A woman should have normal Hb levels to prevent anaemia during bleeding. According to WHO (2011), pregnant women are supposed to have at least a Hb level of 11 g%. If Hb is found to be less than 11 g% in pregnant women, the mother is considered anaemia [24].

Based on the theory and studies that had been conducted, the educational level, occupation, Hb level, and bleeding are related to each other. The lack of education level leads to the lack of access to the knowledge of the proper nutrition fulfilment for women of childbearing age and pregnant women, especially in nutritional intake to prevent anaemia [25]. This is also influenced by the husband's income which indirectly supports the nutritional needs of the mother.

Associated with hydatidiform mole, pregnancy disorder may cause bleeding and becomes the factor causing low Hb levels in sufferers of hydatidiform mole [22]. This vaginal bleeding results from the villi of a hydatidiform mole with a decidua layer [26].

3.4 Gestational age, β -hCG levels, complications, and management

Gestational trophoblastic disease is a disease resulting from abnormal pregnancies that turn into neoplastic lesions and cancer. Generally, GTD appears in a benign form, which is the hydatidiform mole.

Hydatidiform mole is classified into a complete hydatidiform mole and a partial hydatidiform mole. Both have histopathological differences. A hydatidiform mole may be easily detected at <12 weeks – 25 weeks of gestation. A complete hydatidiform mole can be detected at <12 weeks of gestation, while a partial hydatidiform mole is generally detected at 12-25 weeks of age [27]. Previous studies have shown that hydatidiform moles are diagnosed at >10 weeks of gestation with a fundal height greater than gestational age [28]. Initially, hydatidiform mole is detected at 16 weeks of gestation, but as the use of ultrasound develops, the assessment of pregnancy becomes easier. Hydatidiform mole tends to be detected between 8-22 weeks of gestation [29].

The mother will experience symptoms of pregnancy at <12 weeks of gestation, such as amenorrhea, nausea, vomiting, and dizziness. Therefore, the mother is triggered to do a urine examination with a simple test pack before undergoing an ultrasound examination. hCG is a hormone found in pregnant women. This hormone will be detected in the urine to ensure that a woman is experiencing pregnancy. This hCG is produced by the placental tissue so that this hormone can also be produced even though there is an abnormal proliferation in the placenta, hCG is produced after 7 days of ovulation [30]. Nausea and vomiting are normal symptoms experienced by pregnant women. These occur due to increased levels of β -hCG during pregnancy.

Serum hCG produced by the placenta increases the production of estrogen and progesterone in pregnant women thereby stomach acid increases which makes pregnant women experience nausea and vomiting [31]. Serum β -hCG levels show a high increase, up to 100,000 mIU/mL [32]. According to FIGO 2020, the levels of β -hCG in the urine and blood of pregnancies with GTD are much higher compared to normal pregnancies. In complete hydatidiform moles, the β -hCG levels are much higher than the β -hCG levels in partial hydatidiform moles, while the hCG levels in the tissues of hydatidiform moles are visible, compared to partial hydatidiform moles which appear smoother or lighter [33].

Apart from causing hyperemesis gravidarum, the increase in hCG level also triggers other complications, such as hyperthyroidism or thyrotoxicosis. These complications occur due to the cross-response of hCG and TSH. High levels of hCG may stimulate the thyroid gland by suppressing the release of TSH from the pituitary gland [28].

Hyperthyroidisms are found in about 7% of hydatidiform mole cases. The increase in triiodothyronine (T3) and thyroxine (T4) are seen in clinical manifestations, such as tachycardia, excessive sweating, and weight loss [32]. According to a case report, there was a 23-year-old pregnant woman with 2 weeks of gestation, being referred for vaginal bleeding. After an examination was performed, it was found that her hCG level was > 225,000 U/L and she was then diagnosed with a hydatidiform mole with hyperthyroidism [34].

In some studies at five national referral hospitals, the management of GTD, especially hydatidiform mole, was performed using curettage. This was based on safety considerations since it was easy and fast in evacuating the molar tissue to be examined histopathologically [32]. Evacuating a hydatidiform mole with curettage and suction also has diagnostic and therapeutic purposes and is more recommended than using medications only, such as oxytocin or misoprostol [26].

After the evacuation of the hydatidiform mole tissue is performed, it is necessary to monitor the serum hCG level weekly, then 4 weeks apart. This monitoring is conducted for up to 6 months or until the serum hCG level returns to normal, making it easier to diagnose gestational trophoblast neoplasia (GTN) early. The management of GTD, such as a hydatidiform mole with complications, will be different from the management of advanced potentially malignant hydatidiform moles. Treatment given at a referral hospital for GTN is grouped based on the WHO score. If the score is low, the patient will be treated with a low dose of MTX. Hysterectomy may be considered in women with high parity [35].

3.5 Length of stay, duration of treatment, an interval of pregnancy and histopathology

The study discussing the length of stay for a patient with GTD at the hospital is still very rare. This may be because of the level of risk posed after the treatment of a hydatidiform mole. Approximately, 20% of

hydatidiform mole leads to malignancy, thereby the management should be continued with a hysterectomy 7-10 days after the first curettage [32].

The treatment duration described in the present study was 16-20 weeks. Meanwhile, the existing theory proposes that hCG levels monitoring, treatment, and administration of contraceptives should be performed for at least 6 months to detect the risk of malignancy and recurrent GTD [27].

The β -hCG levels representing post-molar GTD are:

- β -hCG levels plateau for four times measurements over 3 weeks or more (on days 1, 7, 14, and 21)
- β -hCG levels elevate for three or more consecutive tests over 2 weeks or more (on days 1, 7, and 14).
- Histopathological diagnosis of carcinoma.
- β -hCG levels increase for 6 months or more after therapy [36].

Based on the theory above, the pregnancy interval in post-molar is expected longer. Studies conducted at the national referral hospital illustrate two results: interval of pregnancy < 4 months and > 12 months. The possibility of mothers of reproductive age getting pregnant again after experiencing molar is much greater. Therefore, in monitoring β -hCG levels, mothers need to be offered to use contraceptives such as condom till the β -hCG reach the normal level and then continue to use combination pills or tubectomy [32].

According to a study at the national referral hospital in Indonesia, the histopathology of GTD development mostly came from a history of complete hydatidiform mole. A study by Irianti (2000) showed that there were about 15-20% of hydatidiform moles turned into a malignant gestational trophoblastic tumor (GTN), even though a suction curettage had been performed [31]. This is in line with the results of a study by Tobing (2021) which showed that there was a significant difference in the histopathology of complete hydatidiform moles (73.5%) [37]. The theory proposes that a complete hydatidiform mole with excessive hyperplasia tends to turn into malignancy in the later course of the disease, which is characterized by loss of growth control. There are three regulatory genes: cell growth promoters (proto-oncogenes), tumor suppressor genes (antioncogenes), and programmed cell death (apoptosis), although the function of several genes in the pathophysiology of hydatidiform moles is not well known. [38].

3.6 Staging, scoring, and metastases

A study on GTD at a national referral hospital revealed that the most common staging, scoring, and metastases found were stage I, score 7, and no metastases, respectively. FIGO 2000 has established a staging and diagnostic scoring system for GTN.

Anatomical Staging				
Stage I	Disease confined to the uterus			
Stage II	GTN extends outside of the uterus but is limited to the genital structures (adnexa vagina, broad ligament)			
Stage III	GNT extends to the lungs, with or without genital tract involvement.			
Stage IV	All other metastatic sites			
(Modification of the WHO prognostic assessment system)				
Score	0	1	2	4
Age (year)	<40	≥ 40	-	-
Antecedent pregnancy	Mole	Abortion	Term	-
The interval from index pregnancy (mo)	<4	4-6	7-12	>12
Pre-treatment serum hCG	<10	10-10	10-10	≥10

(mIU/mL)				
Largest tumor size (including the uterus)	< 3	3-4	≥ 5	-
Site of metastases		Spleen, kidney	Gastro-intestinal tract	Liver, brain
Number of metastases	-	1-4	5-8	>8
Previously failed chemotherapy	-	-	1	≥ 2

(Adapted from FIGO)
 Low Risk = Score of WHO 0-6
 High Risk = Score of WHO ≥ 7

A system that has been established by FIGO 2000 facilitates determining the treatment given to patients in general.

3.7 Referrals and region of origin

Health service referral is the implementation of health services that regulate the reciprocal delegation of duties and responsibilities of health services, both vertically and horizontally, by health insurance participants [39].

A study by Lumentut (2020) showed Prof. Dr R.D. Kandou hospital is a national central general hospital with tertiary-level health facilities, thereby the normal delivery rate supposes to be low [40]. This is related to the existence of primary and secondary-level health facilities that can handle vaginal deliveries. The national referral hospital is a hospital that handles obstetric gynecology emergencies with complete sub-specialities and other departments, such as internal medicine and heart disease [41]. Therefore, the number of vaginal deliveries should be far lower than section caesarea delivery or any other obstetric gynecology disease.

The service system is highly structured by the Healthcare and Social Security Agency in implementing a tiered health service system [42]. The tiered system consists of first-level health facilities (FKTP), which is community health center; advanced-level health facilities (FKTL) which consist of second-level (secondary) health services, notably type C and D hospitals; and third-level (tertiary) health services consist of type B hospitals and type A referral hospital [43].

Based on the results of the present study and the regulation by the health care system, it can be assumed that those are in line with the results of the study at national referral hospitals, where most patients were referred from outside the region of the hospital location. This is due to both vertical and horizontal service levels.

3.8 Ethnicity

Indonesia is a country with a very diverse ethnic composition. There are around 633 tribes obtained from the grouping of tribes and sub-tribes in Indonesia as a result of the collaboration formulation between Statistics Indonesia (BPS) and ISEAS (Institute of South Asian Studies). The thousands of islands in the Unitary State of the Republic of Indonesia are one of the characteristics that Indonesia is a country with a diversity of ethnicities and different cultural backgrounds. Indonesian society is recognized as both vertically and horizontally the most diverse society in the world along with the United States and India [44].

Studies on GTD related to ethnicity are still very rare. In this present study, the most frequent ethnicity at the national referral hospital was the Sundanese. This might be a result of the location of the study. Therefore, due to a large number of ethnic groups, it is very difficult to know whether ethnic characteristics have a significant relationship to GTD.

3.9 Contraceptives

Contraceptive is a method to prevent pregnancy. These may be temporary or permanent. The use of contraception is increasing, especially the use of injectable contraception, but it is necessary to monitor general health such as body weight, blood pressure, menstrual patterns, and other complaints experienced [45].

This present study showed that the incidence of GTD was found mostly in non-contraceptive women. A case regarding a hydatidiform mole was also reported in a 13-year-old African-American teenager who also used Depo-Provera injectable hormonal contraceptive to prevent pregnancy, but this study did not focus on contraceptive use [46].

The theory suggests that the most adverse effect of DMPA contraceptives and implants are menstrual disorders, such as amenorrhea, spotting, cycle, frequency, and length of menstruation alteration, and excessive blood loss [47]. This is in line with a study by Sety (2014) concerning the relationship between the use of injectable hormonal contraceptives and menstrual disorders. Therefore, acceptors of hormonal contraceptives may experience amenorrhea [48].

Studies on GTD discussing the relationship between the use of contraceptive and GTD is barely to find in Indonesia. However, one of the treatments given post-molar evacuation is the administration of contraceptives to delay pregnancy during hCG monitoring [32].

Other studies suggested that although there was no significant impact between BMI and contraceptives on hCG regression, it was necessary to understand patient characteristics that can affect hCG regression [49].

4. Conclusions

There were similarities in the characteristics of the GTD study at five national referral hospitals. These general characteristics in the GTD study may be used as a literature review in a future study on GTD. The common characteristics were age, parity, education level, complaints, history of pregnancy, β -hCG levels, contraceptives, treatment, and metastases. However, there were differences in the characteristics studied in the study at the five national referral hospitals, including marriage age, gestational age, Hb levels, referral cases, length of stay, duration of treatment, occupation of patients and husbands, ethnicity, region of origin, histopathology finding, the interval of pregnancy, staging, scoring, and complications. Out of the 24 characteristics, it is found that there were still different results. Meanwhile, it should be noted that the study of these characteristics may aim to find out the relationship of characteristics to the incidence of GTD or to describe the characteristics found in study subjects or respondents. Based on this present study, it was concluded that there are 16 characteristics studied to find out the relationship of characteristics to GTD, while the other 9 were only subject characteristics in the study.

The future study examining GTD is expected to explore more about those characteristics and to find any other rare characteristics to be studied.

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