



RETROSPECTIVE AND PROSPECTIVE STUDY OF CLINICOPATHOLOGICAL EVALUATION AND MANAGEMENT OF GESTATIONAL TROPHOBLASTIC DISEASE

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KEYWORDS :

INTRODUCTION-

GTD is spectrum of cellular proliferation disorder where trophoblast undergoes hydropic degeneration with or without invasion, hydropic fluid is rich in hCG. It can be complete mole or partial mole depending on presence of fetal tissue and in absence of invasion. if invasion is detected it can be invasive mole, choriocarcinoma, epithelioid trophoblastic tumor (ETT), placental site trophoblastic tumor (PSTT)¹, Invasive disease & PSTT are collectively called GTN. Earlier when means of diagnosis and chemotherapy were not present GTD used to carry very high mortality. Since the advent of USG to help early diagnosis and good facilities for surgical evacuation it has become easily manageable condition while at same time advent of Chemotherapy has made choriocarcinoma one of the most curable tumors even with distant metastasis. β Hcg is very Important biochemical marker for diagnosis and monitoring of GTD. USG & β -HCG² makes mainstay for diagnosis, follow up and early detection of persistence of disease. In case of GTN multispecialty management is required. As GTN may arise after any pregnancy being it H.Mole, normal or abortion making β -hcg an important element of follow up, though GTN may arise at any age but extremes of age favor it, in this study we aim to identify epidemiological factors which increase chances of GTD as well as role of follow up in early diagnosis and treatment of GTN.

AIMS AND OBJECTIVE-

To know magnitude of GTD in area catered by M.G.M. Medical college and S, = .G.P.T. Cancer hospital Indore

To correlate with the epidemiological factors like age, parity, SES etc.

To evaluate presenting clinical features

To determine high risk factors, present and further score cases.

To identify persistent disease in post molar evacuation cases or post hysterectomy.

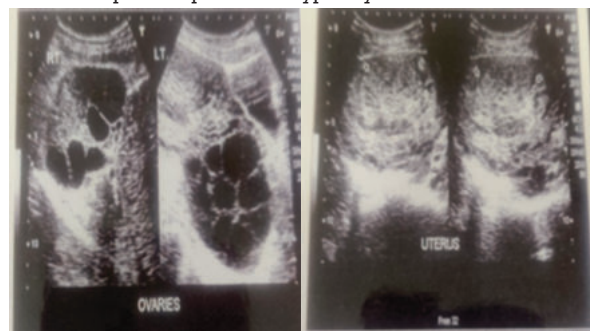
To evaluate role of prophylactic and therapeutic chemotherapy in prevention of development of choriocarcinoma.

MATERIALS AND METHODS

This retrospective and prospective study was undertaken during period of 68 months from Jan 2015 to august 2021.,at M.Y.H & S.G.P.T. Hospital with M.G.M. Medical college Indore .the patients included were from outpatient and inpatient department of Obstetrics and gynecology department of M.Y.H and Cancer Hospital, Indore.

Once patient is selected, she underwent all routine and special investigations, routine investigation included

CBC, LFT, RFT, Thyroid Profile USG abdomen and pelvis, while special investigation included X ray chest CT chest CT abdomen & pelvis. In OPD patient is recognized on the basis of symptoms. History is elicited for period of amenorrhea, bleeding p/v amount and color, abdominal pain, vomiting⁸, edema over feet and body, giddiness cough and chest pain⁹, shortness of breath¹¹, loss of appetite, jaundice, convulsion, features of preeclampsia¹⁰ and hyperthyroidism¹².

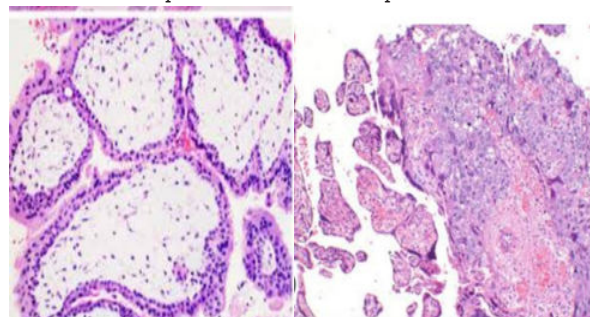


TLC cyst on USG

H.Mole on USG(snow-storm)

General and systemic examination is done to rule out any concerning findings and special reference to lungs. Abdominal examination is done to assess height and feel of uterus, presence /absence of fetal parts, bleeding p/v assessment, to rule out vaginal metastasis, size of cystic ovaries.

Patients of GTD were assessed for WHO score and subjected to different treatment modalities accordingly, i.e. S & E and follow up for low risk¹³ while surgery and chemotherapy¹⁴ and follow up for high risk. During follow up patient is assessed by complain, examination, USG for subinvolution regression of theca lutein cyst and successive regression of β -hCG. Follow up protocol used was different for partial and complete molar pregnancy³. Definitive diagnosis was made only after histopathology. For complete molar pregnancy if β HCG returned to normal in 56 days follow up was done for 6 months from the date of evacuation otherwise follow up should continue for 6 months from the date of normalized HCG. In partial mole follow up concluded once HCG returned to normal on 2 samples at least 4 weeks¹⁵ ap.



Histological picture of H.Mole Vs Choriocarcinoma

WHO SCORING SYSTEM⁴

	0	1	2	4
Age	≤40	≥40		
Antecedent Pregnancy	MOLE	ABORTION	TERM	
Interval (MONTHS)	4	4-6	7-13	≥13
Largest Tumor (Cm)		3-5	≥5	
Metastasis	LUNG	SPLEEN, KIDNEY	GIT	BRAIN, LIVER
Number Of Metastasis	0	1-4	5-8	≥8
Prior Chemotherapy			Single Drug	≥2 Drugs
Hcg Level	≤10 ³	10 ³ - 10 ⁴	10 ⁴ - 10 ⁵	≥10 ⁵

Score of ≤ 6 suggest low risk for choriocarcinoma gestational trophoblastic neoplasia (GTN)⁵

Score of ≥ 6 suggest high risk for GTN⁶.

After treatment patient was advised to use preferably barrier contraceptive for a year²²

RESULTS /OBSERVATION

This study suggested , youngest patient in study was 16 years and oldest was 60 years most patients belonged to age group 21-25 followed by 16-20 years while when ratio was compared it was found to be maximum in ≥40 years as incidence of pregnancy decreases but GTD increases with age .maximum number of cases followed parity 1 than para 0 and 02 while ratio was max for parity 4 and above. Commonest clinical finding was bleeding p/v in 90% leading to anemia in 36%.72 % had uterus larger than period of amenorrhea.

This study included 50 patients in period of 68 months from January 2015-august 2020.all patients were analyzed and data were as follows. On an average incidence was found to be 1:852 in relation to pregnancy while in relation to abortion it was found to be 1:51 spontaneous abortions.

Incidence In Relation To Pregnancy

Year	No Of Pregnancies	No Of GTD	Percentage	Ratio
2015	7086	05	0.07	1:1417
2016	7397	06	0.08	1:1232
2017	7320	09	0.12	1:813
2018	7094	08	0.11	1:886
2019	7930	13	0.16	1:610
2020 August	5800	09	0.15	1:644
Total	42627	50	0.12	1:852

When it was assessed for antecedent pregnancy out of 50 cases , maximum 46% had term delivery.20%abortion and recurrent mole in 10%,rest were primiparous patients.

USG assessment indicated most cases belonged to complete variety, had lutein¹⁶ cyst varying from 1.8-11.2 cm., which regressed on treatment and follow up. None of them needed removal. β- HCG , was used to diagnose and follow up,47/50 cases had range of ≤1000 to 1,00,000 . only3/50 (6%) had very high level to be considered high risk.

hCG Level At Onset Of Treatment

Hcg levels Miu/ml	No of cases	%
≤1000	15	30
1000-10000	20	40
10,000-1,00,000	12	24
≥1,00,000	03	06

WHO scoring system predicted 32/50 (64%) to be low risk while 18/50n(36%) Were considered high risk. 45/50 were treated with S & E out of which 7 received chemotherapy following S & E , while all patients with choriocarcinoma were treated with hysterectomy followed by chemotherapy. In the study 10 cases could not be followed. Most cases belonged to low prognostic

score group and had shown normal regression pattern while 3cases had persistently raised levels of Hcg,1 case presented with rising levels was diagnosed to be case of retained mole and underwent re-evacuation.

DISCUSSION

Incidence of GTD in relation to total number of pregnancies varies from 1:191 to 1:590 in Indian literature .we found it to be 1:852 ,similar to Milar (1989) who reported it to be 1:1000(1989). Geographical variation seen as more incidence in Asian country⁷ ,Philippines 1:82 ,3 times higher than European countries. Incidence in relation to abortion is :52 comparable to Chabal SA,(1966), 1:50 In India & 1:85 In European Countries.

When assessed for age ,max number are found in 21-25 followed by 16-20 years similar to study by V.Rjshekhara(1974)¹⁷ , when total number of cases compared to number of pregnancies above age 35,40 years , the ratio is 1:160 and 1:56 while at age 16-20 years the ratio is 1:1042 indicating rising trend in GTD cases with age and parity Parazzini (1986) said at age≥ 35 ,3 times more and ≥ 40 yrs. ,7 times more risk of GTD . the study reported more parity and. socioeconomic status plays important role in ectogenesis of H.Mole thereby corroborating the statement that GTD Is less prevent in European countries compared to Asian countries , it is suggested low carotene ,low quality protein and rice rich diet increases molar changes¹⁸ ,in this study 845 patients were from poor SES, pertain to fact that study included patients from government medical college.

On examination and history 82% presented with amenorrhea while 3 (6%) had irregular bleeding 3(6%) had lactational amenorrhea. Presenting feature was vaginal bleeding in 90% ,one post molar evacuated case reported exsanguinated and underwent emergency hysterectomy ,turned out to be case of chorioadenoma destruence. V. Rajshekhara(1974) reported amenorrhea in 77% and vaginal bleeding in 97%. Hyperemesis was present in 16% ,cough and dyspnea in 6%,preeclampsia features in 4%.V Rajasekhar and Swigg (1974) reported respiratory complication to be around 27% attributing them to thyroid storm¹⁹ , trophoblastic emboli.in this study uterus size was more compared to period of amenorrhea in 70%, equal in 14% and less in 10%.

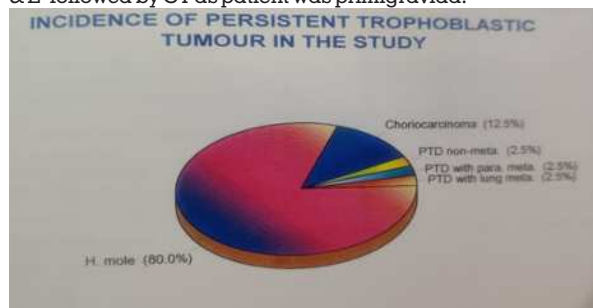
On USG all cases detected to have molar changes ,complete in 82%,partial in 12% .pelvic metastasis could be diagnosed post molar evacuation in one case and 4% had no finding because they were posting hysterectomy with metastasis. Theca lutein cyst was reported in20(40%) cases(4 with GTT, 1 with partial mole and 15 with H. Mole) . they need not be removed as they regress in 2-4 weeks' it contains watery fluid rich in β-Hcg.Montzet al(1984) found incidence of TLC varies from 25-60% varying in size from 1-10 cm.

Serum β-Hcg levels were measured pretreatment for diagnosis and scoring while post treatment levels were measured for follow up of disease²⁰ . Maximum72%patients had pretreatment level of ≤1000 IU , ≥10 000 TO ≤1,00,000 lin 22%.only3(6%) patients had level more than 1,00,000 IU , making it high risk case. these were cases of choriocarcinoma with distant metastasis . follow up could become possible in40/50 cases only. during follow up declining trend was observed in 90% of patients, persistent in3(7.5%), which turned out to be persistent trophoblastic disease (PTD). 1 patient presented with rising titer after 2 weeks which turned out to be retained mole and underwent check curettage, 1 patient reported with 8 weeks of pregnancy after 1 year. in a study by Rajan R 12.5% had persistent titer .

After USG , routine investigation , hCG level assessment and score assignment patients were treated by S & E or hysterectomy with or without chemotherapy. on score

assessment 32 (64%) belonged to low risk, while 18 (36%) were from high-risk group. 45 cases were only H. Mole. Among these 36 were treated by S & E, 7 by S & E with chemotherapy and 2 followed by hysterectomy and chemotherapy. Out of 45 molar cases 13 had high risk score. 9/13 received CT, as 4 absconded, out of these 9 with CT 3 developed PTD and 2 underwent hysterectomy. BSO was done in only one patient as she was postmenopausal, rest all TLC regressed over 2-month period. Incidence of persistent GTT and choriocarcinoma together constituted 8/40 (20%) out of which 12.5% were choriocarcinoma. In study by Rajan R (1984) on 83 patients and follow up persistent GTT was reported in 12.5% cases. Laurin (1983) reported 19% GTT, out of which 2% developed choriocarcinoma.

GTT were detected in total 8/40 (20%) cases as rest 10 were lost to follow up, when assessed against WHO score 1 case was high risk, 7 high risk and 1 was low risk. Therefore 7 underwent hysterectomy²¹ followed by CT while 1 underwent S & E followed by CT as patient was primigravida.



Treatment modality received by GTD (n=50)

	Suction & evacuation	Without CT	With CT	Hysterectomy with CT	%
Mole cases	45	32	07	02	90%
-low risk	32	04			
-high risk	13				
	05			05	10%

CONCLUSION-

It can be said that at outset disease presents as obstetric case, if remain untreated or neglected, later may present as gynecological problem. If not treated disease may metastasize locally or at distant site requiring multidisciplinary approach. Shows rising trend towards malignant changes with increasing age and parity. Main aim of treatment is to provide regular follow up in post evacuation stage with balancing drug use against surgical intervention in invasive disease. Scoring system assist in identifying the risk cases and thereby deciding the management as well need for multidisciplinary approach. Tedious follow up is integral part of GTD management, which help in early diagnosis & management of invasive disease.

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