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RESEARCH ARTICLE
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"EVALUATING CARBETOCIN FOR POSTPARTUM HEMORRHAGE PREVENTION: AN OBSERVATIONAL STUDY FROM NORTHEAST INDIA".

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ABSTRACT

Background: Postpartum hemorrhage (PPH) remains the leading cause of maternal morbidity and mortality worldwide. Carbetocin, a long-acting oxytocin analogue, has been proposed as a superior uterotonic agent for PPH prevention.

Objective: To evaluate the impact of carbetocin administration on postpartum hemorrhage prevention in women undergoing vaginal delivery at a tertiary care facility.

Methods: A prospective observational study was conducted among 80 women who received carbetocin prophylaxis. Demographic data, haemoglobin levels, blood loss at defined intervals, incidence of PPH, need for supplementary uterotonics, and adverse events were recorded.

Results: The mean age of participants was 25.7 years, with 62.5% aged 21–25 years. The mean gestational age was 270 days. Mean blood loss was 302.25 mL at 30 minutes, 317 mL at 1 hour, and 337.6 mL at 2 hours, all below the diagnostic threshold for PPH. The incidence of PPH was limited to 2.5%, and supplementary uterotonics were required in only 2.5% of cases. Haemoglobin concentration declined modestly from 11.66 g/dL pre-delivery to 11.17 g/dL post-delivery, corresponding to a mean reduction of 0.49 g/dL. No blood transfusions were administered. The adverse event profile was favourable: nausea and vomiting occurred in 10% of participants, while 90% reported no adverse effects.

Conclusion: Carbetocin demonstrated high efficacy in reducing blood loss, minimising haemoglobin decline, and lowering PPH incidence, with a favourable safety profile. Its sustained uterotonic activity reduced reliance on adjunct therapy, underscoring its potential role in routine obstetric practice for PPH prevention.

Keywords: Postpartum hemorrhage, Third-Stage Labour, Carbetocin, Efficacy, Northeast India

INTRODUCTION

The third stage of labour, defined as the interval between the delivery of the neonate and the complete expulsion of the placenta and membranes, is arguably the most critical phase for maternal safety. Although it is the shortest stage of labour, it carries the highest risk of life-threatening complications, most notably postpartum hemorrhage (PPH).[1] Historically and currently, PPH remains the leading cause of maternal mortality worldwide, accounting for approximately 25% of maternal deaths globally. The majority of these cases are attributed to uterine atony—the failure of the myometrium to contract effectively after childbirth, leading to rapid and uncontrolled blood loss from the placental site.[2]

To mitigate these risks, the Active Management of the Third Stage of Labour (AMTSL) has been widely adopted as the gold standard in obstetric care. AMTSL typically comprises three key interventions: the administration of a uterotonic agent immediately following the birth of the baby, controlled cord traction, and uterine massage.[3] Among the pharmacological options available, Oxytocin has long served as the first-line prophylactic uterotonic due to its proven efficacy, low cost, and relatively minimal side-effect profile.[4] However, Oxytocin is not without its operational and pharmacological limitations. Its short half-life often necessitates continuous intravenous infusion or repeated intramuscular injections to maintain adequate uterine tone. Furthermore, standard Oxytocin is heat-sensitive, requiring a strict cold chain (2-8°C) that is frequently compromised in low-resource or tropical settings.[5]

In response to the limitations of Oxytocin, Carbetocin, a long-acting synthetic analogue, was developed. Carbetocin is an agonist at the peripheral oxytocin receptors, specifically designed to address the need for a more stable and longer-lasting uterotonic effect. Structurally, Carbetocin differs from Oxytocin through two primary modifications: the replacement of the disulfide bond with a thioether bond and the deamination of the cysteine at the N-terminus. These chemical alterations render the molecule significantly more resistant to degradation by aminopeptidases, which are prevalent in the bloodstream during pregnancy.[6]

From a pharmacokinetic perspective, Carbetocin maintains a biological half-life of approximately 40 minutes—nearly ten times longer than that of Oxytocin. When administered intravenously as a single bolus, its duration of action persists for up to 120 minutes, providing a sustained contraction of the myometrium.[7] This extended activity is clinically significant as it potentially eliminates the need for the "drip-and-pump" setups required for Oxytocin infusions, thereby reducing the workload of healthcare providers and the risk of fluid overload in the patient.

The primary focus of modern obstetric research regarding Carbetocin is its efficacy relative to the established "gold standard." The debate centres on whether the higher unit cost of Carbetocin is offset by its clinical benefits, such as a reduced need for "rescue" uterotonics and a decrease in the incidence of PPH. Large-scale randomised controlled trials (RCTs), including the landmark WHO CHAMPION trial, have compared these two agents extensively, particularly in vaginal deliveries.[8] Strong clinical data show that carbetocin outperforms oxytocin in reducing PPH across vaginal and caesarean deliveries. Meta-analyses highlight its association with fewer cases of PPH, decreased reliance on rescue uterotonics, and reduced transfusion requirements. However, widespread use is constrained by cost, which is estimated to be almost one hundred times higher than oxytocin.[9]

While multiple Indian studies have assessed carbetocin in the management of third-stage labour, data from the Northeastern region are limited. This gap motivated our investigation, which aimed to evaluate the impact of carbetocin administration on postpartum hemorrhage prevention in women undergoing vaginal delivery at a tertiary care facility.

MATERIALS AND METHODS

Study Approach

The investigation was designed as a hospital-based, observational study involving term pregnant women presenting in labour. The study population included women attending the antenatal OPD and labour room of the Department of Obstetrics and Gynaecology at Agartala Government Medical College, Tripura.

Participants

A total of 80 women were enrolled and received Carbetocin prophylaxis.

Study Period and Sampling Method

The study extended over 18 months (78 weeks). Each week, one day was randomly chosen, and on that day, the first patient administered carbetocin was enrolled. This recruitment method was consistently applied until the study concluded.

Recruitment Criteria

1. Inclusion was restricted to term gestations with cephalic presentation resulting in normal vaginal delivery.
2. Exclusion criteria comprised preterm and postdated pregnancies, hypertensive disease, diabetes, anaemia, coagulation disorders, abnormal amniotic fluid volume, multifetal gestations, multigravidas, obstructed labour, fetal macrosomia, abdominal overdistension, and assisted vaginal deliveries.

Study Protocol

Following admission, all participants received systematic history taking and examination. Demographic data, vital signs, and routine laboratory investigations were recorded according to a predefined schedule, with tests repeated when necessary.

Participants were randomly assigned to receive a single intravenous dose of heat-stable carbetocin (100 μg). Administration occurred immediately after delivery, with the third stage of labour managed per WHO guidelines. Following cord clamping and division, blood loss was measured using a calibrated BRASSS-V obstetric drape placed beneath the buttocks.

Blood loss was quantified from the time of delivery until two hours postpartum, with >500 ml after vaginal birth defined as PPH. Additional uterotonic use within this period was documented, noting the agent given. Adverse events—including nausea, vomiting, flushing, headache, dyspnoea, tachycardia, and other drug-related reactions—were systematically captured.

Outcome Assessment

1. Measurement of blood loss from fetal and placental delivery through two hours postpartum.

2. Change in haemoglobin levels, determined by comparing values before delivery and after delivery.

Ethical clearance

Ethical clearance was obtained from the institutional committee, and written informed consent was secured from all participants before study initiation.

Data Interpretation

Documentation was done on a standard proforma. Qualitative variables were analysed with chi-square, and quantitative data expressed as mean ± SD, compared using unpaired t-test or Mann–Whitney U. Statistical significance was defined as $p < 0.05$. Analyses were performed in SPSS v26.0, with figures generated in Excel 2021.

RESULTS

The study cohort had a mean age of 25.7 years. Of patients receiving carbetocin, 62.5% were aged 21–25 years, and 35% were aged 26–30 years. The mean gestational age was 270 days. As shown in Table 1, patients receiving carbetocin experienced a markedly reduced mean blood loss across all observation periods, with values of 302.25 mL at 30 minutes, 317 mL at 1 hour, and 337.6 mL at 2 hours (Figure 1). Table 2 indicates that the incidence of PPH among patients was reduced to 2.5% (Figure 2).

Table 1: Mean comparison of blood loss according to duration (30 minutes, 1 hour, and 2 hours postpartum)

Duration of Blood Loss	Patients treated with carbetocin	Mean blood loss (ml)	SD
30 mins	n=80	302.25	147.88
1 hr		317.00	160.08
2 hrs		337.60	168.57

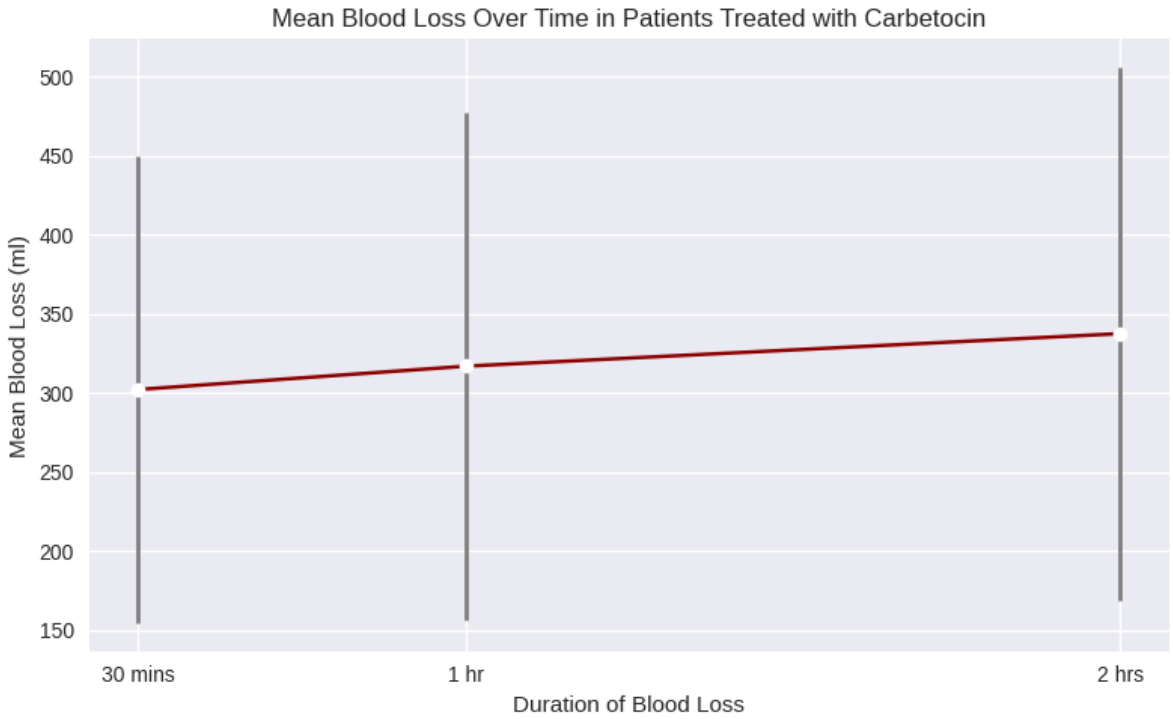


Figure 1: Trend of Postpartum Blood Loss at 30 minutes, 1 hour, and 2 hours

Table 2: Distribution of patients as per the development of PPH

PPH	Patients treated with carbetocin
No	78
	97.5%
Yes	2
	2.5%
Total	80
	100.0%

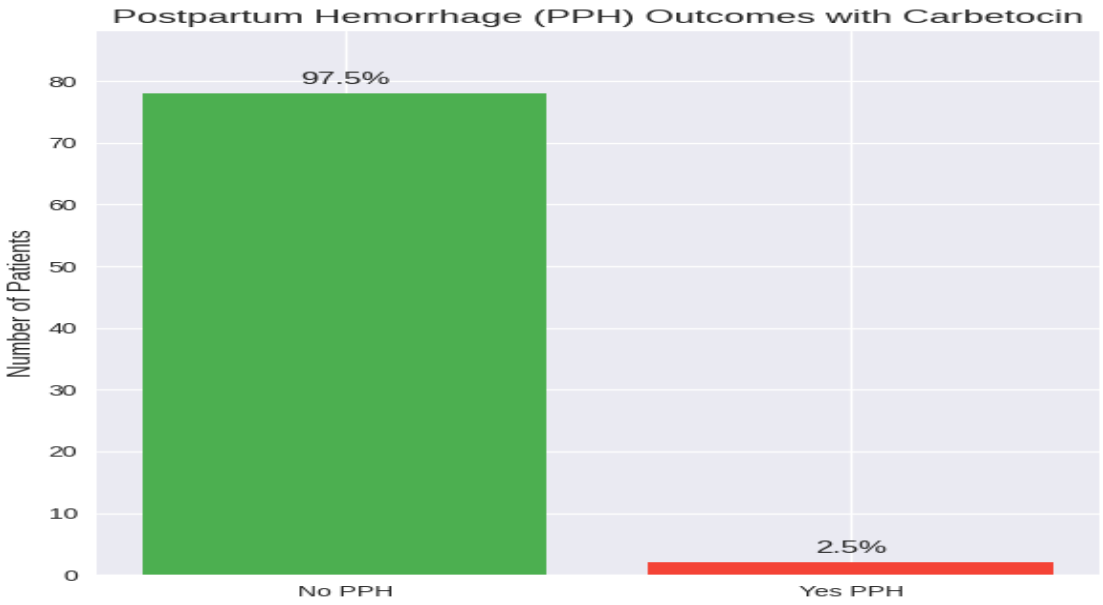


Figure 2: Incidence of PPH in carbetocin-treated patients

Table 3 shows that the mean haemoglobin concentration before delivery was 11.66 g/dL, declining to 11.17 g/dL after delivery, corresponding to a reduction of 0.49 g/dL (Figure 3). No blood transfusions were administered.

Table 3: Comparison of the pre- and post-delivery haemoglobin levels in patients treated with carbetocin

Haemoglobin level	**Patients treated with carbetocin**	**Mean**	**SD**
Pre-delivery	n=80	11.66	0.61
Post-delivery		11.17	0.74
Mean Difference		0.49	0.33

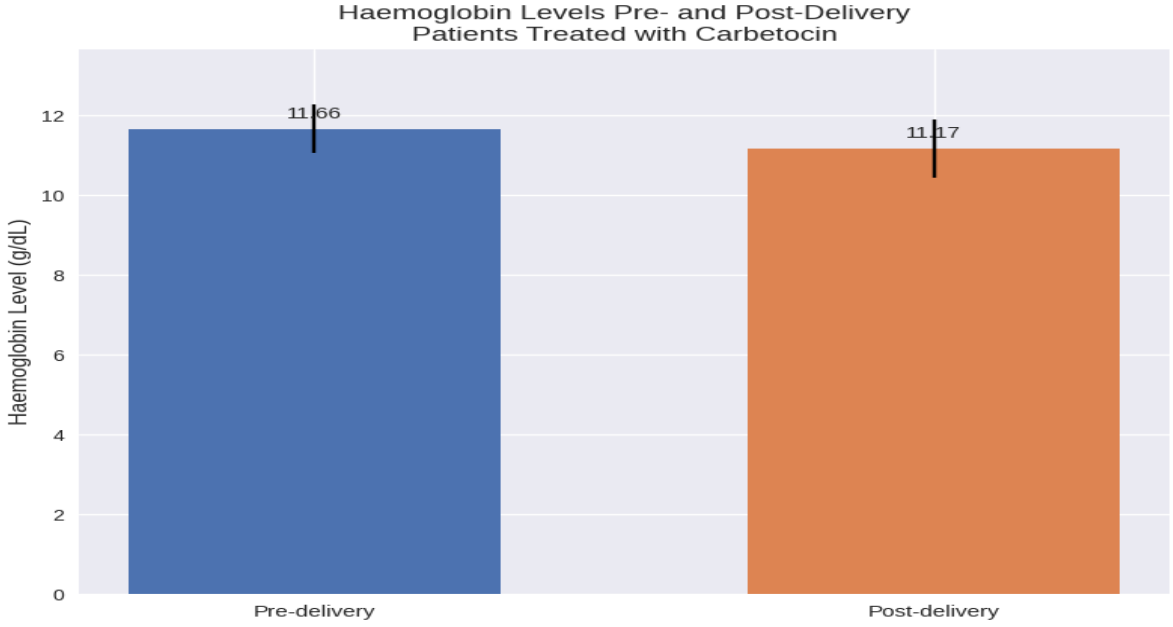


Figure 3: Comparison of the pre- and post-delivery haemoglobin levels in patients treated with carbetocin

Among patients treated with carbetocin, supplementary uterotonic agents were necessary in 2.5% of cases. The adverse event profile demonstrated an absence of headache, with nausea and vomiting documented in 10% of participants. Notably, 90% of recipients reported no adverse effects.

DISCUSSION

The present study evaluated the clinical profile, haemodynamic changes, and outcomes in women receiving carbetocin for the prevention of PPH. The cohort had a relatively young mean age of 25.7 years, with the majority of participants between 21–25 years. This demographic distribution is consistent with reproductive trends in South Asian populations, where childbirth commonly occurs in the mid-twenties.[10] The mean gestational age of 270 days reflects term pregnancies, thereby minimising confounding factors related to prematurity or high-risk obstetric conditions.

Haemoglobin and Blood Loss

The mean haemoglobin concentration declined modestly from 11.66 g/dL before delivery to 11.17 g/dL after delivery, corresponding to a reduction of 0.49 g/dL. Importantly, no transfusions were required, underscoring the efficacy of carbetocin in minimising clinically significant blood loss. These findings align with previous randomised trials comparing carbetocin and oxytocin, which demonstrated that carbetocin is associated with lower post-partum haemoglobin decline and reduced transfusion requirements.[11]

Mean blood loss was consistently low across all observation intervals: 302.25 mL at 30 minutes, 317 mL at 1 hour, and 337.6 mL at 2 hours. These values fall well below the conventional threshold for PPH (>500 mL), highlighting the prophylactic benefit of carbetocin. A systematic review and meta-analysis in 2025 confirmed that carbetocin significantly reduces intraoperative and postoperative blood loss compared to oxytocin, particularly in high-risk women undergoing cesarean delivery.[12] The present study reinforces these findings in vaginal deliveries, suggesting the broad applicability of carbetocin across delivery modes.

Incidence of PPH

The incidence of PPH in this cohort was 2.5%, which is markedly lower than the global average of 6–10% reported in large obstetric registries. This reduction is clinically meaningful, given that PPH remains the leading cause of maternal mortality worldwide. The low rate of PPH observed here supports the growing evidence that carbetocin provides superior uterotonic efficacy compared to oxytocin, with longer duration of action and reduced need for repeat dosing.[13]

Need for Additional Uterotonics

Supplementary uterotonic agents were required in only 2.5% of cases, further demonstrating the sustained activity of carbetocin. Previous comparative studies have reported higher rates of additional uterotonic use with oxytocin, ranging from 10–15%.[14,15] The reduced reliance on adjunct therapy not only improves patient safety but also decreases healthcare costs and resource utilisation.[16]

Adverse Event Profile

The safety profile of carbetocin in this study was favourable. No cases of headache were reported, nausea and vomiting occurred in 10% of participants, and 90% experienced no adverse effects. These findings are consistent with prior literature, which describes carbetocin as well-tolerated, with gastrointestinal symptoms being the most common but generally mild. The absence of serious adverse events underscores the suitability of this approach for routine use in obstetric practice.[17,18]

Clinical Implications

Taken together, the results of this study demonstrate that carbetocin is highly effective in reducing blood loss, minimising haemoglobin decline, and lowering the incidence of PPH. Its prolonged uterotonic effect reduces the need for supplementary agents, while its favourable safety profile enhances patient acceptability. These findings support the incorporation of carbetocin into standard

protocols for active management of the third stage of labour, particularly in settings where PPH contributes significantly to maternal morbidity and mortality.
Future research should focus on larger multicentre trials to validate these outcomes across diverse populations and delivery settings. Cost-effectiveness analyses are also warranted, especially in resource-limited environments where affordability remains a barrier to widespread adoption.

Limitations
- **Single-centre design:** Conducting the study in one tertiary care facility restricts external validity, as outcomes may differ in other geographic regions or healthcare settings.
- **Sample size constraints:** The cohort included only 80 participants, which may limit the statistical power and generalizability of the findings. Larger multicentre studies would provide more robust evidence.
- **Age distribution bias:** The majority of participants were between 21–25 years, which may not fully represent older maternal age groups where PPH risk is higher.
- **Short follow-up period:** Blood loss and haemoglobin changes were monitored only up to 2 hours postpartum. A longer follow-up could reveal delayed complications or late-onset PPH.
- **Limited outcome measures:** The study focused primarily on blood loss, haemoglobin decline, and immediate adverse effects. Broader maternal outcomes such as recovery time, breastfeeding initiation, or neonatal health were not assessed.
- **Absence of comparator arm:** Without a direct comparison group receiving oxytocin or another uterotonic, it is difficult to definitively attribute superiority to carbetocin.
- **Potential reporting bias:** Adverse events were self-reported and may have been underrecognized, especially for mild or transient symptoms.

CONCLUSION
The findings of this study offer robust evidence highlighting carbetocin as an effective uterotonic for the prevention of PPH. Consistent outcomes reveal that carbetocin markedly lowers both the incidence of PPH and the degree of postpartum haemoglobin decline. Notably, these advantages are attained without any corresponding rise in adverse maternal events, underscoring their safety and clinical utility.

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REFERENCES
1. Hersh AR, Carroli G, Hofmeyr GJ, Garg B, Gülmezoglu M, Lumbiganon P, et al. Third stage of labor: evidence-based practice for prevention of adverse maternal and neonatal outcomes. Am J Obstet Gynecol. 2024;230(3S):S1046-S1060.e1.
2. Sorout S. Uterine atony: a primary cause of postpartum hemorrhage. Int J Sci Res Publ. 2024;14(8):218-222.
3. Musaba MW, Dey T, Wandabwa JN, Weeks AD. Carbetocin for the Management of Postpartum Hemorrhage. In: A Comprehensive Textbook of Postpartum Hemorrhage. 2nd ed. Chapter 44 - NEW NEW Both #3.vp
4. Tyagi S, Arya SB, Baghel J, Gupta S. Role of oxytocin versus carbetocin in active management of third stage of labour. Int. J. Adv. Res. 2024;12(11):985-990.
5. Lambert P, McIntosh MP, Widmer M, Evans L, Rauscher M, Kuwana R, et al. Oxytocin quality: evidence to support updated global recommendations on oxytocin for postpartum hemorrhage. J Pharm Policy Pract. 2020;13:14.
6. Nolan MD, Shine C, Scanlan EM, Petracca R. Thioether analogues of the pituitary neuropeptide oxytocin *via* thiol-ene macrocyclisation of unprotected peptides. Org Biomol Chem. 2022;20(42):8192-8196.

7. Mistri S. Carbetocin versus Oxytocin for the Prevention of Postpartum Hemorrhage. Int J Toxicol Pharmacol Res. 2023;13(12):105–109.
8. Widmer M, Piaggio G, Nguyen TMH, Osoti A, Owa OO, Misra S, et al. Heat-Stable Carbetocin versus Oxytocin to Prevent Hemorrhage after Vaginal Birth. N Engl J Med. 2018;379(8):743-752.
9. Delavallade M, Vaunois A, Cellier M, Boukerfa-Bennacer Y, Chauleur C, Raia-Barjat T. Carbetocin versus oxytocin for the prevention of postpartum haemorrhage during caesarean section in patients at high risk of bleeding. Eur J Obstet Gynecol Reprod Biol. 2024;300:206-210.
10. Pandey A, Maheshwari SK, Pandey RK. A prospective study to compare the efficacy of carbetocin with oxytocin in prophylaxis of postpartum hemorrhage in vaginal deliveries. Int J Life Sci Biotechnol Pharma Res. 2024;13(2):531-534.
11. Mehta SD, Shah AN. A comparative study of injection oxytocin with injection carbetocin in the management of postpartum haemorrhage. Int J Clin Obstet Gynaecol. 2025;9(1):99-103
12. El-Goly NA, Maged AM, Kamal WM, Hosny O, Turki D, Helmy NM. Carbetocin versus oxytocin in prevention of postpartum hemorrhage after cesarean delivery in high-risk women. A systematic review and meta-analysis. Arch Gynecol Obstet. 2025;312(2):291-309.
13. Issac E, Anuradha M, Sankar G, Shanmugapriya C. Comparison of the Efficacy of Carbetocin vs Oxytocin in Preventing PPH in Women Undergoing Vaginal Delivery: A Prospective Randomized Controlled Trial from Tamil Nadu, India. J South Asian Feder Obst Gynae 2025;17(Suppl 1):S34–S38.
14. Attilakos G, Psaroudakis D, Ash J, Buchanan R, Winter C, Donald F, et al. Carbetocin versus oxytocin for the prevention of postpartum haemorrhage following caesarean section: the results of a double-blind randomised trial. BJOG. 2010;117(8):929-36.
15. Su LL, Chong YS, Samuel M. Carbetocin for preventing postpartum haemorrhage. Cochrane Database Syst Rev. 2012;(2):CD005457.
16. Onwochei DN, Van Ross J, Singh PM, Salter A, Monks DT. Carbetocin reduces the need for additional uterotonics in elective caesarean delivery: a systematic review, meta-analysis and trial sequential analysis of randomised controlled trials. Int J Obstet Anesth. 2019;40:14-23.
17. Joshi SD, Shirsat A, Shukla V. Efficacy of carbetocin for the prevention of postpartum hemorrhage: a systematic review, meta-analysis, and randomized controlled trial from India. Int J Innovative Res Technol. 2025;12(3):532-537.
18. Mishra A, Singh RP, Pandey D, Singh KP. A comparative study on prophylactic use of oxytocin and carbetocin in cesarean delivery to prevent primary postpartum hemorrhage in a tertiary care centre, Sitapur. Int J Life Sci Biotechnol Pharma Res. 2024;13(7):560-563.