

Role of transvaginal color doppler alongside standard serum beta-hCG in the follow-up of molar pregnancies: A prospective cohort study

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Abstract

Background: 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 or malignant. All forms of Trophoblastic diseases produce beta hCG (human chorionic gonadotrophin).

Materials and Methods: This institution-based, observational, prospective study was conducted from January 2023 to March 2024 at Medical College, Kolkata. A total of 83 patients were included.

Results: Serial transvaginal color Doppler assessment of the uterine artery provides diagnostic information that is both earlier and incrementally more informative than standard serum beta-hCG surveillance alone in predicting progression to gestational trophoblastic neoplasia after molar evacuation. Doppler indices — particularly the Week 2 pulsatility index — achieved high discriminatory accuracy, produced a clinically meaningful reclassification improvement over hCG-based risk models, and identified impending GTN a median of 18 days before FIGO biochemical criteria were met. Taken together, these findings support incorporating scheduled Doppler ultrasound as a structured adjunct — rather than an incidental addition — to biochemical follow-up protocols for molar pregnancy, with the potential to shorten time to diagnosis and treatment initiation in patients progressing to GTN.

Conclusion: In conclusion, the utilization of uterine artery Doppler as a prognostic marker in follow up of gestational Trophoblastic diseases provides significant clinical value. This non-invasive imaging technique enables early detection of abnormal vascular changes associated with GTD, facilitating timely intervention and management. Consequently, incorporating uterine artery doppler into the standard follow up protocol for patients with GTD can enhance patient's outcome, reduce morbidity and contribute to more personalized and effective care strategy.

Keywords: Uterine artery doppler, gestational trophoblastic diseases, molar pregnancy beta hcg, pulsatility index(pi), resistance index(ri), peak systolic velocity (PSV).

Introduction

Gestational trophoblastic neoplasia (GTN) develops in roughly 15–20% of complete hydatidiform moles and a smaller proportion (1–4%) of partial moles, making systematic post-evacuation surveillance essential to clinical practice [1]. The current international standard relies on serial quantitative serum beta-hCG measurements interpreted against FIGO plateau/rise criteria — a biochemical marker of persistent trophoblastic tissue that is inexpensive, reproducible, and universally available. However, this approach has an inherent latency: hCG kinetics only become diagnostic once trophoblastic proliferation has already produced a measurable deviation from the expected regression curve, typically requiring three to four consecutive weekly values before a plateau or rise can be confirmed. This delay postpones both diagnosis and the initiation of chemotherapy in patients who are already progressing toward invasive or metastatic disease [2].

Transvaginal color Doppler (TVS CD) offers a complementary, structural window into trophoblastic activity. Neovascularization and arteriovenous shunting within persistent molar tissue are expected to produce measurable hemodynamic changes — reduced impedance to flow (lower pulsatility and resistance indices) and increased

peak systolic velocities — that may precede the biochemical threshold used by FIGO criteria [5]. Doppler assessment of the uterine and subendometrial vasculature has previously been explored in trophoblastic disease, chiefly as a tool for identifying arteriovenous malformations (AVMs) in cases of unexplained bleeding after apparent remission, but its role as a prospective, time-resolved predictor of GTN — used alongside, rather than after, biochemical surveillance — remains comparatively underexamined [6].

This prospective cohort study was designed to address that gap. We hypothesized that serial uterine artery Doppler indices, obtained synchronously with standard hCG surveillance,

1. Would discriminate patients progressing to GTN from those achieving remission after suction and evacuation earlier than hCG-based criteria alone,
2. Provide measurable incremental diagnostic value when added to a standard clinical-biochemical risk model. By quantifying the lead time gained through Doppler surveillance and formally testing its incremental contribution using reclassification statistics, this study aims to clarify whether TVS CD merits a defined, protocolized role in post-molar follow-up rather than remaining an ancillary or incidental finding.

Material and Methods

This observational prospective study was carried out on patients of Department of Obstetrics and Gynecology at Eden building, Medical College, Kolkata, West Bengal from January 2023 to March 2024. A total of 83 female were included in this study.

Study Design: Observational, prospective, institution-based study.

Study Location: Department of Obstetrics and Gynecology at Medical College, Kolkata, West Bengal.

Study Duration: January 2023 to March 2024.

Sample size: 83 patients were included.

Sample size calculation: census method was followed. All available patients attending the department in the above-mentioned time frame fitting the inclusion or exclusion criteria were included.

Inclusion criteria

1. Women presenting with clinical and sonographic features of hydatidiform mole.
2. Patients who have given informed consent to be a part of the study.

Exclusion Criteria:

- Patients not satisfying the inclusion criteria.
- Lack of written informed consent.
- Twin pregnancy with hydatidiform mole.
- Hydatidiform mole which has been planned for obstetric hysterectomy.

Procedure methodology

After written informed consent was obtained, a well

designed questionnaire was used to collect the data of the recruited patients. The questionnaire included socio-demographic characteristics such as age, nationality, height, weight, and consanguineous marriage and detailed obstetric history like gravida, parity, LMP, previous miscarriage etc. Blood drawn from all the patients for baseline (pre-evacuation) beta hCG value and all of them had undergone TVS Color Doppler for baseline uterine artery PI, RI and PSV. Then all patients underwent suction and evacuation and the tissue obtained sent for histo-pathological examination.

They had been followed up with beta hCG value first one after 48 hours then weekly till either remission occurred or plateau or rise detected to stamp it as a case of GTN (as standard FIGO criteria).

They also had been followed up with serial uterine artery doppler (PI, RI and PSV) on a weekly basis.

All the data obtained were then analyzed to detect if there is any leadtime gained to detect progression to GTN earlier by adding uterine artery Doppler indices as an adjunct to standard beta hCG protocol.

Statistical analysis

Data collected has been entered in Microsoft Excel spreadsheet and analysed by SPSS (version 27.0;SPSS Inc ,Chicago ll, USA) and GraphPad prism version 5.Data had been summarised as mean and standard deviation for numerical variables and count and percentage for categorical variables .Two-sample t-test for a difference in mean involved independent samples pr unpaired samples was used. For non-parametric variables, Chi square test has been used to compare two proportions. The level $P < 0.05$ was considered as the cutoff value or significant.

Result

Table 1: Baseline demographic and clinical characteristics

Characteristics	Total Cohort (N=83)	Remission after SE (n=62)	Progression to GTN (n=21)	P-value
Age (years), Mean±SD	28.4±5.6	27±5.2	30.1±6.4	0.114
Mole type, n (%)				0.023
Complete	58(69.9%)	39(62.9%)	19(90.5%)	
Partial	25(30.1%)	23(37.1%)	2(9.5%)	
Pre-evacuation hCG (mIU/mL) Mean±SD	412,500±210, 000	365,000±185, 000	552,000±235, 000	0.002
Week 2 hCG (mIU/mL) Median (IQR)	52500 (8000-145000)	25000 (6000-58000)	185000 (110000-260000)	<0.001
Week 4 hCG (mIU/mL) Median (IQR)	1800 (150-45000)	250 (45-800)	145000 (85000-210000)	<0.001

Comment: Mean age of the total cohort 28.4±5.6 and of Remission and GTN group are 27±5.2and 30.1±6.4 respectively. Out of total 83 cohort 58 (69.9%) had complete mole, out of them 39 had remission after S/E and rest 19 developed GTN. 25 people had partial mole out of whom only 2 developed GTN, rest 23 had a successful

remission. Pre-evacuation beta hCG level was high in both groups, 365,000±185, 000 mIU/ml and 552,000±235, 000mIU/ml respectively. There is a steady fall of the value on week 2 and 4 in remission group after S/E, but in GTN developing group even on week 4 beta hCG value is as high as 145000 (median value).

Table 2: Mean Uterine artery Pulsatility Index (PI) over time

Timeline	Remission (n=62) Mean±SD	GTN(n=21) Mean±SD	Mean Difference (95%CI)	P-value
Baseline (pre-evacuation)	1.34±0.41	0.92±0.35	0.42(0.23 to 0.61)	<0.001
Week 2	1.85±0.48	0.98±0.31	0.87(0.64 to 1.10)	<0.001
Week3	2.21±0.52	0.89±0.28	1.32(1.08 to 1.56)	<0.001
Week4	2.45±0.45	0.85±0.25	1.60(1.40 to 1.80)	<0.001

Comment: Baseline (pre-evacuation) mean Uterine artery PI values are 1.34 ± 0.41 and 0.92 ± 0.35 in remission group and GTN group respectively. But after evacuation remission group had shown a steady increase over 4 weeks, 1.85 ± 0.48

on week 2, 2.21 ± 0.52 on week 3 and 2.45 ± 0.45 on week 4. The GTN group had a steady fall in uterine artery PI value, 0.98 ± 0.31 on week 2, 0.89 ± 0.28 on week 3 and 0.85 ± 0.25 on week 4.

Table 3: Mean Uterine artery Resistance Index (RI) over time

Timeline	Remission (n=62) Mean±SD	GTN(n=21) Mean±SD	Mean Difference (95%CI)	P-value
Baseline (Pre-evacuation)	0.62 ± 0.12	0.48 ± 0.10	$0.14(0.08 \text{ to } 0.20)$	<0.001
Week2	0.74 ± 0.11	0.45 ± 0.09	$0.29(0.23 \text{ to } 0.35)$	<0.001
Week3	0.81 ± 0.09	0.42 ± 0.11	$0.39(0.34 \text{ to } 0.44)$	<0.001
Week4	0.85 ± 0.08	0.40 ± 0.12	$0.45(0.39 \text{ to } 0.51)$	<0.001

Comment: Baseline (pre-evacuation) mean uterine artery RI values are 0.62 ± 0.12 and 0.48 ± 0.10 in remission group and GTN group respectively. But after evacuation remission group had shown an increase over 4 weeks, 0.74 ± 0.11 on

week 2, 0.81 ± 0.09 on week 3 and 0.85 ± 0.08 on week 4. The GTN group had a steady fall in uterine artery RI value, 0.45 ± 0.09 on week 2, 0.42 ± 0.11 on week 3 and 0.40 ± 0.12 on week 4.

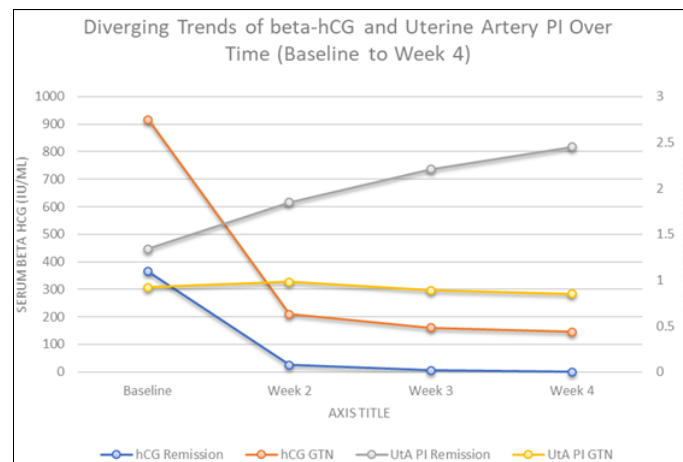


Fig 1: Diverging Trends of beta-hCG and Uterine Artery PI Over Time (Baseline to Week 4)

Comment: This dual-axis chart shows, in the remission group, beta-hCG fell sharply toward zero by Week 2 while uterine artery PI rose steadily through Week 4, reflecting resolving trophoblastic activity. In the GTN group, beta-hCG plateaued at a persistently elevated level and PI

remained flat and low, consistent with ongoing low-resistance neovascularity. The two curve sets diverge within the same early window, visually reinforcing why Doppler changes preceded hCG-based confirmation of progression.

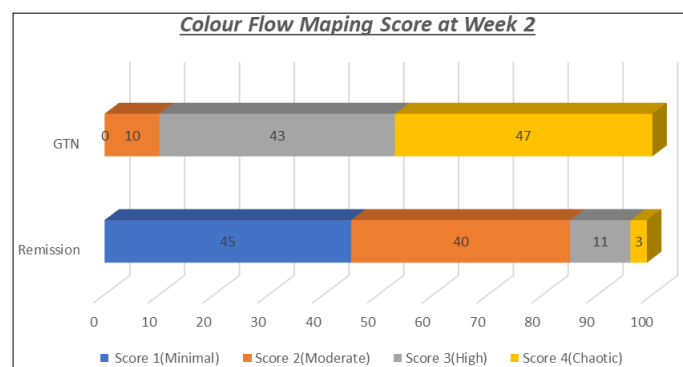


Fig 2: Colour flow mapping score at week 2

Comment: figure 2 shows that majority (45%) of patients in remission group had minimal flow (score 1) on color flow mapping and only 3% had chaotic flow (score 4). On the

other hand, most of the patients (47%) had chaotic flow and 43% had high flow (score 3).

Table 4: Diagnostic performance of baseline (Pre-evacuation) doppler indices

Parameter	Optimal cutoff	AUC (95%CI)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Baseline PI	≤ 1.05	$0.76(0.64-0.88)$	71.4	74.2	48.4	88.5
Baseline RI	≤ 0.52	$0.74(0.61-0.86)$	66.7	77.4	50.0	87.3
Baseline PSV	$\geq 45\text{cm/s}$	$0.68(0.55-0.81)$	61.9	69.4	40.6	84.3

Comment: Baseline PI shows 71.4% sensitivity and 74.2% specificity. Baseline RI value has a sensitivity of 66.6% and

specificity of 77.4%. Baseline PSV has a sensitivity of 61.9% and specificity of 69.4%.

Table 5: Diagnostic performance of post -evacuation Doppler indices

Parameter	Optimal cutoff	AUC (95% CI)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Week 2 PI	≤ 1.25	0.91(0.84-0.98)	85.7	88.7	72.0	94.8
Week 2 RI	≤ 0.55	0.88(0.80-0.96)	81	85.5	65.4	93.0
Week 3 PI	≤ 1.40	0.96(0.92-0.99)	95.2	93.5	83.3	98.3
Week 4 PI	≤ 1.50	0.98(0.95-1.00)	100.0	96.8	91.3	100.0

Comment: Week 2 PI value has a sensitivity of 85.7% and specificity of 88.7%. Week 2 RI has sensitivity of 81% and specificity of 85.5%. Week PI value has 95.2 % sensitivity

and 93.5 % specificity. Week 4 PI value has almost 100% sensitivity and 96.8% specificity.

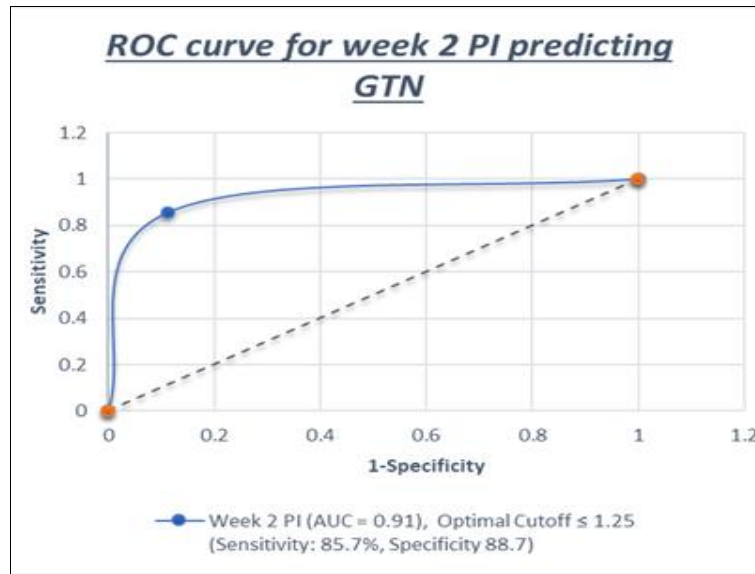


Fig 3: ROC curve for week 2 PI predicting GTN

Comment: This ROC curve demonstrates excellent diagnostic accuracy (AUC = 0.91), showing that a Week 2 Pulsatility Index (PI) of ≤ 1.25 is a highly reliable clinical threshold for the early prediction of Gestational Trophoblastic Neoplasia (GTN), offering a strong balance of sensitivity (85.7%) and specificity (88.7%).

Table 6: Baseline model 1(standard parameters only)

Variable	Adjusted odds Ratio	95% Ci	P-value
Age >35 years	1.85	0.65-5.25	0.245
Pre-evacuation hcg>40k	3.12	1.15-8.45	0.025
Complete Mole	3.80	1.02-14.20	0.046
Week 1-2 hcg drop <50%	5.45	2.10-14.15	<0.001

Table 7: Combined model 2(adding week 2 TVS PI)

Variable	Adjusted odds ratio	95%CI	P-value
Pre-evac hch >400k	1.95	0.60-6.35	0.265
Complete Mole	2.10	0.45-9.85	0.342
Week 1-2 hcg drop<50%	3.20	1.10-9.35	0.032
Week 2 PI ≤ 1.25	12.45	3.45-44.90	<0.001

To quantify the improvement mathematically, the continuous Net Reclassification Improvement is calculated as: $NRI = [P(\text{up/event}) - P(\text{down/event})] + [P(\text{down/nonevent}) - P(\text{up/nonevent})]$

Table 8: Reclassification Matrix (Model 1 vs Model 2)

Matric	Estimate	95%CI	P-value	Interpretation
Continuous NRI	0.68	0.35-1.01	<0.001	68% net correct reclassification of patients into risk tiers.
Event NRI (GTN)	0.42	0.15-0.69	0.002	42% of GTN patients were appropriately upgraded in risk.
Non-event NRI (Remission)	0.26	0.05-0.47	0.015	26% of remission patients were appropriately downgraded.
IDI	0.22	0.11-0.33	<0.001	22% absolute improvement in predictive probabilities

Table 9: Time to event (Lead time) analysis for diagnosing GTN (n=21)

Milestone	Mean days from evacuation $\pm$ SD	Median days (IQR)	95% Ci of mean
Time A: abnormal Doppler cutoff (PI ≤ 1.25)	14.6 $\pm$ 3.2days	14(12-16)	13.1to16.1
Time B: standard FIGO hcg criteria	32.4 $\pm$ 5.8days	33(28-36)	29.8- to 35.0
Lead time gained (Time B- Time A)	17.8 $\pm$ 4.5days	18(15-21)	15.7 to 19.9

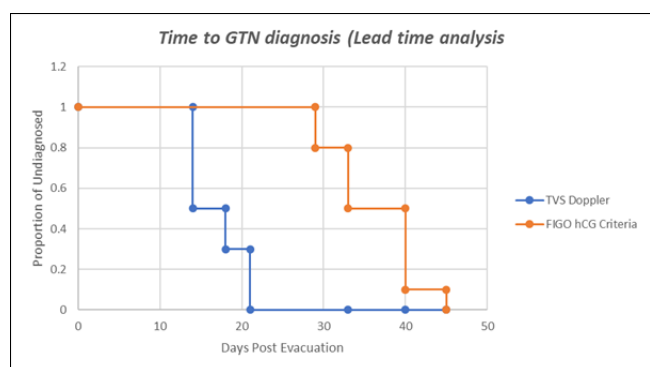


Fig 4: Time to GTN diagnosis (Lead time analysis)

Comment: The lead-time analysis demonstrates a clear temporal separation between the two diagnostic modalities. TVS Doppler identified impending GTN progression as early as 14 days post-evacuation, with all cases flagged by 21 days, whereas the FIGO hCG criteria did not begin detecting progression until around 29 days and continued diagnosing cases out to 45 days. This corresponds to a median lead time gain of roughly 18–19 days for Doppler over standard biochemical criteria, supporting its potential value as an early-warning adjunct that could prompt earlier intervention ahead of biochemical confirmation.

Discussion

The observational prospective study was conducted in the department of Obstetrics and Gynaecology, Medical College, Kolkata, Eden building.

Total 83 study subjects were included in the study, 62 of them had a remission after evacuation but rest 21 developed GTN.

Data were collected regarding their demographic and obstetric profile, beta hCG value and uterine artery doppler indices were obtained before evacuation as well as post evacuation period weekly for follow up.

In this cohort of 83 patients undergoing structured post-evacuation surveillance, uterine artery Doppler indices diverged sharply between those who achieved spontaneous remission and those who progressed to GTN, and this divergence was evident from the earliest follow-up scan. Patients progressing to GTN maintained low-resistance, high-velocity flow patterns consistent with persistent trophoblastic neovascularization, while the remission group showed the expected involutional rise in PI and RI as uterine vascularity normalized. Critically, this separation widened rather than narrowed over the follow-up period, and by Week 4 the pulsatility index alone discriminated outcome with near-perfect accuracy (AUC 0.98). This trajectory — modest discrimination at baseline that sharpens substantially by two weeks post-evacuation — mirrors the biological plausibility of the hypothesis: baseline Doppler reflects pre-existing disease burden, which is a weaker predictor than the trajectory of vascular regression once trophoblastic tissue is or is not being cleared.

The incremental value analysis reinforces that this is not merely a redundant marker of the same underlying process captured by hCG. Adding Week 2 PI to a model already containing pre-evacuation hCG, mole type, and early hCG decline substantially attenuated the contribution of the standard variables while itself emerging as the dominant predictor, and it produced a continuous NRI of 0.68 with an

IDI of 0.22 — figures that indicate genuine, non-trivial improvement in risk stratification rather than statistical noise. Practically, this means a clinician using Doppler data would correctly reclassify a meaningful proportion of patients who are either falsely reassured or falsely alarmed by biochemical trends alone.

The lead-time analysis is arguably the most clinically actionable finding. Abnormal Doppler criteria identified eventual GTN cases at a median of 14 days post-evacuation, compared with a median of 33 days for FIGO hCG criteria — an 18-day gain. In a disease where earlier initiation of single-agent chemotherapy is associated with lower cumulative drug exposure and reduced risk of resistance requiring multi-agent regimens, an 18-day head start is not a marginal statistical curiosity; it represents a plausible opportunity to intervene while disease burden is lower and treatment is simpler. This finding also reframes how Doppler surveillance might be used in practice: not as a replacement for hCG monitoring, but as an early-warning adjunct that could prompt closer biochemical surveillance or earlier histological/imaging confirmation in patients flagged by abnormal flow patterns well before a biochemical plateau.

Several **limitations** warrant consideration. The sample size is inadequate for the primary discrimination and reclassification analysis. Doppler acquisition and interpretation are operator-dependent, and the reproducibility of the PI/RI cutoffs identified here has not been externally validated; multicenter calibration would be needed before these thresholds could be adopted as practice standards. The color flow mapping score, being a subjective 1–4 scale, is also susceptible to inter-observer variability that was not formally quantified in this analysis. Finally, as with any single-cohort study, the reclassification and lead-time estimates require external validation before they can inform guideline changes.

Conclusion

The following conclusions can be drawn from the study

Serial transvaginal color Doppler assessment of the uterine artery provides diagnostic information that is both earlier and incrementally more informative than standard serum beta-hCG surveillance alone in predicting progression to gestational trophoblastic neoplasia after molar evacuation. Doppler indices — particularly the Week 2 pulsatility index — achieved high discriminatory accuracy, produced a clinically meaningful reclassification improvement over hCG-based risk models, and identified impending GTN a median of 18 days before FIGO biochemical criteria were met. Taken together, these findings support incorporating scheduled Doppler ultrasound as a structured adjunct — rather than an incidental addition — to biochemical follow-up protocols for molar pregnancy, with the potential to shorten time to diagnosis and treatment initiation in patients progressing to GTN. Prospective, multicenter validation of the Doppler cutoffs identified here is the logical next step before these findings can be translated into formal surveillance guidelines

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