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Correlation Between Histopathologic Features And β-HCG Levels in the Event of Hydatidiform Mole

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ABSTRACT

Background: Hydatidiform mole is a gestational trophoblastic disease with the highest incidence in Indonesia where the incidence is 1 in 40 pregnancies. The cause of the high incidence of Hydatidiform mole is influenced by the reproductive performance of patients such as disorders of the hypothalamic-pituitary-ovarian system which causes hyperproliferation of trophoblastic cells, hydrophic degeneration of chorionic villi, and increased levels of β-hCG.

Methods: This research was involving human subjects so that was related to the issues of ethical consideration. It was done at the Anatomical Pathology Laboratory and the medical record division of the Hasanuddin University Hospital and Dr Wahidin Sudirohusodo Hospital Makassar from September - November 2019. The number of samples was 28 which used the total sampling method that fulfill the inclusion and exclusion criteria. Data analysis used chi-square.

Results: There are correlation between the histopathologic features with β-hCG levels, they are hydrophic degeneration of chorionic villi with β-hCG levels (p= 0.008) and proliferation of trophoblast cell with β-hCG (p= 0.001).

Conclusions: There is a correlation between the histopathologic features and β-hCG levels in the event of hydatidiform mole at Hasanuddin University Hospital and Dr. Wahidin Sudirohusodo Hospital Makassar. The higher levels of β-hCG, the histopathologic features of hydropic degeneration villi will increase, and trophoblastic cells will become hyperproliferation.

KEYWORDS: Hydatidiform mole- β-hCG level- histopathologic- pregnancy- gestational trophoblastic disease

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INTRODUCTION

Hydatidiform mole, more commonly known as a molar pregnancy, is a pregnancy which characterized by abnormal trophoblast growth. In a hydatidiform mole, the structure formed by the trophoblast is chorionic villi which has bubbles-shaped like grapes. Based on genetic and pathological differences, hydatidiform mole can be divided into two subtypes, that are complete and partial hydatidiform mole.[1] Compared with other gestational trophoblastic diseases, hydatidiform mole is the most common type. In general, the incidence of hydatidiform mole in Asia and Latin America is higher than in western countries. The incidence in Europe and the United States is 1-2 per 1000 pregnancies, while the incidence in Southeast Asia is eight times higher. The incidence of hydatidiform mole in Indonesian hospitals is higher than other countries, which is 1 per 40 pregnancies. It shows that hydatidiform mole is an important disease in Indonesia.[1,2]

Many patients with molar pregnancy are concerned that their condition could affect their reproductive health. Several studies have found that a patient with a hydatidiform mole, especially a complete mole, has a 10-20 times greater risk of mole recurrence than the general population. It can be concluded that 2% of hydatidiform mole patients could have

an abnormal pregnancy after evaluation. To improve post-evaluation reproductive health, we have to know the factors that have correlation with the patient's reproductive performance. In patients with hydatidiform mole, there are several clinical characteristics that can indicate a high risk of developing malignancy and affecting reproductive performance. One of them is the increase of β-hCG levels, conditions that can interrupt hypothalamic-pituitary-ovarian system so may produce different pregnancy outcomes. These clinical symptoms are related to the excessive proliferation of syncytiotrophoblast cell which causes the chorionic villi has hydrophilic degeneration which can be observed on histopathologic features and also has secondary effect of exceeding uterine size for gestational age.[1,2]

This research aims to reveal the correlation of histopathologic feaures with β-hCG levels in hydatidiform mole patients so that it can be used as a screening to detect hydatidiform mole malignancy.[3]

MATERIALS AND METHODS

After gaining approval from ethical recommendation Hasanuddin University Faculty of Medicine No.777/UN4.6.4.5.31/PP36/2019, all women with pathological diagnosed of hydatidifom mole in Hasanuddin University Hospital and Dr Wahidin Sudirohusodo from January 1, 2014 to Desember 2019 were retrospectively reviewed. Patient data was collected from inpatient databases. This study is an analytic observational study with a cross sectional design to see the correlation of histopathologic features with β-hCG levels in hydatidiform mole patients through secondary data.

Statistical analysis

The data analysis used chi-square to see the correlation between histopathologic features and β-hCG levels in hydatidiform mole patients. A p-value <0.05 was considered statistically significant. All statistical analyses were performed using the Statistical Package for Social Sciences (SPSS) versions 17 for Windows.

RESULTS

Patients with hydatidiform mole from the Hasanuddin University Hospital from 2014 to 2019 were 12 samples and from Dr. Wahidin Sudirohusodo had 40 samples. So the total samples of this research are 52 samples. The minimum number of samples is determined by the Slovin formula. The results of minimum sampling are 46 respondents from 52 total population. However, only 28 samples had β-hCG levels and histopathologic features for analysis.

Patient data was analyzed in two phases. At first β-hCG levels were divided in two categories: <100.000 mIU/mL and >100.000 mIU/mL. Next histopathological features of villi that has hydrophilic degeneration were divided in four categories: 10-25%, 25-50%, 50-75%, >75%. And then histopathological features of the proliferating trophoblast were divided I two categories: hypoproliferation and hyperproliferation.

Table 5.1. Correlation of β-hCG levels with histopathologic features of villi that has hydrophilic degeneration.

β-hCG	Histopathological features of villi that has hydrophilic degeneration				Total	p value
	10-25%	25-50%	50-75%	>75%		
β-hCG <100.000	3	3	0	4	10	0.008
β-hCG >100.000	0	1	6	11	18	
Total	3	4	6	15	28	

Table 5.1 shows the correlation between β-hCG levels and the histopathologic of villi that has hydrophilic degeneration. There were 10 respondents who have β-hCG levels <100.000 mIU/mL, including 3 people whose villi had 10-25% hydrophilic degeneration, 3 people whose villi had 25-50% hydrophilic degeneration, no person whose villi had 50-75% hydrophilic degeneration and 4 people whose villi had >75% hydrophilic degeneration. There were 18 respondents who had β-hCG levels >100.000 mIU/mL, which no people whose villi had 10-25% hydrophilic degeneration, 1 person whose villi had 25-50% hydrophilic degeneration, 6 people whose villi had 50-75% hydrophilic degeneration, and 11 people whose villi had >75% hydrophilic degeneration.

The result of statistic tests using the chi square test is p value (0.008) < 0.05, which means there is a correlation between the levels of β-hCG and the histopathologic features of villi that has hydrophilic degeneration.

Table 5.2. The correlation between β-hCG levels and histopathologic features of proliferating trophoblasts

	Histopathological features of the proliferating trophoblast		Total	p value
	Hyperproliferation	Hypoproliferation		
β-hCG <100.000	8	2	10	0.001
β-hCG >100.000	3	15	18	
Total	11	17	28	

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Table 5.2 shows the correlation between β-hCG levels and histopathologic features of proliferating trophoblasts. There were 10 respondents who had β-hCG levels <100.000 mIU/mL, including 8 people had hypoproliferation trophoblasts and 2 people had hyperproliferation trophoblasts. There were 18 respondents who had β-hCG levels >100.000 mIU/mL, including 3 people had hypoproliferation trophoblast and 15 people had hyperproliferation trophoblas. The result of statistical tests using the chi square test is p value (0.001) < 0.05, which means that there is a correlation between β-hCG levels and histopathologic features of proliferating trophoblasts.

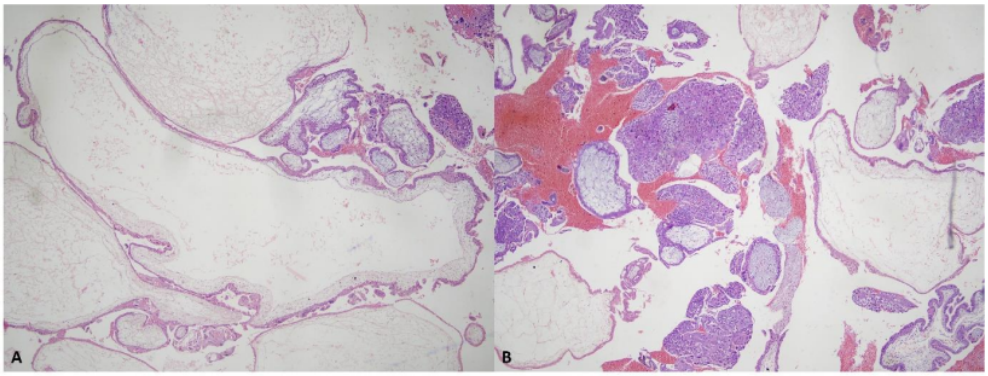

Figure 1. shows the histopathologic features through a microscope with 4x magnification. A. Hypoproliferation trophoblast. B. Hyperproliferation trophoblast.

DISCUSSIONS

The normal placenta consists of trophoblastic cells classified according to their location and cytological shape. Trophoblast cells that grow with chorionic villi are called chorionic villi, while trophoblasts that enter and are found in the decidua, myometrium, and placental blood vessels are called extravillous trophoblasts. Trophoblast is divided into three types namely cytotrophoblast, syncytiotrophoblast, and intermediate trophoblast. The syncytiotrophoblast produces hCG on the 12th day of gestation. Early in normal pregnancy, the serum hCG concentration increases rapidly as the trophoblast increases in size.[4]

Classification of hydatidiform mole is associated with the risk of postmolar gestational trophoblastic neoplastic neoplasia (GTN) and clinical management. The type of hydatidiform mole that is distinguished is usually based on histopathology. The classic histological features of a complete hydatidiform mole (CHM) are villous hydrops (widespread cavitation), trophoblastic proliferation (circumferential distribution, hyperplasia and cytologic atypia), intermediate trophoblast and marked cytological atypia.[5]

The significant histologic features that can distinguish complete hydatidiform mole (CHM) from partial hydatidiform mole (PHM) were central cistern, trophoblastic proliferation, trophoblastic atypia, two populations of villi, presence of fetal vessels and scalloped border. Howat et al. (1993) reported important features in differentiating CHM from PHM were atypical patterns of trophoblastic hyperplasia with circumferential and multifocal patterns. While Ishikawa (Ishikawa et al.,2009) found that the shape of villi and predominance villi with hydropic change were useful to differentiate complete hydatidiform mole from partial hydatidiform mole. The insignificant pathological morphologies that distinguished CHM from PHM in this study were hydropic villi and trophoblastic inclusions which were similar to previous studies (Paradinas et al., 1996; Ishikawa et al., 2009). However, histological criteria for diagnosis type hydatidiform mole are subjective and difficult to imitate. [6]

From a previous study, 72 patients with hydatidiform mole who were treated at the Obstetrics and Gynecology Section of Dr. Wahidin Sudirohusodo Hospital Makassar from January 2002 to December 2005, they were 43 patients who had the sample criteria. The results showed that there were 10 patients with hydatidiform mole in the first trimester (23.3%) which 3 people with low β-hCG levels (7.0%), 4 people with normal β-hCG levels (9.3%) and 3 people with high β-hCG levels (7.0%). In the second trimester there were 33 people (76.7%) with low β-hCG 8 people (18.6%), normal β-hCG 13 people (39.5%), high β-hCG 12 people (27.9%).[6] This shows that β-hCG levels are also influenced by gestational age. However, in this study, it was not categorized based on gestational age. There may be samples with low β-hCG levels or <100,000 mIU/mL due to gestational age in the early trimester, not because partial hydatidiform mole.[7]

Research from the Department of Obstetrics and Gynecology, Faculty of Medicine, Padjajaran University, Dr Hasan Sadikin Hospital, Bandung, said that there was a correlation between preevacuated β-hCG levels, histopathologic features, and lutein cysts with β-hCG performance in patients with hydatidiform mole who progressed to PTG and returned to normal.[8] The study explained that there are three risk factors that support the diagnosis of a hydatidiform mole in patient, they are β-hCG

Corresponding Author: Upik Anderiani Miskad

levels, histopathologic features of villi that has hydrophilic degeneration, and trophoblast proliferation.[8] This is what supports this research.

Correlation of β-hCG levels with histopathologic features of villi that has hydrophilic degeneration

As we know, a normal pregnancy must consist of mother element which will form the embryonal part (child) and the father element which is needed to form the extraembryonic part (placenta, amniotic fluid, etc.). Because there is no maternal element, in a complete hydatidiform mole there is no embryonal (fetus) part, there is only a pathological extraembryonic part in the form of chorionic villi that become hydrophilic degeneration like grapes and in partial hydatidiform mole, some immature villi relative normal and some villi enlarged with hydrophilic degeneration.[9] Hydatidiform moles are divided into 2; partial and complete moles, where partial moles have normal β-hCG levels or <100.000 and have normal chorionic villi or partially hydrophilic degeneration whereas in complete moles, β-hCG levels > 100,000 and have chorionic villi that are almost entirely hydropic degeneration.[10,11] From this study, it can be seen that 10 patients with β-hCG levels <100.000 mIU/mL had chorionic villi which 6 people had partial hydrophilic degeneration and 4 patients had complete hydrophilic degeneration, 18 patients with β-hCG levels >100.000mIU/mL had chorionic villi which 1 person had partial hydrophilic degeneration and 17 people had complete hydropic degeneration.

Correlation of β-hCG levels with histopathologic features of trophoblast proliferation

On research of Obstetrics and Gynecology Department, Faculty of Medicine, Padjadjaran University, Dr Hasan Sadikin Hospital, Bandung, the trophoblast proliferation was divided into 2 categories, they were hyperproliferation and hypo proliferation and it was found that complete hydatidiform mole which has high levels of *β*-hCG >100.000 mIU/mL in 21 of 23 samples and 14 of 23 samples with histopathological features of hyperproliferation.[8]

From this study it can also be seen that 10 patients with β-hCG levels <100.000 mIU/mL which 8 patients had hypoproliferative trophoblast features and 2 patien with hyperproliferative trophoblast, while 18 patients with β-hCG levels >100.000 mIU/mL which 3 people had hypoproliferative trophoblast features and 15 people had hyperproliferation trophoblast features.

Meanwhile, there is a gap where complete hydatidiform mole patients should have β-hCG levels > 100.000 mIU/mL, histopathologic features of villi are all hydrophobic degeneration, and hyperproliferation trophoblast. However, in this study, there were some samples that deviated from having β-hCG levels > 100,000 mIU/mL with histopathologic features of the villi only partially hashydrophilic degeneration and hypoproliferation trophoblasts.[11,12]

high levels of β-hCG which give a low value because the sensitivity of the hCG test is set in the range of 27.300 to 233.000 at 8-11 weeks of gestation. Laboratory errors can occur when the β-hCG level is more than 500,000 mIU/mL. Level measurement *β*-hCG which is found to be *falsely low reading* can appear in patients with hydatidiform mole, where this phenomenon is called the *high dose hook effect*. Several things that cause a *high dose hook effect* include the measurement of ferritin by immunoassay, prolactin, thyrotropin, CA 125, and prostate-specific antigen. High dose hook effect occurs whenever there is an inordinate amount of substance measured by immunoassay that causes incomplete antibody-antigen binding.[12]

CONCLUSION

There is a correlation between β-hCG levels and the histopathologic features of villi that had hydrophilic degeneration. The higher the level of β-hCG, the more villi had hydrophilic degeneration. There is also correlation between β-hCG levels and histopathologic features of proliferating trophoblasts. The higher the level of β-hCG, the trophoblast become hyperproliferation.

REFERENCES

I. Allison A.G., Lawrence H.L, Michelle D., Alexander M., Anthony R., Sue Y., Kevin E., et all. Impact of clinical characteristics on human chorionic gonadotropin regression after molar pregnancy. Clinics (Sao Paulo). Volume 76, 2021, e2830.
II. Jean J. C. The hydatidiform mole. Cell Adh Migr. 2016 Jan-Apr; 10(1-2): 226–235.
III. James L. N., Kenneth H. K., Ronald D. A. Abnormally low hCG in a complete hydatidiform molar pregnancy: The hook effect. Gynecol Oncol Case Rep. 2011 Dec; 1(1): 6–7.
IV. Nihal A. R., Marwa A. R., Thuriya A.H., Shaimaa A. S, Bushra Snand Moza A. K. Gestational Trophoblastic Disease at Sultan Qaboos University Hospital: Prevalence, Risk Factors, Histological Features, Sonographic Findings, and Outcomes. Oman Med J. 2019 May; 34(3): 200–204.
V. Hoskins W. Principles and practice of gynecologic oncology. 4th ed. Williams L, Wilkins, editors. USA; 2005. 21-3.
VI. Triratmachat S, Nakaporntham P, etc. Role of P57KIP2 Immunohistochemical Expression in Histological Diagnosis of Hydatidiform Moles. Asian Pacific Journal of Cancer Prevention, Vol 17, 2016.
VII. Syafii, Aprianti S, Hardjoeno. Kadar beta hCG penderita mola hidatidosa sebelum dan sesudah kuretase. Indones J Clin Pathol Med Lab. 2006;13(1):1-3.

Corresponding Author: Upik Anderiani Miskad

VIII. Harjito VN, Hidayat YM, Amelia I. Hubungan antara karakteristik klinis pasien mola hidatidosa dengan performa reproduksi pascaevakuasi di rumah sakit hasan sadikin bandung. Dep Obstet dan Ginekol Fak Kedokt Univ Padjadjaran. 2017;3:26.

IX. Nodler JL, Kim KH, Alvarez RD. Abnormally low hCG in a complete hydatidiform molar pregnancy: The hook effect. Gynecol Oncol Case. 2011.

X. Hidayat YM, Gandamihardja S, Krisnadi SR. Hubungan kadar βHCG praevakuasi, gambaran histopatologi, dan kista lutein dengan performa βHCG pada penderita mola hidatidosa yang berkembang menjadi PTG dan kembali normal. Dep Obstet dan Ginekol Fak Kedokt Univ Padjadjaran. 2014;46:248.

XI. Manuaba. Buku ajar patologi obstetri. Jakarta: EGC; 2008. 86-7.

XII. Akbar N. D. S., Agustria Z. S., Patiyus A., Theodorus. Malignancy Risk Factors of Hydatidiform Mole. Indonesian Journal of Obstetrics and Gynecology. VOLUME 7 NO. 2 APRIL 2019.

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