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CLINICO-EPIDEMIOLOGICAL PROFILE OF MOLAR PREGNANCIES AT A TERTIARY CARE CENTRE OF INDIA: A PROSPECTIVE OBSERVATIONAL STUDY

Gynaecology

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ABSTRACT

Objective: To study epidemiology & clinical profile of Gestational Trophoblastic Disease and to evaluate its management and outcome. **Method:** It was a prospective observational study of women (50 cases) with molar pregnancy who were diagnosed, treated and followed up at Umaid hospital, Jodhpur, Rajasthan from 1st July 2012 to 31st July 2013. **Results:** Incidence of Gestational Trophoblastic Disease was 1.76 per 1000 pregnancies with mean age distribution of 24.68 years and was found to be most frequent in nulliparous women with low socioeconomic status presenting with amenorrhoea followed by vaginal bleeding. After primary treatment, during follow up all cases were cured including malignant ones. **Conclusion**: Gestational Trophoblastic Disease requires early diagnosis, treatment and strict monitoring to be 100% curable.

KEYWORDS:

Gestational Trophoblastic Disease; Hydatidiform Mole; Gestational Trophoblastic Neoplasia; Fish Hook Effect.

INTRODUCTION

Gestational trophoblastic disease (GTD) is a spectrum of cellular proliferation arising from the placental villous trophoblast encompassing four main clinic-pathologic forms: Hydatid form Mole (H. mole) complete or partial, Invasive Mole, Choriocarcinoma and Placental Site Trophoblastic Tumor (PSTT). The term "Gestational Trophoblastic Neoplasia" (GTN) has been applied collectively to the latter three conditions; which can progress, invade, metastasize, and lead to death if left untreated.[1]

Epidemiological studies have reported wide regional variations in the incidence of H. mole. Estimates from studies conducted in North America, Australia, New Zealand and Europe have shown the incidence of H. mole to range from 0.57–1.1 per 1000 pregnancies, whereas studies in Southeast Asia and Japan have suggested an incidence as high as 2.0 per 1000 pregnancies.[2] The incidence of GTD in India was found to be one per 967 pregnancies in an epidemiological study on GTD in a North Indian population.[3]

The two established risk factors that have emerged are extremes of maternal age and prior molar pregnancy besides other known factors like, prolonged uptake of OCPs, deficiency of protein, iron and folate etc.[4-8] Complete mole most commonly presents with variable period of amenorrhea followed by vaginal bleeding, partial mole being misdiagnosed as incomplete or missed abortion confirmed on histopathological review of curetting's, and GTN has a varied presentation depending on the antecedent pregnancy event, extent of disease, and histopathology. Post molar GTN (invasive mole or choriocarcinoma) most commonly presents as irregular bleeding following evacuation of a H. mole. Molar pregnancies are usually diagnosed incidentally during dating scans supported by β-hCG levels and confirmed finally by histopathological reports.

Suction evacuation and curettage is the preferred primary mode of treatment of a H. mole, independent of uterine size, for patients who wish to maintain their fertility. Serial β-hCG levels after evacuation of a H. mole is essential to detect trophoblastic sequelae (invasive mole or choriocarcinoma), which develop in approximately 15-20% with complete mole and<5% with partial mole.[9-13]

GTDs were historically associated with significant morbidity and mortality. Currently with early detection, effective uterine evacuation and vigilant monitoring, most women with GTD can be cured with their fertility preserved. Also considering the varied incidence rates reported from Asian countries, there is a need to determine risk factors, clinical presentation, management practices outcome and incidence and prevalence rates of GTDs in Indian population, so as to diagnose it at early stage & preventing its malignant transformation.

METHODOLOGY

This prospective longitudinal observational study was carried out in department of Obstetrics and Gynecology, Umaid Hospital, Dr. S. N. Medical College, Jodhpur, Rajasthan (INDIA) after getting ethical committee approval and informed consent from patients. Pregnant patients who had registered in OPD & referred to our institute during a period of 13 months from 1st July 2012 to 31st July 2013 were enrolled. Women diagnosed with H. mole clinically, radiologically and on histopathology were studied.

Over study period a total of 28,301 pregnancies were registeredand 50patientswere diagnosed as having GTD, treated and followed up, and whenever needed referred to medical oncology department. Two out of fifty women were referred to our institute after evacuation for Mole in rural peripheral center with inadequate follow up for post-molar complications and were found to have neoplastic changes. All women under study were subjected to a detailed history as per the preset proforma including age, occupation, socioeconomic status, dietary habits, family history, previous obstetric history, period of amenorrhea, bleeding per vagina, pain abdomen, hyperemesis, pedal oedema, passing vesicles per vagina, neurological symptoms, respiratory symptoms (hemoptysis, dyspnoea) and hematemesis. Further, general physical examination, per abdominal and per vaginal examinations were carried out to evaluate anemia, thyroid related symptoms, size and consistency of uterus, any adnexal mass and signs related to neoplastic transformation of mole.

Routine investigations along with TSH, serum β-hCG, chest x-ray and ultrasonography were done. Suction evacuation under anaesthesia was the primary treatment in almost all cases except one patient of partial mole with complete placenta praevia in which hysterotomy was performed.

For follow up, serum β-hCG within 48 hours of evacuation was taken as initial level. Serumβ-hCG concentrations were measured every two weeks until the values became normal (less than 5mIU/ml). Patients whoseβ-hCG levels normalized within 56 days of uterine evacuation were monitored every month for 6 months from evacuation date. When the first β-hCG reading within the normal range was noted after 56 days, monthly monitoring was continued for 6 months after normalization.[14-15] Secondary curettage was done in selected patients

with heavy vaginal bleeding and sonographic evidence of retained products. Women diagnosed with persistent trophoblastic disease or GTN were scored according to modified WHO scoring system [Table-1].[16]

Further management including chemotherapy was done based on the total score. Patients with WHO scores <7 were considered to be at low risk and the patients with scores > 7 were considered to be at high risk. All patients with low risk disease were given single agent therapy in the form of methotrexate or actinomycin. Those with high risk disease were to be considered for EMA/CO (Etoposide, Methotrexate, Actinomycin D/Vincristine, Cyclophosphamide) multidrug chemotherapy regimen.

RESULTS

In the present study out of 28,301 pregnancies registered at our institution, 50 patients were diagnosed as having GTD. This gives an incidence of 1.76 per 1,000 pregnancies. Among these 50 cases,38 (76%)cases had complete H. mole, 10 (20%) cases had partial H. mole and 2(4%)cases had GTN at the time of presentation. During follow up 2(4%) more patients of complete mole turned into GTN. The incidence of GTN was found to be 0.15per 1000 pregnancies (4 out of 28,301 pregnancies) (Table-2).

Mean age of having GTD was 24.68 years, most of the patients (56%) were in age group of 21-25 years. Majority of patients (54%) are from lower socioeconomic status (monthly income less than 5000 rupees). H.mole was more common in Nulliparous women (30%) than in women with parity one (24%), parity two (24%), parity three (10%) and parity four and above (12%). Minimum duration of amenorrhea at the time of presentation was 8 weeks and maximum duration was 24weeks. Most of the patients (56%)presented in first trimester. Almost all patients had amenorrhea of variable period with 84% having vaginal bleeding followed by hyperemesis in26% and abdominal pain in 24% patients. None of the patients had sign/symptoms of hypertension and dyspnoea. Size of uterus was more than gestational age in 42%, smaller than gestational age in 34% and corresponding to gestational age in 24% patients. Sixty-six percent of patients were found to be anemic with blood transfusion requirement in only 6% patients who were in shock. Most frequent blood group found among patients was O (38%) followed by A (28%) (Table-2).

In present study48(96%) patients were diagnosed on ultrasound during dating scan supported by β-hCG level. Two(4%) patients were misdiagnosed as missed abortion on USG but on dilatation and evacuation found as vesicular mole and confirmed by histopathology. Pre-evacuation β-hCG levels were greater than 1 lac mIU/ml in 40% of the patients and less than 1 lac in 54% of patients [Table-3]. Twenty percent (4 out of 20) of those with β-hCG more than1 lac mIU/ml progressed to GTN. All the patients in our study were found positive on Urine pregnancy test(UPT)except one patient who was repeatedly found UPT negative with initial falsely low levels ofβ-hCG. She was diagnosed radiologically as having H. mole, and confirmed by histopathology. In follow up herβ-hCG were found high by dilution method ofβ-hCG quantification. Herβ-hCG levels shown a rise before the usual fall. This effect is known as high dose HOOK EFFECT [Figure-1].[17-18]

Most (94%) of the patients were treated by suction and evacuation. Hysterotomy was done in a patient who was diagnosed on USG with single live intrauterine fetus of 21 weeks with bulky cystic placenta completely covering the internal os (partial mole with placenta praevia). Three (6%) patients underwent subsequent total abdominal hysterectomy when they were found to have GTN in their follow up (including two post evacuation patients referred from peripheral centers). Secondary curettage was done in two patients in their first follow up visits when they complained of excessive bleeding per vaginum & their USG showed echogenic material in endometrial canal and retained products of conception was found in histopathology. Majority (90%) of patients had spontaneous remission defined as three consecutive β-hCG value undetectable. Eight percent patients progressed to GTN in present study. One patient lost to follow up (2%).Among the four cases of GTN,2(4%) developed invasive mole and 1(2%) developed choriocarcinoma. One of them showed rising titers without any other specific sign & symptom, so was categorized persistent trophoblastic disease and was referred to oncology department for chemotherapy. Because of small number of patients in present study there is higher percentage of GTN [Table-3]. All of these patients were categorized by modified WHO prognostic scoring system as low risk group and all patients had received single-agent methotrexate via the 8-day alternating methotrexate/leucovorin regimen. All of the GTN patients had history of molar pregnancy in past [Table-3].

During follow up most frequent complain of patients was bleeding per vaginum and only 16% patients presented with bleeding of more than 5 days duration. No other specific symptoms for metastasis found in these patients. No mortality found in the present study.

Table-1 Modified WHO prognostic scoring system for GTN as adopted by FIGO.

RISK FACTOR	RISK SCORE			
	0	1	2	4
Age (yrs.)	<40	>40	-	-
Antecedent pregnancy	Mole	Abortion	Term	-
Interval from antecedent pregnancy to chemotherapy (months)	<4	4-6	7-12	>12
hCG concentration (mIU/ml)	$<10^3$	10^3 -$<10^4$	10^4 -10^5	$>10^5$
Number of metastasis	0	1-4	4-8	>8
Site of metastases	Lung	Spleen, Kidney	Gastrointestinal tract	Brain, liver
Largest tumour mass diameter (cm)	-	3-5	>5	-
Previous chemotherapy	-	-	Monotherapy	Combined therapy

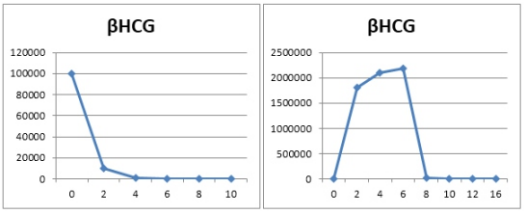
Table-2Incidence, Demographic profile, Risk Factor and Clinical Presentation of Gestational Trophoblastic Disease

S.No.	Demographic Variable		No. of patients	Percentage
1.	Gestational Trophoblastic Disease	Complete and Partial H. mole; and GTN	50	1.93/1000 Pregnancies
2.	Age	Upto 20 years	8	16
		21-25 years	28	56
		26-30 years	10	20
		31-35 years	2	4
		36-40 years	2	4
3.	Monthly Income	<5,000	27	54
		5000-10000	20	40
		>10000	3	6
4.	Parity	Nullipara	15	30
		Para 1	12	24
		Para 2	12	24
		Para 3	5	10
		Para 4 and above	6	12
5.	Amenorrhoea in weeks	Upto 8 weeks	14	28
		9-12 weeks	14	28
		13-16 weeks	13	26
		17-20 weeks	8	16
		>20 weeks	1	2
6.	Presenting Signs/Symptoms	Amenorrhoea	50	100
		Vaginal Bleeding	42	84
		Hyperemesis	13	26
		Abdominal Pain	12	24
		Passage of Vesicle	1	2
		No Symptoms	3	6
7.	Size of the Uterus	Corresponding with Gestational age	12	24
		> Gestational Age	21	42
		< Gestational Age	17	34
8.	Blood Group	O	19	38
		A	14	28
		B	12	24
		AB	5	10
9.	Anaemia	No Anaemia	17	34
		Mild Anaemia (Hb 10-10.9 gm%)	9	18

		Moderate Anaemia (Hb 7-9.9 gm%)	21	42
		Severe Anaemia (Hb<7 gm%)	3	6

Table – 3 Diagnosis, Management and Outcome of Molar Pregnancy

S. No.			No. of Patients	Percentage (%)
1.	Primary Diagnostic Modality	Radiological finding (dating scan for early pregnancy) + βhCG level thereafter	48	96
		Histopathology (Clinically & radiologically diagnosed as Missed Abortion)	2	4
2.	Pre-evacuation βhCG level (mIU/ml)	<103	3	6
		103 - 104	15	30
		104 - 105	9	18
		> 105	20	40
		Not Available	3	6
3.	Treatment Modalities	S + E	42	84
		D & C	2	4
		Hysterotomy	1	2
		S + E f/b Hysterectomy	3	6
		S + E f/b Secondary evacuation	2	4
4.	Post evacuation Outcome	Spontaneous Remission	45	90
		GTN	4	8
		Lost to follow up	1	2
5.	Antecedent Pregnancies among GTN cases	Mole	4	100
		Abortion	0	0
		Term Pregnancy	0	0
6.	Presence of bilateral	Theca Lutein Cyst	9	18



Normal regression of hCG levels after evacuation
High dose HOOK effect

Figure-1 Showing normal regression of β-hCG and high dose HOOK effect

DISCUSSION:

Gestational trophoblastic disease (GTD) encompasses a spectrum of pregnancy related trophoblastic abnormalities which include complete and partial moles, placental site trophoblastic tumors, choriocarcinomas, and invasive moles. Molar pregnancies (hydatidiform mole) represent a significant burden of disease on the spectrum of GTDs.

Published literature on incidence of GTD's from India is rather small. Studies concerning the risk factor, clinical presentation, management practices and outcomes of GTD's are rarely published from india apart from few cases. Also considering the varied incidence rates reported from Asian countries, there was a need to evaluate clinic-epidemiological profile of molar pregnancy in Indian population especially the western Rajasthan population, so as to diagnose it at early stage & preventing its malignant transformation.

In the present study, out of total 28,301 pregnancies admitted in the hospital during study period, 50 cases of GTD were diagnosed, treated and followed up for a period of 6 months. Incidence of GTD was 1.76 per 1000 pregnancies. Total four patients found malignant including the two referred from peripheral centers (two invasive moles, one choriocarcinoma and one Persistent Trophoblastic Disease). The incidence of GTN was 0.15 in 1000 pregnancies. In accordance with our study, Atrash et al in their study conducted in North America, Australia, New Zealand, and Europe reported the incidence of H. mole ranging from 0.57–1.1 per 1000 pregnancies, whereas studies in Southeast Asia and Japan have suggested an incidence as high as 2.0 per 1000 pregnancies.[2] In a study conducted in India by Rauf et al[19] the incidence of GTD was 1/967 pregnancies in a hospital based study. Out of the 50 patients with GTD 38(76%) were had Complete H. mole and 10(20%) were had Partial H.mole and 2 (4%) presented as GTN on admission being referred after evacuation from the peripheral centers. Similar results were found in the study done by Farhat Khanum et al[20] where out of 45 cases of GTD 31(68.8%) were had complete H. mole , 7(15.5%) were had partial H. mole and 7 (15.5%) were had choriocarcinoma.

In present study,40(80%) women were in the age group of 21-35 years, similarly Dr Jyoti Ramesh Chandran et al[21], Vaidya et al [22], Ocheki et al [23] found in their studies maximum incidence in age group 24-30 years. Contrary to our findings, Parazzini et al [4] and Sebire et al [5] showed that the relative risk (RR) of complete mole was elevated for teenage women (RR = 1.9) and for those aged 36-40 (RR = 1.9) or over 40 (RR = 7.5).

In present study maximum number (15; 30%) of patients were nulliparous. Similar results were found by Fatima et al[24] and Altieri et al.[25]Most of the women(54%) belonged to lower socioeconomic group favoring malnutrition as an etiological factor concluding in favors of study by parazzini et al.[26]

Gestational age at presentation was between 8-20 weeks in majority of patients (98%). Our results are comparable to study by Dr Jyoti Ramesh Chandran et al. [21] Most common presenting symptom was amenorrhea (100%) followed by vaginal bleeding(84%). This observation was supported by the studies of Fatima et al [20], Lurain et al [27], Ocheki et al [23], Curry et al [28] and Kohorn et al. [29]

In our study, 42% of patients presented with uterine size more than period of gestation, similarly Curry et al [28] found 46%and Kohorn et al [29] found 38% of patients had uterine size more than period of gestation.

Primary mode of diagnosis in the present study was USG as shown in studies done on role of sonography in detecting molar pregnancy by Santos Ramos[30], Benson CB et al[31] and Vaidya A[22].Majority (38%) of the patients with H. mole belonged to blood group 'O'. Most of the patients who progressed to GTN also had blood group O as found in study by Dr. Jyoti Ramesh Chandran. [21]Anemia was found in 66% of our patients which was similar to the study of Fatima et al[24], where out of 65 patients with molar pregnancy, 58(68.2%) patients had anaemia. All patients in our study had UPT positive except one who was repeatedly found UPT negative with initial false low levels of β-hCG. She was diagnosed radiologically as having H. mole with large bilateral theca lutein cysts, and confirmed by histopathology of specimen collected at Suction Evacuation. In follow up herβ-hCG levels were found high by dilution method of β-hCG quantification. Herβ-hCG levels had shown a rise before the usual fall, an effect known as HIGH DOSE HOOK EFFECT/fish hook effect [17,18] (card pregnancy test is a solid phase sandwich-format immunochromatographic assay for qualitative detection ofβ-hCG. When the concentration of the antigen is sufficiently high (>1lac) to saturate, both the solid migratory phase and fixed detection antibodies independently, it prevents the same molecule from binding the two antibodies and forming a "sandwich" and prevents the formation of color change and leads to a false-negative test). Pre-evacuation β-hCG levels were > 1lac mIU/ml in 40% patients. Twenty percent of those with β-hCG>1lac mIU/ml progressed to GTN and none of the patient with β-hCG <1 lac mIU/ml progressed to GTN. These results were in accordance with Menczer's study.[32] Most (84%) patients were treated primarily by Suction Evacuation. Six percent patients treated by Suction Evacuation followed by Hysterectomy, when they were found to have GTN during their follow up. Suction Evacuation followed by secondary curettage was done in four percent patients who had excessive bleeding per vagina. Hysterotomy was done as primary treatment in a patient who was diagnosed radiologically as partial H. mole with complete placenta praevia. The histopathology of curettings revealed necrotic retained products of conception. The treatment modalities of molar pregnancy were well studied by Hancock BW,

Tidy JA. Soper JT. [33,34] Ninety percent of patients achieved spontaneous remission. Four patients who underwent evacuation for H.mole progressed to GTN. Two patients (4%) who had evacuation at our institute for H.mole progressed to GTN and rest two of these women were referred to our institute after evacuation for H.mole in rural peripheral Centre with inadequate follow up for post-molar complications. All cases with GTN were found as low-risk GTN by modified WHO prognostic scoring system, and achieved remission after single agent chemotherapy. Average time of remission after diagnosis of the patients with spontaneously regressing GTD was 11.5 weeks. Similar results were found by Dr Jyoti Ramesh Chandran[21],in their study 93.6% of patients were low risk and 6.4% were high risk and given multidrug chemotherapy to the patients who developed GTN, peak/plateau was detected at average 7-10 weeks in majority and they regressed to normal after treatment at median 17 weeks. Like the study of Fatima et al[24], there was no mortality in our study due to vigilant follow up and management in contrast to Khanum[20]who reported one mortality in his study results.

Conclusion

Nearly all patients with GTD can now expected to be cured with preservation of fertility in majority of them with no long term serious consequences. Routine USG screening of all pregnancies in the first trimester helps early diagnosis, timely management of the GTDs thereby preventing their progression to GTN. Specimen from all non-viable terminations must be subjected to histopathology. All diagnosed or suspected cases of GTDs from the periphery.

Conflict of interest: There is no conflict of interest.

References:

1. Seckl MJ, Sebire NJ, Berkowitz RS. Gestational trophoblastic disease. Lancet 2010;376: 717–29
2. Atrash HK, Hogue CJR, Grimes DA. Epidemiology of hydatidiform mole during early gestation. Am J Obstet Gynecol 1986;154: 906-9
3. Kumar N, Saxena YK, Rathi AK, Chitra R, Kumar P. Host and risk factors for gestational trophoblastic disease: a hospital-based analysis from India. Med. Sci. Monit 2003;9(10): 442–7
4. Parazzini F, La Vecchia C, S. Pampallona, Parental age and risk of complete and partial hydatidiform mole. Br J Obstet Gynaecol 1986. 93 (6): 582-5
5. Sebire NJ,Foskett M, Fisher RA, Rees H, Seckl M, Newlands E. Risk of partial and complete hydatidiform molar pregnancy in relation to maternal age. BJOG 2002; 109(1): 99-102
6. Berkowitz RS,Im SS,Bernstein MR, Golstein DP. Gestational trophoblastic disease. Subsequent pregnancy outcome, including repeat molar pregnancy. J Reprod Med 1998; 43(1): 81-6
7. Parazzini F, La Vecchia C, Mangili G, Caminiti C, Negri E, Cecchetti G et al. Dietary factors and risk of trophoblastic disease. Am J Obstet Gynecol, 1988; 158(1): 93-9
8. Parazzini F, Cipriani S, Mangili G, Garavaglia E, Guarnerio P, Ricci E et al. Oral contraceptives and risk of gestational trophoblastic disease. Contraception 2002; 65(6): 425-7
9. Berkowitz RS, Goldstein DS. Clinical practice: molar pregnancy. N Engl J Med 2009; 360: 1639-45
10. Feltmate CM, Batorfi J, Fulop V, Goldstein DP, Doszpod J, Berkowitz RS. Human chorionic gonadotropin follow-up in patients with molar pregnancy: a time for reevaluation. Obstet Gynecol 2003; 101: 732-6
11. Hancock BW, Nazir K, Everard JE. Persistent gestational trophoblastic neoplasia after partial hydatidiform mole: incidence and outcome. J Reprod Med 2006; 51: 764-6
12. Feltmate CM, Growdon WB, Wolfberg AJ, Genest DR, Goldstein D P, Genest D R. Clinical characteristics of persistent gestational trophoblastic neoplasia after partial hydatidiform molar pregnancy. J Reprod Med 2006; 51: 902-6
13. Goto S, Yamada A, Ishizuka T, Tomodo Y. Development of postmolar trophoblastic disease after partial molar pregnancy. Gynecol Oncol 1993; 48: 165-70
14. Sebire NJ, Seckl MJ. Gestational trophoblastic disease: current management of hydatidiform mole. BMJ 2008; 337: 1193.
15. Sebire NJ, Foskett M, Short D, Savage P, Stewart W, Thomson M et al. Shortened duration of human chorionic gonadotrophin surveillance following complete or partial hydatidiform mole: evidence for revised protocol of a UK regional trophoblastic disease unit. BJOG 2007; 114(6): 760-2
16. Kohorn EI. The new FIGO 2000 staging and risk factor scoring system for gestational trophoblastic disease:description and critical assessment. Int J gynecol Cancer 2001; 11: 73-7
17. Levavi H, Neri A, Bar J, Regev D, Nordenberg J, Ovadia J. "Hook effect" in complete hydtatidiform molar pregnancy: a false low level of beta hCG. Obstet Gynec 1993; 82(suppl2): 720-1
18. Wheeler CA, Davis S, Degefu S, Thorneycroft IH, O'Quinn AG. Ovarian choriocarcinoma: A difficult diagnosis of an unusual tumor and a review of the hook effect. Obstet Gynecol 1990; 75: 547-9
19. Rauf B, Hassan L, Ahmed S. Management of gestational trophoblastic tumors: a five year clinical experience. J Coll Physicians Surg Pak 2004; 14: 540-4
20. Farhat Khanum, Sadia Shamsher. Gestational trophoblastic disease: experience at a tertiary care hospital of peshawar. Jpmi 2010; 24(02): 127-32
21. Jyoti Ramesh Chandran, Uma Devi N, Sumangala Devi, Sajala Vimal Raj. Epidemiology of Complete Hydatidiform Mole at a Tertiary Hospital and Analysis of Cases over Last 5 Year Period. Indian Journal Of Maternal And Child Health 2011; 13 (4): 1-8
22. Vaidya A. Molar Pregnancy - Clinical Trends at Maternity Hospital. Postgraduate medical journal of national academy of medical science 2008; 8(1): 1-6
23. Amaka N Ocheke, Jonah Musa, Alexander O Uamai. Hydatidiform mole in Jos, Nigeria. Niger Med J 2011; 52(4): 223–6
24. Fatima M, Kasi PM, Baloch SN, Kassi M, Marri SM, Kassi M. Incidence, management, and outcome of molar pregnancies at a tertiary care hospital in quetta, pakistan. ISRN Obstet Gynecol 2011; 2011: 925316
25. Altieri A, Franceschi S, Ferlay J, Smith J, La Vecchia C. Epidemiology and an etiology of gestational trophoblastic disease. Lancet Oncol 2003; 4: 670
26. Parazzini F, LaVecchia C, Mangili G. Dietary factors and risk of trophoblastic disease. Am J Obstet Gynecol 1988; 158: 93-9
27. John R, Lurain MD. 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: 531-39
28. Curry SL, Hammond CB, Tyrey L, Creasman WT, Parker RT. Hydatidiform mole: diagnosis, management, and long-term follow-up of 347 patients. Obstet Gynecol 1975; 45: 1-8
29. Kohorn EI. Molar pregnancy: presentation and diagnosis. Clin Obstet Gynecol 1984; 27: 18-19
30. Santos-Ramos R, Forney JP, Schwarz BE. Sonographic findings and clinical correlations in molar pregnancy. Obstet Gynecol 1980; 56: 186-92
31. Benson CB, Genest DR, Bernstein MR, Soto-Wright V, Goldstein DP, Berkowitz RS. Sonographic appearance of first trimester complete hydatidiform moles. Ultrasound Obstet Gynecol 2000;16:188-91
32. Menczer J, Modan M, Serr DM. Prospective follow-up of patients with hydatidiform mole. Obstet Gynecol 1980; 55: 346-9
33. Hancock BW, Tidy JA. Current management of molar pregnancy. J Reprod Med 2002; 47: 347-54
34. Soper JT. Surgical therapy for gestational trophoblastic disease. J Reprod Med 1994; 39: 168-74