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Monitoring of βHCG in 25 Yemeni women with gestational trophoblastic diseases

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Abstract
We studied 25 cases of gestational trophoblastic diseases from March- September 2014 aiming to monitor βHCG level pre-evacuation, 48 hours post evacuation and the following eight weeks post evacuation. Eight cases received chemotherapy and 17 cases without chemotherapy. During the study, we identified 19 cases vesicular mole (VM), 4 cases partial mole (PM) and 2 cases Choriocarcinoma. The mean age of our patients was (19±0.9 to 29±7) and the mean values of β-HCG was decreased rapidly and significantly post evacuation. A slower decline in the next 3weeks and a steady very slow decline after the 4th week. No significant difference between chemotherapy received cases and other cases regarding the decline in β-HCG. We conclude that good evacuation is the mainstay of treatment for molar pregnancy. Chemotherapy should be postponed as we can if no significant rise occurs post evacuation of VM and PM. Post evacuation chemotherapy should begin after the 4th week if βHCG level is more than 20,000mIU/ml. We advised to postpone chemotherapy if levels are lesser than that and do another evacuation after the 8th week if βHCG level is more than 5000mIU/ ml and not to use chemotherapy except if the level not returns to normal after that.

Keywords: GTD, βHCG, chemotherapy, VM

Introduction
Gestational trophoblastic diseases (GTD) are an uncommon complication of pregnancy. The term GTD describes a group of interrelated diseases including complete vesicular mole (VM), partial mole (PM), Choriocarcinoma (Chorio), placental site trophoblastic tumor and epithelioid trophoblastic tumor. Worldwide the incidence of GTD varies between 0.5 and 0.8 cases per 1000 live births [1].

The history and management of trophoblastic diseases can be considered as one of success stories of modern medicine as the majority if not all the women are potentially curable once prompt diagnosis and treatment commence early enough [2].

GTD diagnosis especially molar pregnancy depends on clinical finding, maternal serum β-HCG level, ultrasound and histopathological examination. Molar pregnancy management is by suction evacuation (method of choice), hysterectomy is an option for good surgical candidates not desirous for further pregnancy and elder women, and prophylactic chemotherapy for patients with high risk for malignancy (greater than 35years, previous vesicular mole, poor follow-up) [3].

Human Chorioonic Gonadotropin (HCG) is a glycoprotein that contains galactose hexosamine. It is produced by syncytiotrophoblast. Like pituitary glycoprotein hormones it is made up of α and β subunits. The α subunit is identical to α subunit of LH, FSH, and TSH. Molecular weight of α subunit is 14000 Dalton and of β subunit is 23500 Dalton. HCG is primarily leutinizing and leuteotropic and has little FSH activity [4].

It can be measured using radio immune assay (RIA), fluro immune assay (FIA) and enzyme immunoassay (ELISA) to sensitive levels below 5 mIU / ml. It can be detected in blood as early as 6 days after conception [5].

The incidence of malignant disease following vesicular mole is about 20-30% so that close follow-up and serial HCG level is essential for every patient [3]. Following evacuation of vesicular mole the patient should have: gynecological examination done one week after evacuation for uterine size, adnexal mass and unless symptoms develops examination should be repeated at 4 weeks interval, serial serum β-HCG level at weekly interval until it declines to non-detectable levels on 3 successive assays [6]. The average disappearance time of serum β-HCG after VM is 99.3 days and after PM is 68.9 days so, it is recommended NOT to start chemotherapy for Persistent Gestational Trophoblastic Diseases before 100 days after VM evacuation provided steady downward course of serum β-HCG levels [7]. Most critical time for observation is 4-6 weeks post-evacuation and about 70% would achieve normal HCG levels within 60 days post-evacuation [3]. It is convenient to ask patients to avoid further pregnancy for 6-12 months following molar pregnancy to enable efficient HCG follow-up [1]. Up to 20% of patients, trophoblastic diseases persist as evidenced by continuing clinical symptoms (particularly vaginal bleeding), excessive uterine size, prominent ovarian theca lutein cysts or marked elevation of HCG levels [8].

Chemotherapy is the mainstay in treatment of choriocarcinoma and metastatic vesicular mole. However, the use of chemotherapy as a routine adjuvant therapy for GTD in our locality should be investigated. In this study we measure β-HCG using electrochemiluminescence technique which is a sensitive technique to follow up the hormone in different GTD to know the cut off values to start chemotherapy.

Materials and methods
We retrospectively and prospectively studied 25 cases of gestational trophoblastic diseases: 19 cases VM, 4 cases PM and 2 cases Choriocarcinoma. The study was performed during

the period from March 2014 to 9 September 2014 in Al-Gomhori Teaching Hospital with the corporation of the First Yemeni Center for Tumor Diagnosis, Taiz, Yemen. We select cases whose files are complete and cooperative during the follow up period. The level of βHCG in these cases was followed up in pre-evacuation, 48 hours post evacuation and the next eight weeks post evacuation. The data collected are age, sex, type of GTD and wither the patient given chemotherapy or not. The level of βHCG was taken from the patient files as well as measured by Cobas machine (cobas e 411- Roche Co-Germany) for analysis of new samples. The kit used is (βHCG Elecsys 03271749, Lot 17509803 Roche). The data collected tabulated and subjected for statistical analysis. We use SAS program (Statistical analysis system) and Excel application of office to make the curves. The results expressed as mean ± SEM. Statistically significant achieved at $p<0.05$.

Results

We studded 25 cases of gestational trophoblastic disease. Nineteen cases were VM, four cases were PM and two cases were chorrcinoma. The mean ages of the cases were 32±2.4 in VM, 19±0.9 in PM and 29±7 in Chorio. The mean values of β-HCG pre-evacuation and 48hs post evacuation are tabulated (Table 1). The mean values of β-HCG in next eight weeks after evacuation were as follows (Table 2).

Table 1: The mean values of β-HCG pre-evacuation and post evacuation

Disease	Age	Pre evacuation	Post evacuation
VM	32±2.4	789340.5[a]	374507.14[a]
PM	19±0.9	875000[a]	598463.5[a]
Chorio	29±7	850000[a]	336308.5[a]
p. value		NS	NS

Table 2: The mean values of B-HCG in the in next eight weeks post evacuation

Disease	No	B-HCG							
		W1	W2	W3	W4	W5	W6	W7	W8
V.M	19	130048	45000	20630[b]	11192	8292	765	679	1178
P.M	4	280400	84587	32871[b]	9807	2970	541	152.9	10
Chorio	2	76592	21715	100946[a]	2834	8890	2253	644.3	312
p. value		NS	NS	0.05 *	NS	NS	NS	NS	NS

* Significant difference between a & b.

The decreasing ranges of β-HCG from post evacuation to W7 in VM, PM and Chorio were tabulated (Table 3). Illustrations of such decreases are provided in Figures 1, 2 and 3.

Table 3: The decreasing range of β-HCG in VM

Disease	No	W1	W2	W3	W4	W5	W6	W7
V.M	19	85049[a]	24370[a]	9483[b]	3900[a]	7527[a]	86[a]	-498.5[a]
P.M		195713[a]	51717[a]	23064[b]	6837[a]	2429[a]	388[a]	143[a]
Chorio		54877[a]	79231[b]	98112[a]	6056[a]	6637[a]	1608[a]	332.5[a]

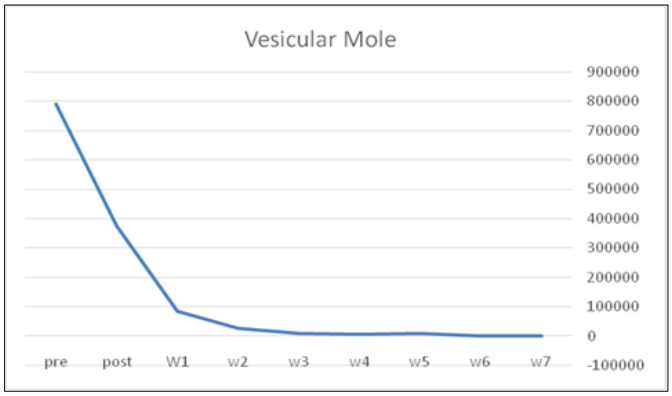

Fig 1: Decreasing range of βHCG in VM

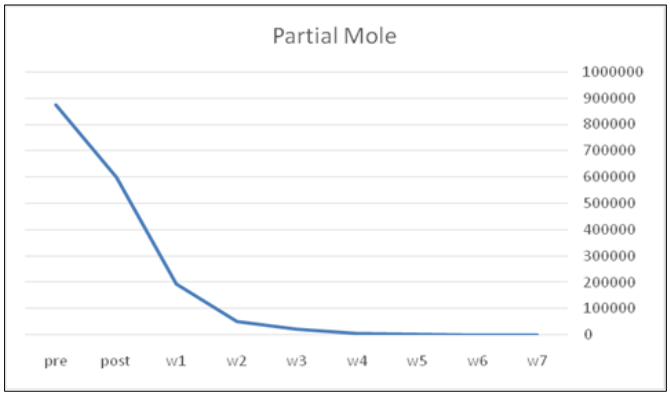

Fig 2: Decreasing range of βHCG in PM

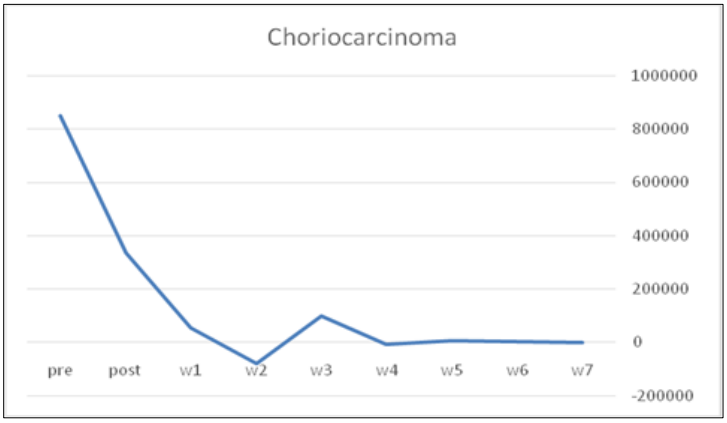

Fig 3: Decreasing range of βHCG in Chorio

The mean values of βHCG in cases received chemotherapy and not received chemotherapy are tabulated in table 4 and illustrated in Figure 4:

Table 4: Mean values of βHCG in cases received and not received chemotherapy

	No	W1	W2	W3	W4	W5	W6	W7	W8
No chemotherapy	17	204409	69697	30098	13364	7364	959	522	1316
Chemotherapy	8	33843	6490	26701	3794	7753	611	742	83
p. value	NS								

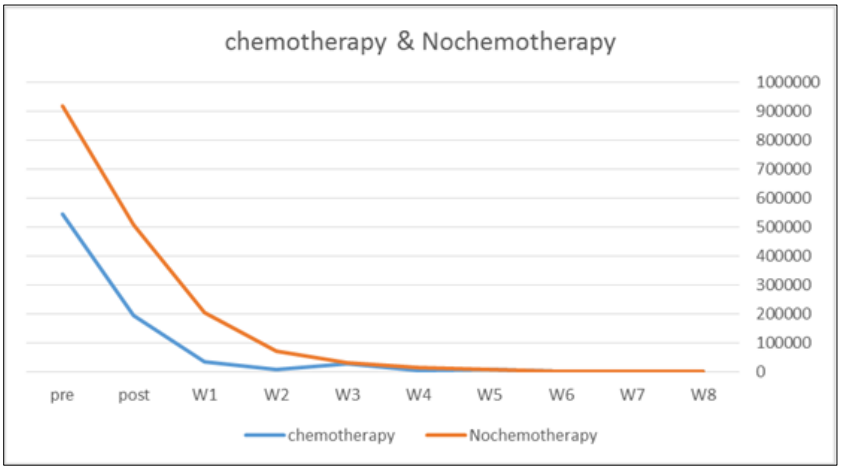

Fig 4: Mean decrease of βHCG in chemotherapy received cases and not received

Discussion

This is the first study carried in Yemen to determine the mean decline of β-HCG in various trophoblastic diseases. We studied 25 cases of GTD; 19 VM, 4 PM and 2 Chorio. Regarding the mean age of each group, we found that PM comes earlier in age than Chorio and VM, this may be due to the low number of PM cases. The mean age of VM and Chorio was 32±2.4 consistent with other studies [9, 10].

Differences between pre and post evacuation level of β-HCG

No significant differences between the mean values of pre-evacuation β-HCG level in all categories of GTD as well as between post evacuations. However, there is significant difference between pre-evacuation and post evacuation levels in each group. These data are consistent with others [10] and indicate the importance of evacuation in lowering tumor burden as it is the main treatment of GTD.

The mean values of βHCG in the eight weeks post evacuation

No significant difference between the levels of β-HCG in all groups as well as within each group during the first, second, fourth, fifth, sixth, seventh as well as the eighth weeks [11].

During the third week, we found significant differences of β-HCG levels between molar pregnancy and Choriocarcinoma, this is because of complete evacuation of Choriocarcinoma could not be achieved. In addition, it means that evacuation is the main treatment of molar pregnancy [12].

Our results suggest that more than 20.000 mIU/ml after the fourth week is the minimum β-HCG value that indicates chemotherapy for GTD and this is consistent with the practice in Royal College of Obstetricians and Gynaecologists [13].

Also we suggest another evacuation after 8 weeks if βHCG still higher than 5000 mIU/ml and not to rush to chemotherapy. This may keeps with other studies [14] which advised chemotherapy if βHCG is higher than 6000 mIU/ml after 6th week post evacuation.

The mean decline of β-HCG in the next eight weeks post evacuation

There is a steady decline after the first week post evacuation but this decline becomes slower after the third week. This slower decline is the rule in most cases and not indicates the need for chemotherapy. This result keeps with others who noticed that the decline of βHCG in VM needs 99 days to return to undetectable levels and 68 days in PM [7].

The mean decline of β-HCG in cases with chemotherapy and cases without chemotherapy

No significant difference in βHCG decline between cases received post evacuation chemotherapy and those not received chemotherapy during the first, second, third, fourth, fifth, sixth, seventh as well as the eighth weeks in all groups. This may be due to the efficacy of evacuation, and the low number of cases of Chorioocarcinoma (2 cases compared to 6 cases VM). We concluded that early chemotherapy in VM is nugatory and this is consistent with others [7].

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