Original Article

DOI: 10.7860/JCDR/2022/52824.16262

Evaluation of Incidence, Risk Factors, Diagnosis and Management of Gestational Trophoblastic Neoplasia: A Retrospective Study

Obstetrics and Gynaecology Section

ANJALI MURALIDAS[1], SHILPA ANN BABY[2]

ABSTRACT

Introduction: Detection of any definite established pattern in aetiological factors can help identify high risk groups among vesicular mole patients, so that the development of Gestational Trophoblastic Neoplasia (GTN) can be anticipated to avoid delay in management of this disease with almost 100% cure rate.

Aim: To determine the incidence of GTN, various factors associated with the condition, and any difference in risk factors between low risk and high risk disease and to evaluate the efficacy of the different treatment protocols used.

Materials and Methods: A retrospective descriptive study done in the Department of Obstetrics and Gynaecology in a tertiary level hospital in South India which included 100 cases of GTN who were registered in the Gestational Trophoblastic Disease (GTD) clinic for a period of 10 years from January 2002 to December 2011. Data analysis was done from January 2020 to August 2020 The hospital incidence of GTN and proportion of GTN among vesicular mole was calculated. The different socio-demographic factors, clinical features and hormonal profile of all cases of GTN were studied in detail.

Results: The incidence of GTN was 0.76 per 1000 deliveries. The proportion of GTN among molar pregnancy was 10.7%. Uterine size greater than period of amenorrhoea, bilateral theca leutin cysts especially with size >6 cm and pre-evacuation human Chorionic Gonadotropin (hCG) >100,000 mIU/mL was associated with development of GTN. GTN was found more in those with complete mole and that was around 71%. Around 81% had low risk GTN and 19% had high risk GTN. Major indication for starting chemotherapy was rising β-hCG (72%). Presence of theca lutein cysts and uterine size greater than period of amenorrhoea were statistically significant risk factors for high risk GTN (p=0.022 and p<0.001, respectively).

Conclusion: Identification of risk factors helps in early recognition of GTN and improves the overall outcome. The choice of chemotherapy depends on risk categorisation based on International Federation of Gynaecology and Obstetrics (FIGO) scoring system. Single agent for low risk and combination chemotherapy for high risk group is often sufficient.

Keywords: Beta-human chorionic gonadotrophin, Choriocarcinoma, Persistent trophoblastic disease, Vesicular mole

INTRODUCTION

Gestational Trophoblastic Neoplasia is a collective term for gestational trophoblastic diseases that invade locally or metastasise. It includes invasive mole, choriocarcinoma, Placental Site Trophoblastic Tumour (PSTT) and Epithelioid trophoblastic tumour (ETT), of which invasive mole and choriocarcinoma are more common. GTNs are among the rare human tumours that can be cured even in the presence of widespread dissemination [1].

The incidence of molar pregnancy in South-east Asia (2 to 10 per 1,000 pregnancies) is much higher than the incidence in Europe or North America (about 0.6 to 1.1 per 1,000 pregnancies). In India and the Middle east the incidence is believed to be 1 in 160 pregnancies [2]. Incidence of GTN has been reported from 18% to 29% after a molar pregnancy [2,3]. The risk of development of GTN after complete mole is around 20% and 1 to 4% in partial mole [1,3-5]. United Kingdom (UK) has a chemotherapy rate of 0.5-1.0% for GTN after partial molar pregnancy and 13-16% after complete molar pregnancy [6].

Management of a molar pregnancy includes suction evacuation, histotogical examination and serial follow-up with β-hCG [1,5]. Postevacuation high hCG values have also been associated with development of GTN [7,8]. Several studies have reported almost full remission for low risk disease with primary therapy [1,9].

Most remaining refractory cases were successfully treated with a second single agent chemotherapy or hysterectomy leading to an overall remission rate of virtually 100% [10,11]. Combination chemotherapy should be continued for two to three cycles after three consecutive β-hCG assays are normal and there is no clinical evidence of disease. In both single agent and combination chemotherapy after achieving remission, twice weekly measurement of β-hCG is done for three months, then monthly for one year. Effective contraception should be advised during follow-up period. Ideally, all patients should have lifelong follow-up.

There is a wide variation in incidence reported in India which has been attributed to genetic, demographic, social, environmental and patient related factors. Keeping the above scenario in mind the study was undertaken to identify and analyse clinical, socio-demographic and hormonal profile of GTN to identify specific risk factors in patients admitted to our hospital. The pattern of incidence over recent years was noted. An attempt has been made to distinguish any difference in risk factors between low risk and high risk cases. The efficacy of treatment protocol used in our hospital was also reviewed.

MATERIALS AND METHODS

The present retrospective descriptive study was conducted in the Department of Obstetrics and Gynaecology in, a tertiary care teaching hospital Government Medical College, Thiruvananthapuram, South India after taking the Ethical Committee clearance (IEC. No.8/3/2011. MCT). The case sheets of all the patients who attended the vesicular mole clinic over a period of 10 years from January 2002 to December 2011 were taken and study subjects were identified

using the criteria given below for diagnosing postmolar GTN. The collected data was analysed from January 2020 to August 2020.

The FIGO criteria for diagnosing postmolar GTN includes [5,7]:

- Four values or more of hCG documenting a plateau (+-10% of hcg value) over at least three weeks.
- A rise of hCG of 10% or greater for three values or longer over at least two weeks.
- Presence of histologic choriocarcinoma.
- Persistence of hCG six months after mole evacuation, even if still falling.

Treatment used is based on the modified World Health Organisation (WHO) scoring system as adapted by FIGO for GTN. Low risk cases (score ≤6) receive single agent (methotrexate) chemotherapy and high risk cases (≥7) receive combination, Etoposide, Methotrexate, Actinomycin D, Cyclophosphamide (EMA-CO) and Vincristine chemotherapy [1,5,7,11,12].

In both single agent and combination chemotherapy after achieving remission, twice weekly measurement of β-hCG is done for three months, then monthly for one year. Effective contraception is advised during follow-up period.

Inclusion criteria: All cases of postmolar GTN diagnosed as per FIGO criteria during the study period who had regular follow-up with complete records.

Exclusion criteria: Cases of GTN with irregular follow-up and incomplete records were excluded. Cases of GTN outside the study period were also excluded.

Study Procedure

There were a total of 100 cases of GTN during the study period. Various epidemiological factors were obtained from the details which had been meticulously noted in the old records. They were retrospectively analysed. The hospital incidence of GTN and proportion of GTN among vesicular mole was calculated. The different socio-demographic factors, clinical features and hormonal profile of all cases of GTN were studied in detail.

Type of chemotherapy, indication and outcome were obtained from the follow-up details in the records. Each case was categorised into a low risk or a high risk group according to modified WHO scoring system as adapted by FIGO [5,7,11]. The above said variables were compared in high risk and low risk groups to find out any statistically significant association. Cases of invasive mole were diagnosed based on radiological or histological evidence and its effect on treatment was noted by the type and courses of chemotherapy in those patients.

STATISTICAL ANALYSIS

Data was entered in excel sheet and analysed using Statistical Package of the Social Sciences (SPSS) version 27.0 software. The distribution of each variable was studied. Chi-square test was used to measure the association between the various variables with high risk and low risk groups of GTN.

RESULTS

There were 933 cases of vesicular mole during the study period of which 100 developed GTN. The incidence of vesicular mole was 7.13 per 1000 deliveries during the study period. The incidence of GTN was 0.76 per 1000 deliveries. The proportion of GTN among molar pregnancy varied from 2.29% to 15.9% per year with an average value of 10.7%. Majority of GTN cases were found between 21 and 30 years with a mean age of 25 years, standard deviation of 4 and a range from 18 to 44 years [Table/Fig-1]. Age of marriage of majority of cases was between 21 and 25. Mean age of the husband was 29 years, majority were between 26 and 35 years.

Variable	Frequency (n)	Percentage (%)
Age of patient		
≤20 years	12	12%
21 - 30 years	83	83%
31 - 40 years	4	4%
>40 years	1	1%
Contraception used		
Yes	51	51%
No	49	49%
Previous GTD		
Yes	4	4%
No	96	96%
Blood group of wife		
A	32	32%
B	25	25%
AB	14	14%
O	29	29%
Parity		
Nullipara	47	47%
1	47	47%
>=2	6	6%

[Table/Fig-1]: Demographic profile.

About 46% of GTN cases had blood group A and AB; among them 63% had high risk disease. Blood groups A and AB may be associated with development of high risk GTN. Contraceptives (oral contraceptive pills/barrier methods/intrauterine devices) were used by 51% of women prior to pregnancy. Family history of GTD was seen in 2% of subjects. Previous pregnancy was a normal term pregnancy in 81.1% of patients. Only four of them had a previous history of GTD. Recurrence rate of vesicular mole in cases was 5.1%. The index pregnancy in all cases of GTN in the present study was a vesicular mole.

A 44% of patients presented with uterine size greater than period of amenorrhoea, at the time of diagnosis of molar pregnancy [Table/Fig-2]. Range was from five weeks to 24 weeks. The mean period of amenorrhoea at diagnosis was 11.4 weeks and the standard deviation was 4.5. A 41% cases had period of amenorrhoea more than 12 weeks, when they were diagnosed to have vesicular mole. The most common clinical presentation at diagnosis of GTD was bleeding per vaginum (69%). An 18% were diagnosed to have vesicular mole on routine ultrasonogram. About 3% presented with passage of vesicles. Preeclampsia developed in 1% only.

Variables	Frequency (n)	Percentage (%)
Uterine size at diagnosis		
Lesser than period of amenorrhoea	21	21%
Equal to period of amenorrhoea	35	35%
Greater than period of amenorrhoea	44	44%
Presence of theca leutin cyst		
Yes	40	40%
No	60	60%
Indications for chemotherapy		
Rising hCG	72	72%
Rising hCG with invasive mole	16	16%
Plateauing hCG	9	9%
hCG >20000 IU four weeks postevacuation	3	3%

[Table/Fig-2]: Clinical profile.

About 40% of the patients had theca lutein cysts in the ovary, among them 60% had cysts greater than 6 cm and bilateral cysts were noted in 70%. Bilateral cyst with size greater than 6 cm was associated

with development of GTN and presence of theca lutein cysts was a statistically significant risk factor for high risk GTN (p=0.022) [Table/Fig-2]. GTN was found more in those with complete mole (71%). All patients had stage one disease; none of them had any distant metastasis. An 81% had low risk GTN and 19% had high risk GTN. Major indication for starting chemotherapy was rising β-hCG (72%) on follow-up [Table/Fig-2]. Invasive mole was present in 16% of cases. In those with invasive mole, 75% had low risk disease.

Hysterectomy was done in two patients with persistent trophoblastic disease. Both had invasive mole and belonged to the high risk group. Due to inadequate response to therapy hysterectomy was done. Both achieved complete remission with further courses of combination chemotherapy. Minimum number of courses of single drug chemotherapy was one and maximum was nine. Minimum number of courses of combination chemotherapy was one and maximum was eight. Average number of courses in both single drug and combination chemotherapy was five.

Majority of the patients had a pre-evacuation β-hCG greater than one lac (47%), association exits between pre-evacuation hCG greater than one lac and development of GTN [Table/Fig-3]. But pre-evacuation β-hCG values had no statistical association to the type of chemotherapy (p=0.117).

β-hCG hCG values in mIU/mL	No. of patients (pre-evacuation)	No. of patients (pretreatment)
<1000	1	31
1000-10000	21	38
10000-100000	31	27
>100000	47	4

[Table/Fig-3]: Pre-evacuation and pretreatment β-hCG values.

A 69% of patients had pretreatment hCG values greater than 1000 mIU/mL. Only 13% of study subjects had postevacuation β-hCG (after 48 hours) greater than or equal to 100,000 mIU/mL which was not statistically significant. A hCG value greater than 1000 mIU/mL, especially four months postevacuation may be associated with development of GTN. About 69% of persistent trophoblastic disease was diagnosed >4 months after evacuation of a molar pregnancy [Table/Fig-4].

About 31.6% of patients in the combination chemotherapy group had a pre-evacuation β-hCG value more than 1 lac mIU/mL, whereas only 8.6% of patients of single drug group had pre-evacuation hCG greater than one lac. When pretreatment β-hCG is greater than 1,00,000 mIU/mL there is a statistically significant increase in number of combination chemotherapy (p<0.001) [Table/Fig-5].

Interval from index pregnancy	No. of cases of GTN (N)
<4 months	30
4 to 6 months	11
7 to 12 months	20
>12 months	39

[Table/Fig-4]: Interval from index pregnancy.

β-hCG Pretreatment	Type of chemotherapy				Total	
	Single drug		Combination chemotherapy			
	n	%	n	%	n	%
>100000	0	0.0	4	21.1	4	4.0
≤100000	81	100.0	15	78.9	96	96.0
Total	81	100.0	19	100.0	100	100.0

[Table/Fig-5]: Pretreatment β-hCG and type of chemotherapy.
*Fisher's-exact test p<0.001

Of the 16 invasive mole, only four received combination chemotherapy, type of chemotherapy had no relation with uterine myometrial invasion (p=0.749,); but more number of courses of chemotherapy had to be given for them (p=0.007). Eight cases out of the 12 (66.6%) who took single agent chemotherapy had to be given more than five courses of chemotherapy (p=0.007). No statistically significant association was observed between the type of mole and myometrial invasion (p=0.324). When uterine size was greater than period of amenorrhoea there is a statistically significant increase in the number of high risk disease (p<0.001) [Table/Fig-6]. Presence of theca lutein cysts is a statistically significant risk factor for high risk GTN (p=0.022).

DISCUSSION

In the present study, the hospital was a referral centre, most of the cases of vesicular mole were referred (61%). The incidence of vesicular mole was 7.13 per 1000 deliveries. It was 2.3 per 1000 deliveries in the study by Lakra P et al., [13]. The incidence of GTD in another study by Kumar D et al., in India was 4.5 per 1000 deliveries [14]. The incidence of GTN was 0.76 per 1000 deliveries. Majority of GTN cases was found between 21 and 30 years with a mean age of 25 years and a range from 18 to 44 years, comparable to Indian studies by Lakra P et al., and Hussain A et al., [13,15]. Advanced maternal age has been postulated as a risk factor for GTN [1,11], but this was not seen probably because of early marriage in the community and main bulk of the pregnant patients were between 20 and 35 years of age. No relation was observed between gravidity, parity and development of GTN.

Variables		Low risk		High risk		Total		p-value
		Count	% within FIGO score gp	Count	% within FIGO score gp	Count	% within FIGO score gp	
Age of wife (years)	>35	0	0	1	5.3%	1	1.0%	p=0.190
	<=35	81	100.0%	18	94.7%	99	99.0%	
Age of husband (years)	>35	0	0	4	21.1%	4	4%	p=0.001
	<=35	81	100%	15	78.9%	96	96%	
Period of amenorrhoea	>=12 weeks	35	43.2%	7	36.8%	42	42%	χ^2=0.256 p=0.613
	<12 weeks	46	56.8%	12	63.2%	58	58%	
Uterine size	>POA	28	34.6%	16	84.2%	44	44%	χ^2=17.27 p=0.001
	<POA	19	23.5%	2	10.5%	21	21%	
	=POA	34	42%	1	5.3%	35	35%	
Theca leutin cysts	Yes	28	34.6%	12	63.2%	40	40%	χ^2=5.241 p=0.022
	No	53	65.4%	7	36.8%	60	60%	
Myometrial invasion	Yes	12	14.8%	4	21.1%	16	16%	χ^2=0.102 p=0.0749
	No	69	85.2%	15	78.9%	84	84%	
Pretreatment hCG (IU)	>100000	0	0	4	100%	4	4%	p=0.001
	<=100000	81	84.38%	15	15.6%	96	96%	

[Table/Fig-6]: Comparison of clinical, demographic and hormonal factors in high risk and low risk disease.

The index pregnancy in all cases of GTN in the present study was a vesicular mole. Incidence of GTN has been reported from 18% to 29% after a molar pregnancy. The risk of development of GTN after complete mole is around 20% and 1 to 4% in partial mole [1,3-5]. The proportion of GTN among molar pregnancy was 10.7% in the present study. Recurrence rate of vesicular mole was found to be 5.1%. GTN occurred more frequently in those with complete mole (71%). Of the hundred cases of GTN,16 had invasive mole while the remainder (84%) of the cases had persistent trophoblastic disease with no myometrial invasion diagnosed by rising/plateauing hCG or elevated hCG four weeks postevacuation. There was no histologically proven case of choriocarcinoma.

Uterine size greater than period of gestation, high pre-evacuation β-hCG levels (>1 lac mIU/mL), uterus large for date, bilateral theca lutein cysts and cyst size >6 cm, respiratory distress syndrome after molar evacuation, and eclampsia, have been postulated as a risk factor for development of GTN [1,3,5]. Among the GTN cases in the present study majority had uterine size greater than period of amenorrhoea. When uterine size was greater than period of amenorrhoea there is a statistically significant increase in the number of high risk disease (p<0.001). The mean period of amenorrhoea at diagnosis of GTD was 11.4 weeks, comparable to study by Lakra P et al., [13]. In the present study, it was found that bilateral theca leutin cysts with size greater than 6 cm is associated with development of GTN and presence of theca lutein cysts is a statistically significant risk factor for high risk GTN (p=0.022). When paternal age was greater than 35 years, there were more cases of high risk GTN.

Risk groups were assigned according to modified WHO scoring system as adapted by FIGO. Low risk group received single drug (methotrexate) and high risk group received combination (EMA/CO) chemotherapy [1,5,11,16,17]. All cases of low risk GTN received single agent chemotherapy with methotrexate alternating with folinic acid. Minimum number of courses of single-drug chemotherapy was one and maximum was nine. All cases achieved complete remission with methotrexate. Minimum number of courses of combination chemotherapy was one and maximum was eight. Average number of courses in both single drug and combination chemotherapy was five. In the study by Hussain A et al., average number of courses was 7.6 in high risk and 6.1 in low risk groups [15]. Hysterectomy was done in two patients with GTN. Both had invasive mole and belonged to high risk group and was initially started on EMA/CO regimen. Due to inadequate response to therapy hysterectomy was done. Both had completed their families at that time. Both achieved complete remission with further courses of combination chemotherapy. There were no case fatalities.

Of the 16 cases of invasive mole, only four received combination chemotherapy, more number of courses of chemotherapy had to be given for them (p=0.007), eight cases out of the 12 (66.6%) who took single agent chemotherapy had to be given more than five courses of chemotherapy (p=0.007). So, myometrial invasion requires significantly more number of chemotherapy than usual even though majority required single drug only. In the study by Moradi B et al., also, there was in increase in duration of treatment based on myometrial invasion detected in ultrasound [18].

Single agent chemotherapy for low risk GTN vary according to instituitional preferences. In the present study, all cases of low risk GTN received methotrexate including 12 cases of invasive mole. Further studies are required to find out, whether switching to an alternative drug or combination chemotherapy will help to reduce the number of courses to achieve remission of disease.

Pre-evacuation β-hCG greater than one lac has been associated with development of GTN [2,5]. The same finding was also observed in the present study. When pretreatment β-hCG is greater than 1,00,000 mIU/mL, there is a statistically significant increase in number of combination chemotherapy (p<0.001).

Braga A et al., reported that postevacuation β-hCG values following complete molar evacuation can be used to predict development of gestational trophoblastic neoplasia [8]. A 69% of patients had pretreatment hCG values (>4 months postmolar evacuation) greater than 1000 mIU/mL. A hCG value greater than 1000 mIU/mL especially four months postevacuation was found to be associated with development of GTN in the present study.

The GTN being a highly curable disease, aim of treatment should be early diagnosis and effective management with minimum relapse. The present study demonstrates that meticulous follow with accurate documentation was done for all cases and all achieved complete remission. Also, there were no fatalities.

Limitation(s)

The retrospective nature of the study and the long period of patient enrolment, were major study limitations. The toxicity profile of the chemotherapy agents were not reviewed in the present study. Another study limitation was information belonged to only the patients with GTN at the hospital, providing a partial representation of the country. Further studies are required to assess the future obstetric outcome of patients, who received chemotherapy for GTN.

CONCLUSION(S)

It is important that GTN be diagnosed early so that proper intervention can be done and chemotherapy which is curative in almost all cases can be started. Prompt identification of risk factors like complete molar pregnancy, bilateral theca leutin cysts, especially with cyst size greater than 6 cm, uterine size greater than period of amenorrhoea and serum β-hCG and hCG value greater than 1 lac mIU/mL helps in early identification of GTN. The choice of chemotherapy depends on risk categorisation based on FIGO scoring system. Single agent in low risk group and combination chemotherapy in high risk group is often sufficient. Effective counselling of patient and partner with meticulous follow-up helps in early detection of GTN.

REFERENCES

[1] Berkowitz SR, Horowitz SN, Goldstein PD. Gestational trophoblastic Disease. In Berkowitz SR editor, Berecks and Novack's gynaecology. California, Wolters Kluwer. Sixteenth edition. 2020:2758-2788.

[2] Daftary SN, Padubidri VG. Gestational trophoblastic diseases, Trophoblastic diseases. In Padubidri VG, Daftary SN editor. Shaw's Textbook of Gynaecology. Elsevier. 16th edition. 2016:311-319.

[3] Abu-Rustum NR, Yashar CM, Bean S, Bradley K, Campos SM, Chon HS, et al. Gestational Trophoblastic Neoplasia, Version 2.2019, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw. 2019;17(11):1374-91. Doi: 10.6004/jnccn.2019.0053. PMID: 31693991.

[4] Lok C, Frijstein M, van Trommel N. Clinical presentation and diagnosis of Gestational Trophoblastic Disease. Best Practice & Research Clinical Obstetrics & Gynaecology. 2021;74:42-52.

[5] Seshadri L. Gestational trophoblastic Disease. In Seshadri L editor. Essentials of Gynaecology. India, Wolters Kluwer. Second edition. 2017:500-14.

[6] Management of Gestational Trophoblastic Disease: Green-top Guideline No. 38- June 2020. BJOG. 2021;128(3):e1-27. Doi: 10.1111/1471-0528.16266. Epub 2020 Sep 29. PMID: 32996207.

[7] Ngan HYS, Seckl MJ, Berkowitz RS, Xiang Y, Golfier F, Sekharan PK, et al. Update on the diagnosis and management of gestational trophoblastic disease. Int J Gynaecol Obstet. 2018;143 Suppl 2:79-85. Doi: 10.1002/ijgo.12615. PMID: 30306586.

[8] Braga A, Biscaro A, do Amaral Giordani JM, Viggiano M, Elias KM, Berkowitz RS, et al. Does a human chorionic gonadotropin level of over 20,000 IU/L four weeks after uterine evacuation for complete hydatidiform mole constitute an indication for chemotherapy for gestational trophoblastic neoplasia? Eur J Obstet Gynecol Reprod Biol. 2018;223:50-55. Doi: 10.1016/j.ejogrb.2018.02.001. Epub 2018 Feb 15. PMID: 29477553.

[9] Wang Q, Fu J, Hu L, Fang F, Xie L, Chen H, et al. Prophylactic chemotherapy for hydatidiform mole to prevent gestational trophoblastic neoplasia. Cochrane Database Syst Rev. 2017;9(9):CD007289. Doi: 10.1002/14651858.CD007289.pub3. PMID: 28892119; PMCID: PMC6483742.

[10] Winter MC. Treatment of low-risk gestational trophoblastic neoplasia. Best Practice & Research Clinical Obstetrics & Gynaecology. 2021;74:67-80.

[11] Seckl JM. Gestational Trophoblastic Neoplasia. Edmonds KD, Lees C, Bourne T (eds.) In: Dewhurst's Textbook of Obstetrics & Gynaecology. Blackwell publishing Ltd. 9th edition; 2018:575-586.

[12] Braga A, Mora P, de Melo AC, Nogueira-Rodrigues A, Amim-Junior J, Rezende-Filho J, et al. Challenges in the diagnosis and treatment of gestational trophoblastic neoplasia worldwide. World J Clin Oncol. 2019;10(2):28-37. Doi: 10.5306/wjco.v10.i2.28. PMID: 30815369; PMCID: PMC6390119.
[13] Lakra P, Sangwan V, Siwach S, Kansal R, Mahendru R, Sharma A. Outcome of gestational trophoblastic disease in a rural tertiary centre of Haryana, India. Int J Reprod Contracept Obstet Gynecol. 2017;6:271-75.
[14] Dineshkumar, Ajitkumar Singh Y, Somenkumar Singh L, Ranjit Singh L, Liyak P, Vaz A. A study of molar pregnancy at tertiary centre of India. IOSR Journal of Dental and Medical Sciences (IOSR-JDMS). 2016;15(9):49-52. p-ISSN: 2279-0861.
[15] Hussain A, Aziz SA, Bhatt GM, Lone AR, Hussain HI, Wani B, et al. Gestational trophoblastic neoplasia: Experience from a tertiary care center of India. J Obstet Gynaecol India. 2016;66(6):404-08. Doi: 10.1007/s13224-015-0710-0.
[16] Braga A, Elias KM, Horowitz NS, Berkowitz RS. Treatment of high-risk gestational trophoblastic neoplasia and chemoresistance/relapsed disease. Best Practice & Research Clinical Obstetrics & Gynaecology. 2021;74:81-96.
[17] Balakrishnan S. Gestational Trophoblastic Disease. In Balakrishnan S editor, Textbook of Gynaecology. India, Paras Medical Publisher. Second edition. 2016:314-317.
[18] Moradi B, Borhani A, Yarandi F, Rahmani M, Shirali E, et al. Post-molar stage i low-risk gestational trophoblastic neoplasia: transvaginal ultrasound findings and their correlation with chemotherapy response. Iran J Radiol. 2020;17(1):e92005. Doi: 10.5812/iranjradiol.92005.

PARTICULARS OF CONTRIBUTORS:
1. Assistant Professor, Department of Obstetrics and Gynaecology, Believers Church Medical College Hospital, Thiruvalla, Kerala, India.
2. Assistant Professor, Department of Obstetrics and Gynaecology, Believers Church Medical College Hospital, Thiruvalla, Kerala, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Anjali Muralidas,
Assistant Professor, Department of Obstetrics and Gynaecology, Believers Church Medical College Hospital, Thiruvalla, Pathanamthitta-689103, Kerala, India.
E-mail: anjalimuralidas@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Oct 12, 2021
- Manual Googling: Jan 12, 2022
- iThenticate Software: Jan 17, 2022 (10%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? NA
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Oct 11, 2021**
Date of Peer Review: **Dec 08, 2021**
Date of Acceptance: **Jan 13, 2022**
Date of Publishing: **Apr 01, 2022**