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RESEARCH ARTICLE

ROLE OF UTERINE ARTERY DOPPLER IN EARLIER PREDICTION OF RESOLUTION IN POST MOLAR PREGNANCY SURVEILLANCE

***,[1]Dr. Jothi Sundaram and [2]Dr. Chithra**

[1]Associate professor, Department of O&G, Madurai Medical College
[2]Associate professor, Government Rajaji Hospital, Madurai

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ABSTRACT

Background: Gestational trophoblastic disease (GTD) is an uncommon complication of pregnancy, worldwide the incidence varying between 0.5 & 0.8 cases per 1000 live births. β-hCG has been used as standard tool for monitoring the biological activity of trophoblastic diseases and as a tumour marker. The abundant vascular supply of the tumour makes Colour Doppler Ultrasound a potentially useful tool to study its clinical behaviour.

Objective: To evaluate the role of uterine artery doppler in earlier prediction of resolution in post molar surveillance compared to serial β-hCG follow up.

Methods: A longitudinal prospective cohort study was conducted in Government Rajaji Hospital, Madurai over a period of 12 months from August 2015 to August 2016.40 cases of vesicular molewere studied andassessed before and after suction evacuation by measuring serum β-hCG level and finding its relation with Uterine ArteryResistance Index (RI).

Results: Out of the forty patients,36 patients showed resolution of mole characterised by fall in b-hcg values and rise in U/A RI while 4 patients showed progression to invasive mole characterised by plateauing or rise in b-hcg values and a fall in U/A RI in the post evacuation period compared to pre evacuation values.Based on these observations,patients were grouped as molar pregnancy resolution(↑UARI with ↓ßHCG – 90.00%) and molar pregnancy progression(↓UARI with ↑ or plateau ßHCG – 90.00%) groups showing a statistically significant differencewith a p value of <0.05 implying that variation in UARI measurement in relation to ßHCG levels correlate strongly, inversely and negatively.

Conclusion: Finding such a significant correlation between serum β-hCG level and Doppler indices suggest that uterine artery Doppler may be used to predict the course of the disease much earlier than serial follow up with B-hcg.

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INTRODUCTION

Gestational Trophoblastic disease is an umbrella term used to describe the heterogeneous group of interrelated lesions that arise from abnormal proliferation of placental trophoblast. They can be Benign and malignant and vary histologically. Conventionally complete mole was diagnosed with the following features-Abnormal Bleeding per vaginum-commonest presentation, uterus large for GA(25%,) Hyperemesis (10%), Hyperthyroidism (10%), Early onset gestational hypertension (5%,), Anemia, Pulmonary trophoblosticemboli, Prominent theca lutein cyst. Partial mole presented with less severe symptoms more often diagnosed as missed abortion or incomplete miscarriage. All forms of Gestational Trophoblastic disease produce βhCG. Hence it is an excellent tool for screening, diagnosis, monitoring therapeutic response and follow up of the disease. Due to early prenatal and antenatal care and universal use of sonography, molar pregnancies are detected much earlier and before complications ensue with an average gestational age at diagnosis being 10 weeks. But post molar surveillance requires a longer period of follow up with β-hCG with which our Indian women may not be compliant.

***Corresponding author: Dr. Jothi Sundaram**
Associate professor, Department of O&G, Madurai Medical College

Study Design

This longitudinal prospective cohort study was conducted in Department of Obstetrics and Gynaecology, Government RajajiHospital,Madurai over a period of twelve months from august 2015 to august 2016.40 patients entered the study.

INCLUSION CRITERIA

- Amenorrheic women presenting with clinical &sonographic evidence of hydatidiform mole,

- Patients who have given informed consent to undergo the study

Exclusion Criteria

- Not satisfying inclusion criteria
- Lack of written informed consent
- Chronic hypertension
- Anomalous fetus
- Other causes of increased pelvic blood flow like Pelvic inflammatory disease, ectopic pregnancy, non trophoblastic pelvic malignancy, uterine arteriovenous malformations.

- Uterine artery Doppler velocimetry – uterine artery resistance index (UARI)

Then evacuation was done by the means of suction evacuation and specimens were sent for histopathology. All the cases were given low dose combined oral contraceptive pills after evacuation of the molar pregnancy. During follow up, Uterine artery resistance index was recorded 48 hours after evacuation of the uterus and post evacuation serial β-hCG levels monitored at 48 hours, 2nd,4th and 8th week. Uterine artery examination (right and left sides) was done using Transabdominal probe with pulsed and colour Doppler facilities by our institutional radiologist.

Groups

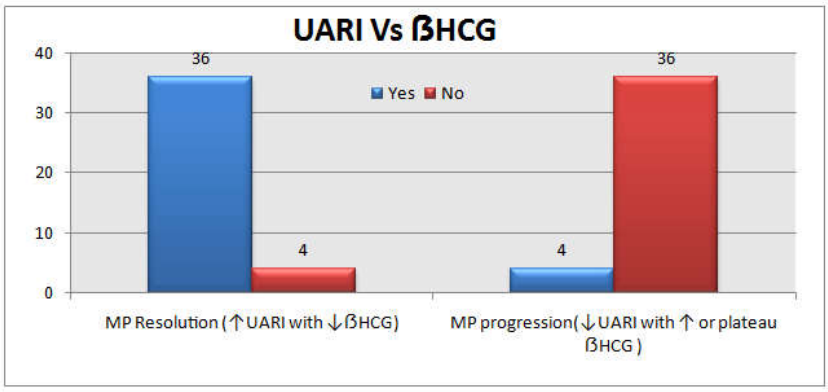
Groups	Definition	Number
MP Resolution	Without Invasive mole progression	36
MP Progression	With Invasive mole progression	4

Serum ßhCG Level

Serum ßhCG Level (mIU/L)		Preevacuation	Post evacuation (48 hrs)	Post evacuation (2nd wk)	Post evacuation (4th wk)	Post evacuation (8th wk)
MP Resolution	Mean	3013.75	493.31	157.17	42.05	0.27
	SD	5972.95	393.98	146.28	28.85	0.33
MP Progression	Mean	33223.00	4008.75	976.50	1374.95	
	SD	54580.16	5871.20	105.12	1231.10	1366.00
P value Unpaired t Test		0.0012	0.0003	<0.0001	<0.0001	<0.0001

Uterine Artery Resistance Index

Uterine Artery Resistance Index		Preevacuation	Post evacuation	P value Paired t Test
MP Resolution	Mean	0.57	0.85	<0.0001
	SD	0.06	0.07	
MP Progression	Mean	0.65	0.52	0.0414
	SD	0.06	0.09	
P value Unpaired t Test		0.0182	<0.0001	



UARI Vs ßHCG	MP Resolution (↑UARI with ↓ßHCG)	MP progression(↓UARI with ↑ or plateau ßHCG)	MP Resolution (↑UARI with ↓ßHCG) %	MP progression(↓UARI with ↑ or plateau ßHCG) %
Yes	36	4	90.00	10.00
No	4	36	10.00	90.00
Total	40	40	100	100
	P value Chi Squared Test			<0.0001

MATERIALS AND METHODS

The patients satisfying inclusion criteria were evaluated the day before evacuation of the uterus. This evaluation included:

- Clinical assessment involving general, abdominal and bimanual pelvic examination.
- Serum level of β-hCG.

Human Chorionic Gonadotropin

Human chorionic gonadotropin (hCG) is a heterodimericglycoprotein composed of 237 amino acids with a molecular weight of 25.7 kDa, produced by human placental syncytiotrophoblast. It has an α (alpha) subunit and β (beta) subunit. β human chorionic gonadotropin can be detected in maternal urine and plasma as early as 6 to 9 days after

ovulation. There is an exponential increase in hCG level with a doubling time of 1.5 days in first 6 weeks, peaks around 1 lakh IU/L at 8 to 10 weeks, starts decreasing from 12th week and plateaus at approximately 30000 IU/L from 20th week until term. In the postpartum period β hCG shows a slower decline than intact hCG. All forms of GTDs produce high levels of hCG except for placental site trophoblastic tumor. Hence serial hCG measurement is a well known indicator and predictor of the course of the disease, reassuring sustained remission, recognizing relapse, and malignant transformation.

Uterine Artery Resistance Index

In a molar pregnancy, abnormal trophoblastic proliferation leads to exaggerated invasion of the myometrial arteries. As a result, Doppler shows high-velocity, lowimpedance flow.The Doppler ultrasound is used to evaluate uterine artery by measuring the blood flow velocity at peak systole (maximal contraction of the heart) and peak diastole (maximal relaxation of the heart). These values are then computed to derive a ratio called Uterine Artery Resistance Index (UARI) in which the peak of systole is divided by the sum of systole and diastole.

UARI= peak systole / (peak systole + peak diastole)

RESULTS

The mean serum ßhCG levels were significantly lesser in MP resolution group compared to MP progression group by a mean difference of 7364.99 mIU/L (91% lesser). During the preevacuation period there was a 11 times increase in titre of mean serum ßhCG levels in MP progression group compared to MP resolution group which came down to 8 times increase in 48 hrs post evacuation, 6 times increase in 2nd week and started to increase to 33 times more in 4th week and finally it was 3838 times increased at 8th week post evacuation. This difference is significant with a p-value of 0.0003 as per unpaired t-test. Among the study patients, there was a statistically significant difference in relation to uterine artery resistance index distribution between MP resolution group (mean – 0.71, SD 0.06) and MP progression group (mean – 0.58, SD – 0.07) with a p value of <0.05 as per unpaired t test. In this study we can safely conclude that uterine artery resistance index has an inverse relationship in molar pregnancy pre and post evacuation. In MP progression group it significantly decreases in post evacuation period. But in MP resolution group it significantly increases in post evacuation period. Among the study patients, there was a statistically significant difference between uterine artery resistance index and ß HCG levels in MP resolution group (↑UARI with ↓ßHCG – 90.00%) and MP progression group (↓UARI with ↑ or plateau ßHCG – 90.00%)with a p value of <0.05 as per chi squared test.In this study we can safely conclude that variation in UARI measurement in relation to ßHCG levels correlates strongly, inversely and negatively.

DISCUSSION

There was a significant fall in post evacuation ß-hCG values in patients with resolution of molar pregnancy and rise in those with progression of molar pregnancy.

There was a significant fall in post evacuation UARI in patients with persistence of molar pregnancy, while there was a significant rise in the post evacuation UARI in patients with resolution of molar pregnancy. A strong correlation is observed with the post evacuation rise in UARI with fall in ß hcg and vice versa.

Conclusion

In our study we concluded that Uterine Artery Resistance Index (UARI) is a non invasive, reproducible and reliable diagnostic approach in earlier prediction of resolution or persistence of Gestational Trophoblastic Disease in conjunction with βhCG.

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