Rev. Fac. Med. Hum. January 2020;20(1):64-69.
DOI 10.25176/RFMH.v20i1.2547
ORIGINAL PAPER
ISSN Version Online: 2308-0531
Faculty of Human Medicine URP

FACTORS ASSOCIATED WITH GESTATIONAL TROFOBLASTIC DISEASE IN A PERUVIAN REFERENCE HOSPITAL

FACTORES ASOCIADOS A ENFERMEDAD TROFOBLÁSTICA GESTACIONAL EN UN HOSPITAL DE REFERENCIA PERUANO

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ABSTRACT

Objective: To determine the risk factors associated with gestational trophoblastic disease in patients treated in an outpatient office of the Gynecobstetrics service of the National Hospital Hipólito Unanue between January 2014 and December 2018. **Methods:** An observational, retrospective, analytical study of cases and controls was conducted. A total of 60 cases were taken as a sample and 120 stories were reviewed as a control group. The information obtained from the review of medical records was recorded in the data collection form. The odds ratio was determined with their respective confidence intervals (CI = 95%). For the multivariate analysis, a binary logistic regression model was used. **Results:** In the bivariate analysis, the factors associated with gestational trophoblastic disease were the history of abortion (OR 6.54; 95% CI 3.12 - 13.74; p <0.001) and multiparity (OR 3.35; 95% CI: 1.47 - 7.65; p <0.001). Age under 20 years was associated with a lower frequency (OR: 0.13; CI: 0.03-0.48 p <0.001). In the multivariate analysis, the only variables that showed significance were the history of abortion (OR 4.85; 95% CI 1.82-12.91; p = 0.002) as a risk factor and age under 20 years as a protective factor (OR 0.08; 95% CI 0.02 -0.32; p <0.001). **Conclusion:** The history of abortion and multiparity were associated with the presence of gestational trophoblastic disease, while the age under 20 years behaved as a protective factor.

Key words: Gestational Trophoblastic Disease; Hydatidiform mole; Risk factors; Trophoblasts. (source: MeSH NLM)

RESUMEN

Objetivo: Determinar los factores de riesgo asociados a enfermedad trofoblástica gestacional en pacientes atendidas en consultorio externo del servicio de Ginecobstetricia del Hospital Nacional Hipólito Unanue entre enero 2014 y diciembre del 2018. **Métodos:** Se realizó un estudio observacional, retrospectivo, analítico de tipo casos y controles. Se tomó como muestra un total de 60 casos y se revisaron 120 historias como grupo control. La información obtenida de la revisión de historias clínicas fue registrada en la ficha de recolección de datos. Se determinó el odds ratio con sus respectivos intervalos de confianza (IC=95%). Para el análisis multivariado se empleó un modelo de regresión logística binaria. **Resultados:** En el análisis bivariado los factores asociados a enfermedad trofoblástica gestacional fueron el antecedente de aborto (OR 6,54; IC 95% 3.12 - 13.74; p <0.001) y la multiparidad (OR 3.35; IC 95%: 1.47 - 7.65; p <0,001). La edad menor a 20 años se asoció a una menor frecuencia (OR: 0.13; IC: 0.03-0.48 p<0.001). En el análisis multivariado las únicas variables que mostraron significancia fueron el antecedente de aborto (OR 4.85; IC95% 1.82-12.91; p=0.002) como factor de riesgo y la edad menor a 20 años como factor protector (OR 0.08; IC95% 0.02-0.32; p<0.001). **Conclusión:** El antecedente de aborto y la multiparidad se asociaron a la presencia de enfermedad trofoblástica gestacional, mientras que la edad menor a 20 años se comportó como un factor protector.

Palabras clave: Enfermedad Trofoblástica Gestacional; Mola hidatiforme; Factores de riesgo; Trofoblastos. (fuente: DeCS BIREME)

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Cite as: Johana Huanca-Llamo, German Aranzabal-Alegria, Willer Chanduví. Factors associated with gestational trofoblastic disease in a peruvian reference hospital. Rev. Fac. Med. Hum. January 2020; 20(1):64-69. DOI 10.25176/RFMH.v20i1.2547

Journal home page: http://revistas.urp.edu.pe/index.php/RFMH

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INTRODUCTION

Gestational trophoblastic disease is an old pathology. About 2500 years ago, Hippocrates in his theory of the 4 humors described hydatidiform mole as hydrops or fluid retention in the uterus which he attributed to unhealthy water[1,2].

The incidence and prevalence of this disease depends on the geographical area; The Asian continent has the highest incidence 1 out of every 500 pregnancies; Also with greater capacity for malignancy, in western countries the incidence is 1 in 1500 pregnancies where only 5 to 10% persists the disease or becomes malignant, in Latin America the incidence ranges from 4.6 per 1000 pregnancies, in our country the incidence ranges from approximately 2.33 to 4.77 per 1000 pregnancies[3].

The term of gestational trophoblastic disease is used to describe a group of tumors that are characterized by abnormal trophoblast proliferation. Trophoblast produces human chorionic gonadotropin, which is why it is important to quantify this peptide for the diagnosis, treatment and follow-up of this disease[4].

From a histological point of view, gestational trophoblastic disease is divided into hydatidiform mole, which is recognized by the presence of villi and non-molar trophoblastic neoplasia, which lacks villi[5-7].

Hydatidiform moles are excessively immature placentas and edematous. These comprise partial, complete and malignant invasive hydatidiform moles. Non-molar trophoblastic neoplasia include choriocarcinoma, placental trophoblastic tumor, and epithelioid trophoblastic tumor. Gestational trophoblastic neoplasia include invasive mole, choriocarcinoma, placental trophoblastic tumor, and epithelioid trophoblastic tumor[8, 9].

In relation to risk factors, the age under 20 years and over 35 are factors associated with the development of the pathology. Multiparity, history of abortion, history of molar pregnancy among others are factors associated with the development of the disease and some find significant association in relation to the occupation of the father[10].

In the past, metastatic tumors had a high mortality rate, but thanks to chemotherapy, most tumors are curable[11].

Therefore, our study aimed to evaluate the incidence and factors associated with gestational trophoblastic disease in patients treated at Hipolito Unanue National Hospital.

METHODS

Type of study

We conducted an observational, retrospective and analytical study of types of cases and controls.

Population

The population consisted of pregnant women treated in the Gynecobstetrics Service of the Hipolito Unanue National Hospital during a period of 6 years. Patients with complete and available medical records were included; While those with incomplete data were excluded. After applying the selection criteria, we took 60 cases of trophoblastic disease and 120 controls from patients from the same service without trophoblastic disease.

Study procedures and variables

The necessary permits were requested for access to the clinical records of the Gynecobstetrics Service of Hipolito Unanue National Hospital, extracting the clinical records according to the list of cases and controls previously selected at random. The incidence of trophophastic disease was determined. Data were obtained from the website of the statistics department of the HNHU, considering the population at risk those patients who were discharged from the postpartum period.

Age, socioeconomic level (based on incomes reported by the family), parity, history of abortion, history of molar pregnancy, use of contraceptives, menarche younger than 12 years and blood group were evaluated as variables potentially associated with gestational trophoblastic disease [12].

Statistical analysis

The bivariate analysis for the evaluation of factors associated with gestational trophoblastic disease was performed using the chi square test. Likewise, we determined the odds ratio with their respective confidence intervals (95% CI) using binary logistic regression. Subsequently, a multivariate analysis was performed including the variables significantly associated in the bivariate analysis. A p value <0.05 was considered statistically significant. The calculations were performed using the statistical package SPSS v25.

Ethical aspects

The identity of the patients was respected and the entire protocol was executed with the institutional approval of the Ricardo Palma University and the Hipolito Unanue National Hospital.

RESULTS

Incidence results were 0.7 % during 2014; In 2015 were 0.6%; In 2016 were 0.8% and in 2017 were 0.8%.

Of the total number of patients studied, the most frequent age range was 20 to 35 years, with 65%, and also the majority (53%) had a low socioeconomic level. On the other hand, about a third were multiparous (32.2%) while the majority were primiparous (38.9%). The other general characteristics are shown in table 1.

Table 1. General characteristics of the patients treated at Hipolito Unanue National Hospital.

	Frequency	Percentage
Age		
Under 20 years	12	6,7%
Between 20 y 35 years	117	65,0%
Over 35 years	51	28,3%
Socioeconomic level		
Low	96	53,3%
Medium	84	46,7%
Parity		
Nulliparous	46	25,6%
Primiparous	70	38,9%
Multiparous	58	32,2%
Grand Multiparous	6	3,3%
History of twin pregnancy		
Yes	1	0,6%
No	179	99,4%
History of abortion		
Yes	44	24,4%
No	136	75,6%
Use of contraceptives methods		
Yes	13	7,2%
No	167	92,8%
Menarche before 12 years		
Yes	14	7,8%
No	166	92,2%
Blood Group		
O	176	97,8%
A	4	2,2%

As can be seen in table 2, the most frequent histological type was complete hydatidiform mole with 66.6%; Followed by partial hydatidiform mole with 26.7%; The other histological types had smaller proportions.

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Table 2. Histological type of cases of trophoblastic disease of patients treated at Hipolito Unanue National Hospital.

Histological Type	Recount	Percentage
Complete Hydatidiform Mole	40	66,6 %
Partial Hydatidiform Mole	16	26,7 %
Invasive Mole	2	3,3 %
Choriocarcinoma	1	1,7 %
Placental Site Tumor	1	1,7 %
Total	60	100 %

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When performing the bivariate analysis, we found that gestational trophoblastic disease was associated with being younger than 20 years, being multiparous and having a history of abortion.

Table 3. Bivariate analysis of the factors associated with developing gestational trophoblastic disease in patients treated at Hipolito Unanue National Hospital.

Risk Factors		Cases N (%)	Controls N (%)	OR	95% CI	P Value
Age	20-35	8 (13,3 %)	4 (3,3 %)			
	<20	25 (41,7 %)	92 (76,7 %)	0,13	0,03-0,48	0,002
	>35	27 (45 %)	24 (20 %)	0,56	0,15-2,10	0,393
Socioeconomic Level	Low	38 (63,3 %)	58 (48,3 %)	1,84	0,97-3,48	
	Medium	22 (36,7 %)	62 (51,7 %)			0,057
Parity	Nulliparous	13 (21,7 %)	33 (27,5 %)			
	Primiparous	10 (16,7 %)	60 (50 %)	0,42	0,16 - 1,07	0,069
	Multiparous	33 (55 %)	25 (20,8 %)	3,35	1,46 - 7,65	0,004
	Grand Multiparous	4 (6,6 %)	2 (1,7 %)	5,07	0,82 - 31,16	0,079
History of Molar Pregnancy	Yes	1 (1,7 %)	0 (0 %)	3,034	2,462 - 3,739	0,156
	No	59 (98,3 %)	120 (100 %)			
	Yes	29 (48,3 %)	15 (12,5 %)	6,548	3,121-13,739	<0,001
History of Abortion	No	31 (51,7 %)	105 (87,5 %)			
Use of Contraceptive Methods	Yes	7 (11,7 %)	6 (5 %)	2,509	0,804-7,831	0,103
	No	53 (88,3 %)	114 (95 %)			
Menarche < 12 years	Si	8 (13,3 %)	6 (5 %)	2,923	0,965-8,853	0,049
	No	52 (86,7 %)	114 (95 %)			
Blood Group	O	57 (95 %)	119 (99,2 %)	6,263	0,637-61,545	0,074
	A	3 (5 %)	1 (0,8 %)			

When performing the multivariate analysis, the only variables that showed significance were history of abortion as a risk factor and age under 20 years as a protective factor.

Table 4. Multivariate analysis to determine the risk of developing gestational trophoblastic disease of patients treated at Hipolito Unanue National Hospital.

Variables	Adjusted OR	95% CI		P value
Age 20 – 35	Ref			
Age <20	0,08	0,02	0,32	<0,001
Age <35	0,22	0,06	1,13	0,073
Nulliparous	Ref			
Primiparous	0,485	0,17	1,37	0,172
Multiparous	1,759	0,60	5,09	0,298
Grand Multiparous	3,873	0,50	29,09	0,193
History of Abortion	4,84	1,81	12,91	0,002

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DISCUSSION

Gestational trophoblastic disease constitutes a diverse group of lesions with specific pathogenesis, morphological characteristics and clinical characteristics[13]. There are few studies whose objectives were to identify possible risk factors associated with the development of gestational trophoblastic disease. Regarding the frequency of gestational trophoblastic disease in our study we found 7 cases per thousand postpartum women, similar to what was described in a study carried out in Mexico in 2016[13].

Of the factors studied, the most frequent in the study population was history of abortion, which was present in 48.3% of cases and was associated with an increase of more than six times the risk of developing trophoblastic disease compared to women who had no history of abortion. This result is similar to that found by Shamshiri H. et al[14] where the risk of developing the disease was 3.17 times, postulating that the woman must have a certain predisposition for the formation, in addition, the presence of recurrent abortions associated with molar pregnancy and multiparity are protective against the whole mole.

Regarding multiparity, which is an important risk factor in pregnancy, childbirth and postpartum for various morbidities. Our study found that 55% of cases had multiparity; However, the relationship found in the bivariate analysis was not found in the multivariate analysis. A study carried out by Garcia L. et al[15] found an OR of 5.41 associated with multiparity in agreement with what was found by Sanchez A.[16] in his study, associating it to the educational level of the population concerned. In contrast, it is worth mentioning that in a study by Fletcher et al[17] the nulliparity associated with the development of gestational trophoblastic disease was analyzed, finding that more than 60% of patients reported a molar pregnancy during their first pregnancy, which agrees with what was found in the present study.

The analysis of the age variable showed that 13.3% of the cases were younger than 20 years and 45% were older than 35 years. It was also found that the age younger than 20 years had an OR lower than 1, behaving as a protective factor for gestational trophoblastic disease, a relationship corroborated in the multivariate analysis. It is worth mentioning that Shamshiri H. et al[14] reported that the younger the greater the risk of developing gestational trophoblastic disease, this explains a relationship between the risk of molar pregnancy and maternal age extremes; With an increased risk of 10 times in women over 40 years and 1.3 times in adolescents. While the highest risk in older women is consistently high, due to declining fertility in this age group. While the effect of aging on eggs can cause abnormal gametogenesis and/or fertilization may be part of the explanation in advanced maternal age, this does not explain the data on adolescents[18].

Regarding socioeconomic level, in the present study no significant association was found. No significant association was found with previous molar pregnancy. This is corroborated by Shamshiri et al[14], who associated trophoblastic disease with educational level, observing that this pathology was more frequent in patients with low educational level. These findings are reported in countries of Latin America and Asia where there may be some bias given the high poverty of this region, it is reported that this incidence would decrease through better medical control from the beginning of pregnancy and better access to food sources[18].

In turn, no association was found with the use of contraceptive methods. This contrasts with the

findings of Palmer et al.[19]; Those who found an association with a history of oral contraceptive use sometime before pregnancy, increasing the risk of trophoblastic disease as the duration of contraceptive use increased. However, Vecchia C. et al[20] in their study found no association between these variables, which attributed to the use of the intrauterine device that was frequent in their environment; This is in line with the present study. This may be due to the increased use of injectable or depot contraceptive methods.

Likewise, no significant association was found in relation to blood group A and trophoblastic disease, the same was found in other studies, such as that carried out by Sharifi N. et al[8] who observed that there was a positive relationship of molar disease with blood group and raised the need to know the blood group of the father, an element also recommended by WHO.

The present study had the limitations that other factors such as diet or genetic factors were not measured. However, the relevance of the factors evaluated and found shed light to perform the respective interventions in order to prevent this disease.

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CONCLUSION

The only risk factor associated with gestational trophoblastic disease in the adjusted analysis was history of abortion, while age under 20 years behaved as a protective factor.

Authorship Contributions: The authors participated in the genesis of the idea, project design, data collection and interpretation, analysis of results and preparation of the manuscript of this research paper.

Financing: Self-financed

Interest conflict: The authors declare no conflict of interest in the publication of this article.

Received: October 25, 2019

Approved: December 10, 2019

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BIBLIOGRAPHIC REFERENCES

1. Rodríguez Sánchez AL. Características clínico-epidemiológicas y factores de riesgo de enfermedad trofoblástica gestacional en el Hospital Nacional Dos de Mayo, 2005-2015 [Internet]. 2018 [citado 2019 dic 8]; Disponible en: http://cybertesis.unmsm.edu.pe/handle/cybertesis/7595.

2. Candelier J-J. The hydatidiform mole. Cell Adhes Migr 2016;10:226–35. https://doi.org/10.1080/19336918.2015.1093275.

3. Vázquez Martinez YE, Brito Garcia A, Delgado Peruyera L, Vázquez Merayo EJ. Caracterización clínica de la enfermedad trofoblástica gestacional, Hospital Ginecobstétrico "Ramón González Coro" (2008-2012). Rev Cuba Hig Epidemiol 2014;52:173–81. Disponible en: http://scielo.sld.cu/scielo.php?script=sci_arttext&pid=S1561-30032014000200004

4. Tse KY, Chan KKL, Tam KF, Ngan HYS. Gestational trophoblastic disease. Obstet Gynaecol Reprod Med 2009;19:89–97. https://doi.org/10.1016/j.ogrm.2008.12.002.

5. Biscaro A, Silveira SK, Locks G de F, Mileo LR, da Silva Júnior JP, Pretto P. Frequency of hydatidiform mole in tissue obtained by curettage. Rev Bras Ginecol E Obstet Rev Fed Bras Soc Ginecol E Obstet 2012;34:254–8. Disponible en: https://www.ncbi.nlm.nih.gov/pubmed/22801599

6. Lurain JR. Gestational trophoblastic disease I: epidemiology, pathology, clinical presentation and diagnosis of gestational trophoblastic disease, and management of hydatidiform mole. Am J Obstet Gynecol 2010;203:531–9. https://doi.org/10.1016/j.ajog.2010.06.073.

7. Kitange B, Matovelo D, Konje E, Massinde A, Rambau P. Hydatidiform moles among patients with incomplete abortion in Mwanza City, North western Tanzania. Afr Health Sci 2015;15:1081–6. https://doi.org/10.4314/ahs.v15i4.5.

8. Sharifi N, Shahidsales S, Haghighi F, Hosseini S. Gestational throphoblastic diseases in North East of Iran: 10 years (2001-2010) prospective epidemiological and clinicopathological study. Adv Biomed Res 2014;3. https://doi.org/10.4103/2277-9175.125801.

9. Khachani I, Alami MH, Bezad R. Implementation and Monitoring of a Gestational Trophoblastic Disease Management Program in a Tertiary Hospital in Morocco: Opportunities and Challenges. Obstet Gynecol Int 2017;2017. https://doi.org/10.1155/2017/5093472.

10. Boufettal H, Coullin P, Mahdaoui S, Noun M, Hermas S, Samouh N. Les môles hydatiformes complètes au Maroc : étude épidémiologique et clinique. Journal de Gynécologie Obstétrique et Biologie de la Reproduction 2011;40:419–29. https://doi.org/10.1016/j.jgyn.2011.02.008.

11. Mamouni N, Boumhaoued S, Erraghay S, Boubou M, Bouchikhi C, Banani A. Clinical and radiological features of gestational trophoblastic tumors. Pan Afr Med J 2017;28:228. https://doi.org/10.11604/pamj.2017.28.228.13267.

12. Veiga de Cabo J, Fuente Díez E de la, Zimmermann Verdejo M. Modelos de estudios en investigación aplicada: conceptos y criterios para el diseño. Med Segur Trab 2008;54:81–8. Disponible en: http://scielo.isciii.es/scielo.php?script=sci_arttext&pid=S0465-546X2008000100011

13. Schwentner L, Schmitt W, Bartusek G, Kreienberg R, Herr D. Cervical hydatidiform mole pregnancy after missed abortion presenting with severe vaginal bleeding: case report and review of the literature. Eur J Obstet Gynecol Reprod Biol 2011;156:9–11. https://doi.org/10.1016/j.ejogrb.2010.12.029.

14. Shamshiri Milani H, Abdollahi M, Torbati S, Asbaghi T, Azargashb E. Risk Factors for Hydatidiform Mole: Is Husband's Job a Major Risk Factor? Asian Pac J Cancer Prev APJCP 2017;18:2657–62. https://doi.org/10.22034/APJCP.2017.18.10.2657.

15. Ramírez CAG, Rangel E, Mantilla HAT. Factores de riesgo, diagnóstico histológico y concentraciones de beta-hCG en pacientes con mola hidatiforme. Rev Médicas UIS 2018;31:39–46. Disponible en: https://revistas.uis.edu.co/index.php/revistamedicasuis/article/view/8192

16. Sánchez Carranza A. Factores de riesgo asociados a embarazo molar en gestantes atendidas en el servicio de gineco-obstetricia del Hospital Regional de Loreto entre enero 2010 - diciembre 2014 [Internet]. 2015 [citado 2019 dic 8]; Disponible en: http://repositorio.unapiquitos.edu.pe/handle/UNAP/3771.

17. Fletcher J, Guillén J, Romero JC, Sandoval J. Factores Asociados al Desarrollo de Mola Hidatidiforme. Hospital Santo Tomás. Panamá. 1994-2001. Rev Méd Científica 2002;15. Disponible en: http://revistamedicocientifica.org/index.php/rmc/article/view/194

18. Steigrad SJ. Epidemiology of gestational trophoblastic diseases. Best Pract Res Clin Obstet Gynaecol 2003;17:837–47. https://doi.org/10.1016/s1521-6934(03)00049-x.

19. Palmer JR, Driscoll SG, Rosenberg L, Berkowitz RS, Lurain JR, Soper J, et al. Oral contraceptive use and risk of gestational trophoblastic tumors. J Natl Cancer Inst 1999;91:635–40. https://doi.org/10.1093/jnci/91.7.635.

20. La Vecchia C, Franceschi S, Parazzini F, Fasoli M, Decarli A, Gallus G, et al. Risk factors for gestational trophoblastic disease in Italy. Am J Epidemiol 1985;121:457–64. https://doi.org/10.1093/oxfordjournals.aje.a114018.