ECRONICON OPEN ACCESS

EC GYNAECOLOGY
Research Article

Incidence and Clinical Profiles of Gestational Trophoblastic Diseases in South West Ethiopia

Admasu Taye[1], Habtamu Jarso[2] and Yesuf Ahmed[1]*

[1]Department of Obstetrics and Gynecology, Institute of Health, Jimma University, Jimma, Ethiopia

[2]Department of Epidemiology, Institute of Health, Jimma University, Ethiopia

***Corresponding Author**: Yesuf Ahmed, Department of Obstetrics and Gynecology, Institute of Health, Jimma University, Jimma, Ethiopia.

Received: November 05, 2018; **Published:** January 17, 2019

Abstract

Background: Gestational trophoblastic diseases (GTD) include a spectrum of diseases which can be grouped into a benign hydatidiform mole and malignant gestational trophoblastic neoplasia (GTN). The prevalence of the disease has demonstrated marked geographic and ethnic differences throughout the world. In Ethiopia only few published literatures exist about the disease and the magnitude is not known. This study was carried out to determine the incidence and clinical profile of GTD in south western Ethiopia.

Methods: Prospective hospital based cross sectional study was conducted to determine the incidence of GTD from September 01, 2015 - August 30, 2017. All patients diagnosed as GTD during the study period were included. Structured questionnaire were prepared and data was collected partly by interviewing the patient and partly from patient's charts. Data were cleaned, edited and entered into a computer and analyzed using SPSS version 20. Demographic characteristics, clinical presentation, management methods and complications of molar pregnancy were studied.

Results: There were a total of 83 cases of GTD diagnosed and 11,453 deliveries in JUMC during the study period making the incidence of GTD to be 7.2 per 1000 deliveries. The mean age of patients was 32.5 (± 6.5) years. More than half (54.2%) of the cases were in the age group 35 years and above, while 37.3% were grand multiparas. Vaginal bleeding was the presenting symptom in 84.5% of patients. Anemia and thyrotoxicosis were the most common complications and were present in 29 (34.9%) and 27 (32.5%) respectively. The most common type of hydatidiform mole was complete mole which was diagnosed in 54 (70.1%) patients. Suction and evacuation was the management modality for 45 (54.2%) patients while hysterectomy was done for 38 (45.8%). Age above or equal to 40 years was found to be an independently associated factor with development of malignant GTD (p = 0.01, AOR: 11.9 (95% CI 2 - 13.3)).

Conclusion: The prevalence of gestational trophoblastic was high in south west Ethiopia. Complete mole was the most common spectrum of disease diagnosed. Older age groups are at higher risk of developing malignant GTD.

Keywords: *Gestational Trophoblastic Diseases (GTD); Gestational Trophoblastic Neoplasia (GTN)*

Introduction

Gestational trophoblastic disease (GTD) is the term used to describe the heterogeneous group of interrelated lesions that arise from abnormal proliferation of placental trophoblasts. GTD lesions are histological distinct and can be benign or malignant. Benign lesions consist of hydatidiform moles, complete and partial, whereas malignant lesions consist of invasive mole, placental-site trophoblastic tumor (PSTT), and choriocarcinoma. This subset of malignant lesions that have varying propensities for local invasion and metastasis is referred to as gestational trophoblastic neoplasia (GTN). GTNs are among the rare human tumors that can be cured even in the presence of widespread dissemination [1,2].

Hydatidiform mole is an abnormal pregnancy characterized grossly by multiple grapelike vesicles filling and distending the uterus, usually in the absence of an intact fetus. Most are recognizable on gross examination, but some are small and may seem to be ordinary abortes uses [3-5].

Estimated in incidence of gestational trophoblastic disease varies in different part of the world, lowest in united states of America 0.6 to 1.1 per 1000 pregnancies to 2 per 1000 pregnancies in Japan and highest in 1 in 125 pregnancies in Taiwan [6,7].

The clinical presentation of patients in gestational trophoblastic disease significantly decreased in developed countries, this is because of routine ultrasound in early pregnancy but in developing countries most patients present late with different kind of symptoms. Most studies clinical presentation ranges from comment of vaginal bleeding too large for date uterus, hyperemises, symptom of severe pre-eclampsia and other rarely symptoms of hyperthyroidisms [5-7].

The preferred management of complete mole is evacuation of uterine content regardless of size of uterus. But for patients who complete their family size and age above 40 years, hysterectomy will be the preferred management options [2,5,7]. Follow up patients with quantitative B-hCG is the best one to detect the development of gestational trophoblastic neoplasia or recurrence but there are paucity of resource in most developing countries likes Ethiopia [5,7].

Methods and Materials

The study was conducted from September 01, 2015 - June 30, 2017 in the Oromia region, Jimma zone, Jimma town, JUMC which is located 357 kilometer South-West of Addis Ababa.

Currently Jimma university medical centre is the only teaching and referral hospital in the southwestern part of the country. It has 700 beds and more than 750 staff of both supportive and professional. It provides services for approximately 9000 inpatient and 80000 outpatient attendances per year coming to the hospital from the catchment population of about 15 million people and as well as the neighboring regions. The hospital delivers health services in many specialty areas including comprehensive services in gynecology and obstetrics with eight seniors and 43 residents

The study design was institution based study in the health facility including all patients who diagnosed gestational trophoblastic disease and followed the management of patients till discharge. Because of the rarity of the disease, the sample was taken all patients in the study period.

Sociodemographic data, previous reproductive performance, current pregnancy symptoms, gestational age were collected from face to face interview and laboratory investigation, histopathology and ultrasound results were collected from patients charts. AT discharge also patients were interviewed about complication and charts also revised to confirm the management's outcomes and what was given in the hospital stay. The investigators were checked completeness of the data before the patients discharge.

Data were cleaned, entered to computer and analyzed using SPSS version 20. Univariate and logistic regression were made to identify associated factors for gestational trophoblastic neoplasia and declared significant association when p-value < 0.05. Ethical clearance was obtained from ethical review committee of institute of health of Jimma university.

Data collection tool and techniques

Data about the socio-demographic characteristics and obstetric and gynecologic conditions of the patients were collected by interviewing the mother using structured questionnaire. Some of the part two like blood group and history of previous molar pregnancy and part three questionnaires were collected by reviewing the mother's charts using checklist. Tissue samples of all patients diagnosed or suspected of GTD based on ultrasound findings was taken during management with hysterectomy or suction and evacuation were sent for histopathologic evaluation and results were obtained on time communicating with pathology department. Two Obstetrics and Gynecology residents and two ward nurses were oriented on the data collection instruments. All mothers with GTD were followed from the time of admission to time of discharge. In addition, each day the responsible ward nurse/resident approaches the mother to find out any complication until discharge.

Data quality control

Questionnaires were prepared in English and revised by advisors; Data collectors were selected from obstetrics and gynecology resident's year-II and ward nurses working at gynecology ward.

Vague points and other problems encountered about the questionnaire were given explanation and clarification. Close supervision were undertaken during data collection. Each questionnaire was crosschecked daily by the principal investigator.

Data analysis and presentation

After data collection, each questionnaire was checked for completeness. Codes given before data entry, the collected data were cleaned, fed to computer every day and finally after data entry was completed, analysis were made using SPSS software program version 20.

Results were presented by narration and tables. Univariate and multivariate logistic regression were performed to see the existence of association between histologic features of GTDs and independent variables.

Ethical consideration

Ethical clearance was obtained from the Ethics Review Committee of Institute of Health, Jimma University. Verbal informed consent was also obtained from every study participant before the interview by explaining the objective of the study. All the information collected from the study participants were handled confidentially by omitting their personal identification, conducting the interview in private place and using the data for the research purpose only.

Results

Incidence of gestational trophoblastic disease

During study period, there were 11,453 total deliveries at Jimma University Medical Center. There were also 83 cases of gestational trophoblastic diseases diagnosed and managed at gynecology ward of the center making the incidence of GTD 7.25 per 1000 deliveries. In other words the rate at which GTD was diagnosed in the hospital was 1 per 138 deliveries or the hospital is managing 1 case of GTD every 8 days on average.

Socio-demographic and reproductive characteristics

Majority of the patients were Oromo 54 (65.1%) by ethnicity and Muslim 55 (66.3%) by religion. The mean age of patients was 32.5 years with standard deviation of 6.5. More than half 45 (54.2%) were 35 years and above while only five (6%) were below 20 years. Thirty five (42.2%) were housewives and majority 57 (68.2%) can't read and write. Nearly half 41 (49.4%) have a monthly income of less than or equal to 1000 Ethiopian birr (Table 1).

Variables	Categories	Number	Percentage (%)
Age	< 20	5	6
	20 - 24	7	8.4
	25 - 29	12	14.5
	30 - 34	14	16.9
	35 - 39	36	43.4
	≥ 40	9	10.8
Ethnicity	Oromo	54	65.1
	Amhara	11	13.3
	Gurage	7	8.4
	Dawuro	4	4.8
	Others	7	8.4
Religion	Muslim	55	66.3
	Orthodox	18	21.7
	Protestant	8	9.6
	Others	2	2.4
Occupation	House wife	55	66.3
	Farmer	14	16.8
	Merchant	10	12
	Civil servant	4	4.8
Educational status	Can't read and write	57	68.7
	Grade 1 - 8	13	15.7
	Grade 9 - 12	10	12
	Diploma+	3	3.6
House hold income	< 1000	41	49.4
	≥ 1000	42	51.6
Maternal blood group	A	31	37.3
	O	30	36.1
	B	18	21.7
	AB	4	4.8

Table 1: *Socio-demographic characteristics of patient with GTD.*

Majority of the patients were gravida five and above 54 (65.1%) while four (4.8%) were primigravida. Nine (10.8%) were nulliparous while 31 (37.5%) of them were grand multiparous. Ten patients (12%) had a past history of molar pregnancy and 30 (36%) had experienced at least one spontaneous pregnancy loss at gestational age below 5 months. About one third 27 (32.5%) had recent or past history of contraceptive use; the most common being injectables 18 (21.7%) while combined oral contraceptive was used only by two (2.4%) (Table 2). Blood groups A and O were the commonest blood group found accounting for 31 (37.3%) and 30 (36.1%) respectively. Almost two third 52 (62.7%) of patients presented at or later than 4 months of amenorrhea and fundal height at presentation was greater than 16 weeks sized for nearly three quarter 60 (72.3%) of patients. The mean fundal height was 19 week size gravid uterus, with range of < 12 weeks to 28 weeks.

Variables	Categories	Frequency	Percentage (%)
FH at presentation	≤ 12 weeks	2	2.4
	13 - 16 weeks	21	25.3
	17 - 20 weeks	40	48.2
	> 20 weeks	20	24.1
Duration of amenorrhea	2 months and below	8	9.6
	3 months	23	27.7
	4 months	33	39.8
	5 months and above	19	22.9
Gravidity	1	4	4.8
	2 - 4	25	30.1
	≥ 5	54	65.1
Parity	0	9	10.8
	1	11	13.3
	2-4	32	38.6
	≥5	31	37.3
Spontaneous abortion	None	53	63.9
	1	26	31.3
	2 and above	4	4.8
Previous mole	None	73	88
	Yes	10	12
Contraception use and type	None	56	67.5
	Injectables	18	21.7
	Implants	4	4.8
	COC	2	2.4
	Others*	3	3.6

Table 2: *Gynecologic and obstetric variables distribution in patient with GTD.*

Clinical profiles of patients

Vaginal bleeding was the commonest presenting symptom in 70 (84.3%) followed by excessive nausea and vomiting which accounted for fourteen (16.9%). Passages of vesicles were reported by only two (2.4%) patients. About two third (63.8%) had at least one complication at presentation while 21 (25.3%) patients had two or more complications, the two most common being anemia and thyrotoxicosis accounting for 29 (35%) and 27 (32.5%) respectively (Table 3). From 83 cases of GTD during the study period, histopathology was confirmed for 77 (92.8%) of the cases. The most common type of hydatidiform mole was complete mole which was diagnosed in 54 (70.1%) patients, while invasive mole was the most common type of GTN, diagnosed in 5 (6.5%) of patients (Figure 2).

Variables	Categories	Frequency	Percentage (%)
Presentation	Vaginal bleeding	70	84.5
	Nausea and vomiting	14	16.9
	Abdominal mass	3	3.6
	Passage of vesicles	2	2.4
	Cough and hemopthysis	1	1.2
Complications	Anemia	29	34.9
	Thyrotoxicosis	27	32.5
	Preeclampsia	12	14.4
	Hyperemesis gravidarium	7	8.4
	Need of ICU admission	3	3.6
	Heart failure	1	1.2

Table 3: *Presenting symptoms and complication of patients with GTD.*

Management modalities and outcome of GTDs

There are different options of management of gestational trophoblastic disease; the surgical management was the major management option in the study area.

Suction and evacuation was the management modality for 45 (54.2%) patients while hysterectomy was done for 38 (45.8%). Prophylactic chemotherapy with single agent oral methotrexate was given for 5 patients with complete mole after being managed with suction and evacuation initially. Among two of the patients with choriocarcinoma, one patient was initially managed by hysterectomy then provided oral methotrexate but failed to respond and finally referred for combination chemotherapy to oncology centre and the other died in ICU after being managed with hysterectomy plus oral methotrexate. Among five patients diagnosed with invasive mole, two of them managed with hysterectomy alone, three of them managed with hysterectomy plus oral methotrexate.

Variables		Hydatidiform mole (n = 70)	GTN (n=7)	Univariate result		Multivariate result	
				P value	COR and 95% CI	P value	AOR and 95% CI
Age	≥ 40 yrs	4 (5.7)	4 (57.1)	0.001	22 (3.6 - 134)	0.01	11.9 (2 - 13.3)
	< 40yrs	66 (94.3)	3 (42.9)		1.0		1
Parity	≥ 5	25 (35.7)	6 (85.7)	0.03	10.8 (1.2 - 94)	0.13	6 (.6 - 63)
	< 5	45 (64.3)	1 (14.3)		1.0		1
Any previous spontaneous abortion	Yes	23 (32.9)	5 (71.4)	.06	5.1 (.9 - 28)	0.26	3 (.4 - 22)
	None	47 (67.1)	2 (28.6)		1.0		1
Gravidity	≥ 5	46 (65.7)	6 (85.7)	0.3	3 (.4 - 27)		
	< 5	24 (34.3)	1 (14.3)		1.0		
History of contraceptive use	Yes	24 (34.3)	2 (28.6)	.76	.76 (.13 - 4)		
	None	46 (65.7)	5 (71.4)		1.0		
Irregular menstrual cycle	Yes	40 (57.1)	3 (42.9)	.47	.56 (.11 - 2)		
	None	30 (42.9)	4 (57.1)		1.0		
GA at Presentation	≥ 5 months	13 (18.6)	3 (42.9)	.15	3.2 (.66 - 16)		
	< 5 months	57 (81.4)	4 (57.1)		1.0		

Table 4: *Univariete and multivariate analysis of risk factor for the development gestational trophoblastic neoplastic.*

Factors associated with histological features of GTD

To identify factors associated with histological features of GTD, we compared different characteristics of GTN patients with that of hydatidiform mole. According to the results of univariate analysis, age ≥ 40 yrs (p = 0.001) and grand multiparity (p = 0.03) are significantly at increased risk for the development of GTN. But with multivariate analysis only age above or equal to 40 years was found to be an independent risk factor with statistically significant association for the development of malignant GTN (p = 0.01, AOR 11.9 (95% CI 2 - 13.3)) (Figure 1 and Table 4).

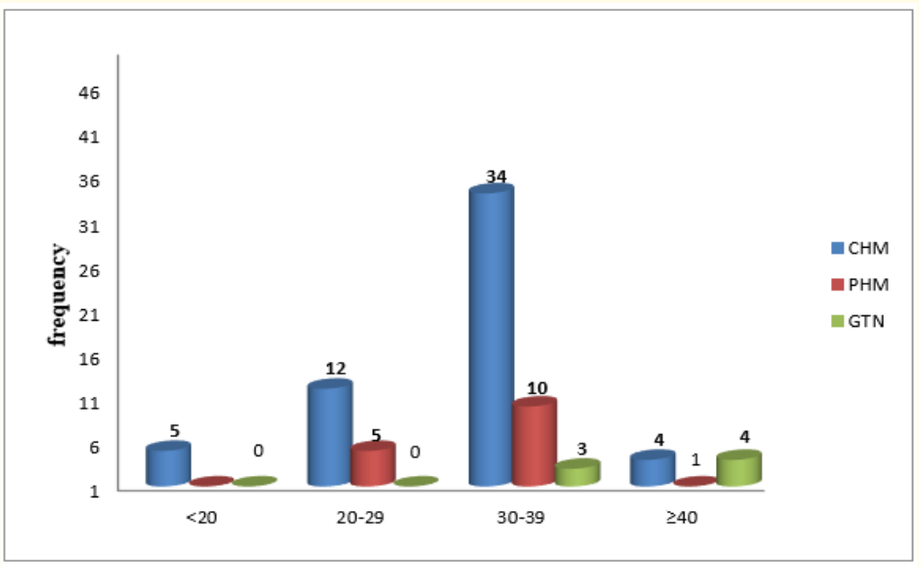

Figure 1: *Distribution of GTD with age.*

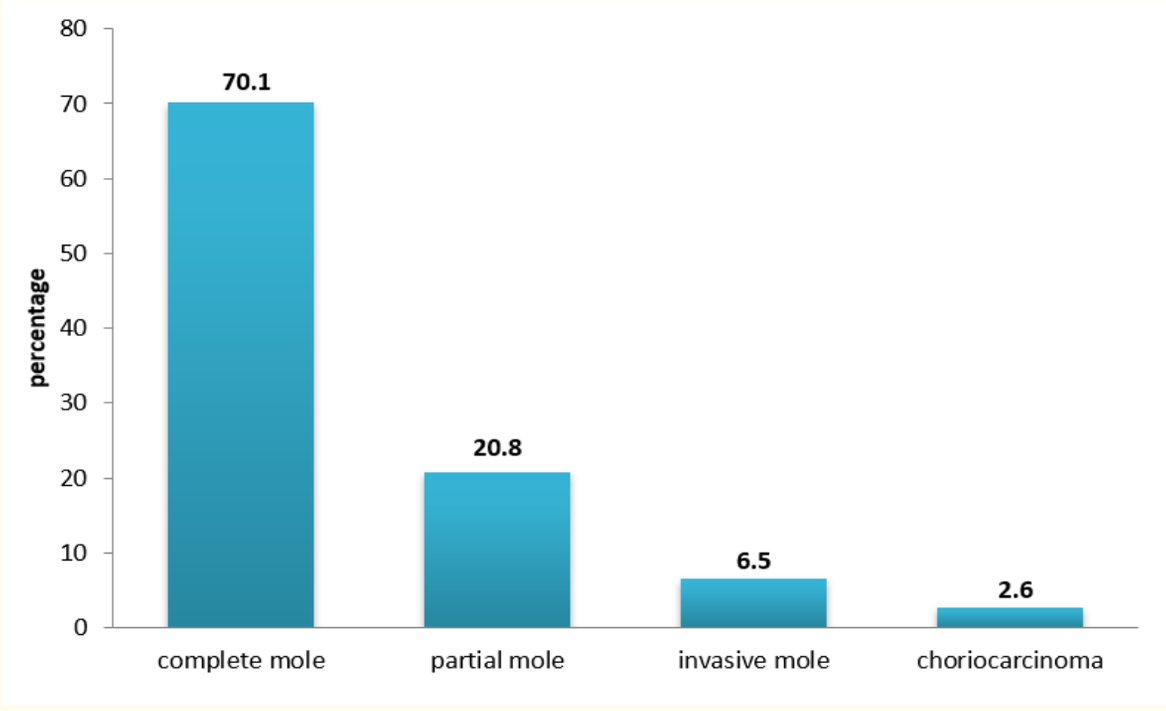

Figure 2: *Proportion of the different histologic type of GTD.*

Discussion and Conclusion

The incidence of GTD in this study was 7.2 per 1000 deliveries. It is much higher than 2.8 per 1000 deliveries in Black lion and Saint Paul hospitals in the capital Addis Ababa [8]. In other way the study was retrospective from review of medical records which included no cases of partial mole which may have been missed. It is also very much higher than incidence rate of 0.6 - 1.1 per 1000 pregnancies in North American and European countries which are largely population based studies and regional differences [6,9]. However it is comparable with figures in some Asian countries like Taiwan and Philippines which is 1 per 125 pregnancies and 7 per 1000 deliveries respectively and slightly lower than 1 per 100 pregnancies in Indonesia [10,11].

Jimma University Teaching Hospital is the only referral tertiary hospital in south western part of Ethiopia, the cases and deliveries represent large proportion of cases that visit the hospital for treatment. However as deliveries also happen at home, surrounding district hospitals, health centers and private institutions while most of the GTD patients are referred to our hospital, the prevalence may be lower if population based study done.

Majority 45 (54.2%) of GTD are aged 35 and above which is a consistent risk factor in different studies while only 6% are aged 20 years and below [12,13]. Half (49.4%) of the cases have income less than 1000 Ethiopian birr which below poverty line as per scale of the country and can be one of the reasons for high incidence.. In our study 32.5% of patients have history of ever use of contraception the most common contraceptive used by patients being injectable contraception Medroxy progesterone acetate while oral contraception was used only by 3.6% of the cases (2.4% Combined oral contraceptives, 1.4% Progestin only pills).

Large proportion of cases occurred in those gravid ≥ 5 (65.1%) and grand multiparous (37.3%). How different studies fail to show real association between gravidity and molar pregnancy when matched with age [14]. In our study 36.1% has history of spontaneous abortion, in earlier study by Parazzini., *et al.* previous spontaneous abortion at least doubles the risk of developing molar Pregnancy [35].

In this study 90.9% of cases are hydatidiform mole, 77.1% complete and 22.9% partial mole while GTN was diagnosed in 9.1% of patients. The most common GTN was invasive mole 6.5% and choriocarcinoma accounts for 2.6% of GTD. There was no patient diagnosed with PSTT in the current study. Complete mole is more common than partial mole in our study which is also the case in many other studies in Africa and Asia [8,15,16]. However study from Canada, by Altman., *et al.* and Ireland have shown partial mole to be more common than

complete mole [17,18]. This difference may be due to variations in the prevalence of risk factors different settings and in part due to the fact that some cases of partial mole may misdiagnosed as incomplete and missed abortion. The proportion of invasive mole and choriocarcinoma in this study is comparable with different literatures [2,5,9]. But it is in contrary to the study by in capital which shows 15.1% choriocarcinoma and 12.9% invasive mole [8]. High proportion of choriocarcinoma, 30% and 33% is also reported in South Africa and Nigeria respectively [12,19]. This may be due to availability of chemotherapy only in few centers in Africa where cases of choriocarcinoma are managed.

Vaginal bleeding was the most common presenting symptom in 84.5% in our study. Anemia and clinical hyperthyroidism were diagnosed in just one third of patients, 34.9% and 32.5% respectively. Preeclampsia and HEG also complicated 14.4% and 8.4% of cases while one patient (1.2%) developed high output heart failure secondary to thyrotoxicosis. This shows that complication is still common in this area as compared studies from developed countries where these complications are rare currently as compared to the past [7,20]. This is due to still low Antenatal care practice in this area and hence patients present late mostly after experiencing complication of vaginal bleeding. This was found in our study as 62.9% presented after 4 months of amenorrhea and 22.9% presented after 5 months, mean (± SD) fundal height was 19 (± 3.6) weeks. This study shows that patients present very late as compared to study from western countries where average gestational age at presentation is 10 weeks [7,21]. One patient with choriocarcinoma died during our study period after presenting late with widespread metastasis. There was however no cases with trophoblastic embolization and treatment related uterine perforation.

In our study we tried compare different characteristics of patients with gestational trophoblastic neoplasia with that of hydatidiform mole. Multivariate analysis result showed patients who are 40 years and above are more likely to develop malignant form of GTD, about 12 times than those who are less than 40 years p = 0.01, AOR 11.9 (95% CI 2 - 13.3). This is also confirmed in different other studies [20]. But presence of previous spontaneous abortion doesn't significantly differ among patients with hydatidiform mole and those with GTN in our study. Whereas other study showed that increase risk twice [22].

High percentages (45.8%) of patients are managed with hysterectomy while this is not the case in other studies [5,20]. Almost two third (65.1%) are gravid 5 and above, while more than half (54.2%) are 35 years and above which is one reason. On the other hand due to absence of chemotherapy and difficulty of post molar surveillance physicians prefer to do hysterectomy if family size is completed. But still there is 3 - 5% chance of persistence disease after hysterectomy for high risk mole [20]. Hysterectomy was the primary management modality for GTN as it was done for all cases. Literatures however suggest that it should be done only for selected cases of GTN and never be the primary treatment unless PSTT [5,20]. So management of GTD in our hospital is suboptimal because of lack of chemotherapy unit which contributed for the death of one patient during our study, may have survived if give combination chemotherapy. This also made post molar surveillance difficult due lack of appropriate management plan if persistent disease is diagnosed. In addition most patients are from far rural areas and can't complain with the standard follow up.

In conclusion, the incidence of GTD higher in this study and patient's clinical presentation late and that makes the managements suboptimal.

Bibliography

1. Berkowitz RS and Goldstein DP. "The management of molar pregnancy and gestational trophoblastic tumors". In: Knapp RC, Berkowitz RS, editors. Gynecologic oncology. 2nd Edition. New York: McGraw-Hill (1993): 328-338.

2. Bagshawe KD. "Risks and prognostic factors in trophoblastic neoplasia". *Cancer* 38.3 (1976): 1373-1385.

3. Berkowitz RS and Goldstein DP. "Molar Pregnancy". *New England Journal of Medicine* 360 (2009): 1639-1645.

4. Goldstein DP and Berkowitz RS. "Current management of complete and partial molar pregnancy". *Journal of Reproductive Medicine* 39.3 (1994): 139-146.

5. Paola A. "Gestational Trophoblastic Disease". In: Current diagnosis and treatment obstetrics and gynecology. Alan HD, Lauren N, Murphy TG, Neri L (Eds). 11th edition McGraw Hill, New York (2007): 885-895.

6. Palmer JR. "Advances in the epidemiology of gestational trophoblastic disease". *Journal of Reproductive Medicine* 39.3 (1994): 155-162.

7. Mangili G., *et al*. "Clinical presentation of hydatidiform mole in northern Italy: has it changed in the last 20 years?" *American Journal of Obstetrics and Gynecology* 198.3 (2008): 302.e1-302.e4.

8. Dereje N and Tefera B. "Profile of gestational trophoblastic diseases in two teaching hospitals in Addis Ababa-Ethiopia". *Ethiopian Journal of Health Sciences* 14.4 (2008): 195-201.

9. Harma M.., *et al*. "Gestational trophoblastic disease in Sanliurfa, southeast Anatolia, Turkey". *European Journal of Gynaecological Oncology* 26.3 (2005): 306-308.

10. Cagayan MS. "Hydatidiform mole and its complications: review of patient profiles and management at the university of the Philippines-Philippine General Hospital". *Journal of Reproductive Medicine* 59.5-6 (2014): 235-240.

11. Aziz MF., *et al*. "Epidemiology of gestational trophoblastic neoplasm at the Dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia". *Advances in Experimental Medicine and Biology* 176 (1984): 165-175.

12. Ibrahim Y., *et al*. "Gestational Trophoblastic Diseases in a Teaching Hospital in Northern, Nigeria". *American Journal of BioScience* 3.1 (2015): 7-10.

13. Parazzini F., *et al*. "Parental age and risk of complete and partial hydatidiform mole". *British Journal of Obstetrics and Gynaecology* 93.6 (1986): 582-585.

14. Pezeshki M., *et al*. "The role of repeat uterine evacuation in the management of persistent gestational trophoblastic disease". *Gynecologic Oncology* 95.3 (2004): 423-429.

15. Agrawal., *et al*. "Clinico-epidemiological profile of molar pregnancies in a tertiary care centre of Eastern Nepal: a retrospective review of medical records". *Gynecologic Oncology Research and Practice* 2 (2015): 9.

16. Çakmak., *et al*. "Incidence of gestational trophoblastic disease in Tokat province, Turkey". *Journal of the Turkish-German Gynecological Association* 15.1 (2014): 22-24.

17. Altman AD., *et al*. "Maternal age-related rates of gestational trophoblastic disease". *Obstetrics and Gynecology* 112 (2008): 244-250.

18. Jeffers MD., *et al*. "Partial hydatidiform mole: a common but underdiagnosed condition". *International Journal of Gynecological Pathology* 12.4 (1993): 315-323.

19. Moodley M., *et al*. "Gestational trophoblastic syndrome: an audit of 112 patients. A South African experience". *International Journal of Gynecological Cancer* 13.2 (2003): 234-239.

20. Cunningham FG., *et al*. "Williams Obstetrics. 24th edition". Gestational Trophoblastic Disease. USA: McGraw-Hill (2010): 818-830.

21. Gemer O., *et al*. "The current clinical presentation of complete molar pregnancy". *Archives of Gynecology and Obstetrics* 264.1 (2000): 33-34.

22. Messerli ML., *et al*. "Risk factors for gestational trophoblastic neoplasia". *American Journal of Obstetrics and Gynecology* 153.3 (1985): 294-300.

Volume 8 Issue 2 February 2019