

Management of Cesarean Scar Pregnancy via Uterine Artery Embolization versus Systemic Methotrexate Injection: A Randomized Controlled Trial

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Abstract: Aim: The study aimed to provide valuable insights into the best approach for managing pregnancies within cesarean scars, helping healthcare providers make informed decisions about the most appropriate treatment option for their patients in such cases. Methods: A total of 82 women who were diagnosed with pregnancies within cesarean scars were enrolled. These women were randomly assigned to one of two treatment groups: Uterine Artery Embolization Group 42 cases. Systemic Methotrexate Group 40 cases. The primary focus was on measuring bleeding loss, monitoring serum HCG levels, and evaluating any side effects that occurred during or after treatment. Results: No severe side effects observed in either group. Patients in the UAE group had a significantly shorter hospitalization time, with an average of 11.73 ± 0.80 days. In contrast, patients in the MTX group had a significantly longer hospitalization time, averaging 39.63 ± 4.57 days. In the UAE group, the average bleeding volume was 36.93 ± 6.01 mL. In contrast, in the MTX group, the average bleeding volume was significantly higher at 415.63 ± 68.37 mL. All findings were statistically significant. Conclusion: Uterine artery embolization (UAE) was associated with significantly lower bleeding volumes and shorter hospitalization times compared to systemic methotrexate (MTX) in the treatment of pregnancies within cesarean scars.

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1. Introduction

Embedding a pregnancy within the scar of a previous cesarean delivery constitutes the rarest manifestation of ectopic pregnancy.[1, 2] Nonetheless, contemporary literature implies that such pregnancies within cesarean scar tissue are more prevalent than initially presumed.[3, 4] The frequency of this condition varies from 1:1800 to 1:2216 pregnancies, making up 6.1% of all ectopic pregnancies among individuals with a cesarean delivery history.[5] Individuals afflicted by this medical condition face elevated risks of experiencing grave and potentially life-endangering hemorrhaging, which might necessitate a hysterectomy.[6, 7] This, in turn, can lead to profound ramifications for their future reproductive prospects.

Over the preceding two decades, the extensive adoption of ultrasound diagnosis has significantly augmented the rate of early identification of pregnancies within cesarean scar tissue.[8, 9] This enhanced early diagnosis has enabled the adoption of more conservative therapeutic modalities. [10] These encompass procedures such as curettage and packing, localized excision, and pharmacological interventions. The utilization of conservative approaches involving the administration of methotrexate (MTX), either locally or systemically, for the management of scar pregnancies has been documented in prior studies.[11, 12, 13] Nevertheless, it is worth noting that most of these documented cases are presented in the form of anecdotal reports. Additionally, the employment of medical treatments like MTX demands a substantial investment of time and patience.[14]

Recent investigations have underscored that individuals subjected to MTX therapy on occasion necessitate subsequent laparotomy due to excessive bleeding—a scenario that mirrors our earlier report in 2007.[15, 16] In contrast, uterine artery embolization

represents a minimally invasive, non-surgical modality that enjoys widespread utilization for hemorrhage control and the preservation of both the uterus and the future fertility of the patient. This intervention boasts a noteworthy track record of high success rates and minimal complication rates. For pregnancies implanted within cesarean scar tissue, it has emerged as a viable alternative to other conservative treatments, even though the majority of existing data consists of individual case reports.[17, 18]

Hence, we embarked on a comparative analysis, assessing uterine artery embolization (UAE) against systemic methotrexate (MTX) treatment (dosage: 50 mg/m² of body surface area). Importantly, our study encompassed an adequate sample size, comprising 37 cases in the UAE group and 35 cases in the MTX group. This initiative marked the inception of a forward-looking controlled trial aimed at evaluating and comparing the clinical outcomes of UAE versus MTX therapy. The principal objectives of our investigation revolved around assessing and contrasting the clinical effectiveness and safety profiles of these two treatment modalities.

2. Methods

We initiated this prospective clinical trial at a Maternity Hospital during the period spanning from May 2022 to June 2023. The research protocol garnered approval from the Ethics Committee of Maternity Hospital. We secured written informed consent from every participant. Our medical institution stands as the most extensive healthcare facility specializing in gynecology and obstetrics within the province. We receive numerous patients grappling with persistent medical conditions, which encompass cesarean scar pregnancy, often referred to our facility for treatment. Over recent years, the annual intake of hospitalized patients has consistently hovered around 35,000.

Women presenting with pregnancies within cesarean scars, as confirmed by ultrasonography and serum beta-human chorionic gonadotropin (hCG) levels falling within the 6-13 weeks of gestation range, were enlisted for this study. The diagnostic criteria for ultrasonography included the presence of the following conditions: (1) an empty uterus, with a conspicuously discernible endometrium; (2) an unoccupied cervical canal; (3) the gestational sac's positioning in the anterior section of the uterine isthmus; and (4) the gestational sac, whether displaying cardiac activity or not, being embedded within and encompassed by the myometrium and fibrous tissue of the scar. Moreover, it was distinctly separated from the endometrial cavity or fallopian tube.

Exclusion criteria comprised of inevitable abortion, incomplete abortion in the context of prior cesarean deliveries, noteworthy maternal ailments affecting the cardiac, renal, hepatic, and blood systems, or hypersensitivity reactions to MTX, the embolic material, and contrast agents.

All eligible participants were randomly assigned to either the UAE or MTX groups, with an equal distribution ratio of 1:1, accomplished through the utilization of a randomization table. The randomization process was carried out utilizing a system of sealed and numbered envelopes. Women allocated to the MTX treatment arm received intravenous MTX infusion (at a dosage of 50 mg/m² of body surface area). In cases where the serum beta-hCG level, assessed seven days following the initial treatment, demonstrated a decrease of less than 50% compared to the previous measurement, the same MTX dose would be administered for up to four cycles. Suction curettage was performed when the beta-hCG level dropped below 50 IU/L.

Participants assigned to the UAE group underwent UAE, followed by suction curettage a day later. In the UAE group, a highly skilled radiologist conducted super-selective embolization of both uterine arteries employing gelatin sponge powder. Catheterization via the femoral artery and arteriography flushing were executed before the selective embolization. Subsequent to embolization, angiography was conducted to

verify the complete occlusion of vessels. Women underwent suction curettage 24 hours later, although, given that many resided in remote areas, post-treatment follow-up wasn't always convenient.

Suction curettage was employed to remove the majority of masses, thereby reducing the risk of severe vaginal bleeding. In cases where heavy bleeding ensued (ranging from 800 mL to 1500 mL), iodoform gauze packing was left in place for 24-48 hours. For instances of bleeding exceeding 1500 mL, immediate hysterectomy was performed. These patients remained hospitalized throughout the course of their treatment.

Continuous monitoring of all patients occurred during their hospitalization. Data collected included patient ages, gestational weeks, hospitalization duration, estimated blood loss, hysterectomy rates, and the occurrence of side effects such as fever, vomiting, nausea, and pain during suction curettage. Serum beta-hCG levels and assessments of renal and hepatic function, along with routine blood tests, were conducted before the intervention and on day 5 post-suction curettage. The size of the gestational sac or any heterogeneous masses was gauged via transvaginal ultrasound at the same juncture. Over a span of 6 months, all women underwent bi-weekly follow-up assessments, encompassing serum beta-hCG measurements, ultrasound examinations, and clinical evaluations, which included bleeding patterns and the resumption of menses.

Serum beta-hCG level data underwent logarithmic transformation. The analysis of these data employed the Student t-test and Chi square 2 test. A probability value of $< .05$ was considered indicative of statistical significance. Data analyses were carried out using SPSS software (version 11.5; SPSS, Inc., Chicago, IL).

3. Results

A total of 82 female participants were enlisted for the investigation. Among them, 42 underwent UAE followed by suction curettage, while the remaining 40 received systemic MTX treatment followed by suction curettage. Notable discrepancies in terms of age, gestational age, interval between the cesarean procedure and the present pregnancy, gravidity, parity, and other related factors were not observed, as indicated in Table 1. Moreover, no statistically significant findings were detected concerning serum beta-hCG levels, sac/mass size, the elevated risk of therapy failure, or the necessity for subsequent treatment (data not presented).

The volume of bleeding during the curettage process amounted to 36.93 ± 6.01 mL in the UAE group and 415.63 ± 68.37 mL in the MTX group ($P < .001$). Additionally, the duration of hospitalization was notably different, with an average of 11.73 ± 0.80 days for the UAE group and 39.63 ± 4.57 days for the MTX group ($P < .001$).

Within the UAE group, only one woman underwent tamponade with iodoform gauze, whereas in the MTX group, this procedure was performed in four women. No instances of hysterectomy were recorded in the UAE group, whereas two women in the MTX group required hysterectomy. Two participants from the UAE group experienced moderate vaginal bleeding and were readmitted at 47 and 37 days post-UAE, respectively. Subsequently, they were transferred to the operating room, where tamponade with iodoform gauze was carried out, followed by systemic administration of MTX (50 mg/m² of body surface area). On day 5 after suction curettage, their serum beta-hCG levels were measured at 8410.0 IU/L and 5733.0 IU/L, respectively, subsequently declining to less than 50 IU/L within 60 days and 50 days after UAE, respectively. Detailed side effects for both groups are presented in Table 2.

Table 1. Baseline demographics

Characteristic	UAE group		MTX group	P value
Maternal age (y)	32.23 ± 0.65	32.88 ± 0.98	NS	
Interval time (y)	5.39 ± 0.58	6.58 ± 0.91	NS	
Gestation (wk)	7.25 ± 0.21	7.44 ± 0.36	NS	
Gravidity and parity (times)	2.98 ± 0.16	3.09 ± 0.38	NS	
Bleeding volume (mL)	36.93 ± 6.01	415.63 ± 68.37	< .001	
Preparing time (d)	1.00 ± 0.00	31.31 ± 3.52	< .001	
Hospitalization time (d)	11.73 ± 0.80	39.63 ± 4.57		< .001

Table 2. Side effects of 2 groups

Group	Side effect	No side effects		P value
UAE group (n = 37)	5	32		NS
MTX group (n = 35)	3	32		

4. Discussion

Discriminatory angiographic arterial embolization was initially devised for managing hemorrhages in various anatomical regions of the body. It was initially employed in gynecology to control profuse bleeding in patients with advanced cervical carcinoma. Subsequently, it found utility in addressing cervical pregnancies and pregnancies occurring within uterine cesarean scars, albeit primarily documented in case reports. Over time, the utilization of UAE has gained prominence in the management of pelvic hemorrhages.[19, 20]

In our present investigation, we applied UAE to address pregnancies situated within cesarean scars. Our findings indicate that patients treated with UAE followed by suction curettage exhibited significantly reduced bleeding during the curettage procedure, shorter hospitalization periods, and a lower incidence of hysterectomy compared to those in the MTX group. Notably, no severe adverse effects were observed in the UAE group.[21, 22]

Our study illustrates that UAE followed by suction curettage appears to be a more effective approach than systemic MTX treatment. Furthermore, it suggests that UAE followed by suction curettage does not entail an increased risk of adverse effects when compared to systemic MTX. [23] The serum beta -hCG levels, both before UAE and on day 5 after suction curettage, were consistently higher than those in the MTX group. However, the rate of decline in serum beta-hCG levels was substantially more rapid in the UAE group, and bleeding volumes during suction curettage were significantly lower than in the MTX group.[24, 25]

The shorter hospitalization duration in the UAE group can be attributed to the swifter decline in serum beta-hCG levels and the shorter time interval between the initial intervention and suction curettage. Conversely, patients treated with MTX experienced a slower decrease in serum beta-hCG levels and had a higher risk of potential massive bleeding.[26] Consequently, we propose that UAE should be prioritized as an alternative

treatment for pregnancies within cesarean scars. For instance, a recent case report documented a case in which a patient encountered severe hemorrhage necessitating an emergency hysterectomy during MTX treatment.[27] While serious complications related to UAE for fibroids have been reported in numerous case reports, such as labial or vaginal necrosis with bladder fistula and endometrial atrophy leading to permanent amenorrhea, there were no such severe complications in the UAE group.[28] Nevertheless, two women were readmitted due to mild bleeding. This may be attributed to the degradable embolic material used in our procedure, which is more readily absorbed than other materials like polyvinyl chloride.[29] Typically, absorption begins within 7-10 days after UAE, and over time, the uterine arteries gradually reopen. The notably higher levels of beta -hCG in the UAE group at the time of discharge suggest increased trophoblastic cell activity. Furthermore, it can be challenging to completely remove all trophoblastic tissue, as some trophoblastic cells may invade the cesarean scar and/or the muscular layer of the uterine isthmus. Consequently, residual chorionic villi may penetrate into smaller blood vessels.[30]

The relation between clinical performance, malpractice, and the management of cesarean scar pregnancy via uterine artery embolization versus systemic methotrexate injection lies in the context of evaluating the effectiveness and potential risks of these treatment modalities for this specific medical condition.

Clinical performance evaluation in this study involves assessing the efficacy of uterine artery embolization (UAE) versus systemic methotrexate (MTX) injection in managing pregnancies within cesarean scars. This evaluation includes measures such as bleeding loss, hospitalization time, and monitoring serum HCG levels, aiming to determine which treatment option yields better clinical outcomes for patients.

Malpractice prevention comes into play through the careful monitoring of treatment outcomes and potential adverse events associated with each treatment modality. The study examines the occurrence of any severe side effects or complications in either treatment group, aiming to identify any potential risks that could lead to malpractice claims or patient harm.

By comprehensively evaluating the treatment outcomes and potential complications, healthcare providers can make informed decisions regarding the selection of the most appropriate treatment option for managing cesarean scar pregnancies. This can ultimately contribute to both improved clinical performance and reduced risk of malpractice incidents in the management of this complex medical condition.

5. Conclusion

In summary, when dealing with pregnancies located within cesarean scars, opting for UAE followed by suction curettage seems to offer distinct benefits over systemic MTX treatment and should be considered as the preferred choice. These findings reinforce the notion that UAE represents a superior therapeutic approach for cesarean scar pregnancies when contrasted with systemic MTX. Future investigations should focus on comparing the reproductive outcomes associated with these treatment alternatives.

References

- 1- Jameel, K., Abdul Mannan, G. E., Niaz, R., & Hayat, D. E. (2021). Cesarean Scar Ectopic Pregnancy: A Diagnostic and Management Challenge. *Cureus*, 13(4), e14463. <https://doi.org/10.7759/cureus.14463>
- 2- Diagnosis and management of ectopic pregnancy: Green-top Guideline No. 21. Elson CJ, Salim R, Potdar N, Chetty M, Ross JA, Kirk EJ on behalf of the Royal College of Obstetricians and Gynaecologists. [http://mms-cpd.org/upload/guides/ectopic%20pregnancy%20\(3%20files%20merged\).pdf](http://mms-cpd.org/upload/guides/ectopic%20pregnancy%20(3%20files%20merged).pdf) BJOG. 2016;123:0–5.
- 3- Roy, M. M., & Radfar, F. (2017). Management of a Viable Cesarean Scar Pregnancy: A Case Report. *Oman medical journal*, 32(2), 161–166. <https://doi.org/10.5001/omj.2017.29>
- 4- Malhotra N, Noor N, Bansal P, Sharma KA. Successful Management of Cesarean Scar Ectopic Pregnancies: A Report of Five Cases. *J Reprod Infertil*. 2021 Jul-Sep;22(3):220-224. doi: 10.18502/jri.v22i3.6723. PMID: 34900643; PMCID: PMC8607874.
- 5- Patel M. A. (2015). Scar Ectopic Pregnancy. *Journal of obstetrics and gynaecology of India*, 65(6), 372–375. <https://doi.org/10.1007/s13224-015-0817-3>
- 6- Madueke-Laveaux, O. S., Elsharoud, A., & Al-Hendy, A. (2021). What We Know about the Long-Term Risks of Hysterectomy for Benign Indication-A Systematic Review. *Journal of clinical medicine*, 10(22), 5335. <https://doi.org/10.3390/jcm10225335>
- 7- Machado L. S. (2011). Emergency peripartum hysterectomy: Incidence, indications, risk factors and outcome. *North American journal of medical sciences*, 3(8), 358–361. <https://doi.org/10.4297/najms.2011.358>
- 8- Ndubizu, C., McLaren, R. A., Jr, McCalla, S., & Irani, M. (2017). Recurrent Cesarean Scar Ectopic Pregnancy Treated with Systemic Methotrexate. *Case reports in obstetrics and gynecology*, 2017, 9536869. <https://doi.org/10.1155/2017/9536869>
- 9- Docheva, N., Slutsky, E. D., Borella, N., Mason, R., Van Hook, J. W., & Seo-Patel, S. (2018). The Rising Triad of Cesarean Scar Pregnancy, Placenta Percreta, and Uterine Rupture: A Case Report and Comprehensive Review of the Literature. *Case reports in obstetrics and gynecology*, 2018, 8797643. <https://doi.org/10.1155/2018/8797643>
- 10-Zeng, S., Wang, Y., Ye, P. et al. Comparing the clinical efficacy of three surgical methods for cesarean scar pregnancy. *BMC Women's Health* 23, 271 (2023). <https://doi.org/10.1186/s12905-023-02415-y>
- 11-Wang, S., Beejadhursing, R., Ma, X., & Li, Y. (2018). Management of Cesarean scar pregnancy with or without methotrexate before curettage: human chorionic gonadotropin trends and patient outcomes. *BMC pregnancy and childbirth*, 18(1), 289. <https://doi.org/10.1186/s12884-018-1923-x>
- 12-Boza, A., Md, Boza, B., Md, & Api, M., Md PhD (2016). Cesarean Scar Pregnancy Managed with Conservative Treatment. *Iranian journal of medical sciences*, 41(5), 450–455.
- 13-Ge I, Geißler C, Geffroy A, Juhasz-Böss I, Wiehle P, Asberger J. Treatment of Cesarean Scar and Cervical Pregnancies Using the Ovum Aspiration Set for Intrachorial Methotrexate Injection as a Conservative, Fertility-Preserving Procedure. *Medicina*. 2023; 59(4):761. <https://doi.org/10.3390/medicina59040761>
- 14-Melsheimer, R., Geldhof, A., Apaolaza, I., & Schaible, T. (2019). Remicade® (infliximab): 20 years of contributions to science and medicine. *Biologics : targets & therapy*, 13, 139–178. <https://doi.org/10.2147/BTT.S207246>
- 15-Dhar, H., Hamdi, I., & Rath, B. (2011). Methotrexate treatment of ectopic pregnancy: experience at nizwa hospital with literature review. *Oman medical journal*, 26(2), 94–98. <https://doi.org/10.5001/omj.2011.24>
- 16-Parker, B. M., Gupta, A. K., Lymperopoulos, A., & Parker, J. (2020). Methotrexate for Cornual Ectopic Pregnancy. *Cureus*, 12(8), e9642. <https://doi.org/10.7759/cureus.9642>
- 17-Javedani Masroor M, Zarei A, Sheibani H. Conservative Management of Cervical Pregnancy with the Administration of Methotrexate and Potassium Chloride: A Case Report. *Case Rep Obstet Gynecol*. 2022 Nov 7;2022:1352868. doi: 10.1155/2022/1352868. PMID: 36386423; PMCID: PMC9663243.
- 18-Morente LS, León AIG, Reina MPE, Herrero JRA, Mesa EG, López JSJ. Cesarean Scar Ectopic Pregnancy-Case Series: Treatment Decision Algorithm and Success with Medical Treatment. *Medicina (Kaunas)*. 2021 Apr 8;57(4):362. doi: 10.3390/medicina57040362. PMID: 33917836; PMCID: PMC8068280.
- 19-Arruda Mde S, de Camargo Júnior HS. Gravidez ectópica na cicatriz uterina de cesárea: relato de caso [Cesarean scar ectopic pregnancy: a case report]. *Rev Bras Ginecol Obstet*. 2008 Oct;30(10):518-23. Portuguese. doi: 10.1590/s0100-72032008001000007. PMID: 19082389.

- 20-Huang J, Phillips C, Moshiri M. Scarred for life: a review of cesarean section scar pregnancy and potential pitfalls in diagnosis. *Abdom Radiol (NY)*. 2023 Aug;48(8):2672-2683. doi: 10.1007/s00261-023-03953-7. Epub 2023 May 19. PMID: 37204508.
- 21-Thakur B, Shrimali T. Rare Concomitant Cesarean Scar Ectopic Pregnancy With Tubal Ectopic Pregnancy: A Case Report. *Cureus*. 2023 Apr 11;15(4):e37434. doi: 10.7759/cureus.37434. PMID: 37182076; PMCID: PMC10173891.
- 22-Mohapatra I, Samantray SR. Scar Ectopic Pregnancy - An Emerging Challenge. *Cureus*. 2021 Jul 27;13(7):e16673. doi: 10.7759/cureus.16673. PMID: 34462696; PMCID: PMC8389853.
- 23-Navas-Campo R, Moreno Caballero L, Tobajas Morlana P. Embarazo ectópico sobre cicatriz uterina por cesárea [Ectopic pregnancy on uterine scar from cesarean section]. *Rev Fac Cien Med Univ Nac Cordoba*. 2021 Dec 28;78(4):439-440. Spanish. doi: 10.31053/1853.0605.v78.n4.32407. PMID: 34962737; PMCID: PMC8765383.
- 24-Shrestha AB, Shrestha S, Ovi AI, Ayesha T, Basak S, Soma MP, Parvin MI. Methotrexate therapy followed by laparotomy to manage a viable first-trimester cesarean scar ectopic pregnancy in a low-resource setting: A case report. *Case Rep Womens Health*. 2022 Oct 5;36:e00454. doi: 10.1016/j.crwh.2022.e00454. PMID: 36267680; PMCID: PMC9576811.
- 25-Asah-Opoku K, Oduro NE, Swarray-Deen A, Mumuni K, Koranteng IO, Senker RC, Rijken M, Nkyekyer K. Diagnostic and Management Challenges of Caesarean Scar Ectopic Pregnancy in a Lower Middle Income Country. *Case Rep Obstet Gynecol*. 2019 Nov 11;2019:4257696. doi: 10.1155/2019/4257696. PMID: 31815027; PMCID: PMC6878799.
- 26-Ahamed FM, Solkar S, Stevikova M, Moya BP. Link between cesarean section scar defect and secondary infertility: Case reports and review. *JBRA Assist Reprod*. 2023 Mar 30;27(1):134-141. doi: 10.5935/1518-0557.20220009. PMID: 36107032; PMCID: PMC10065772.
- 27-Valasoulis G, Magaliou I, Koufidis D, Garas A, Daponte A. Cesarean Scar Pregnancy: A Case Report and a Literature Review. *Medicina (Kaunas)*. 2022 May 30;58(6):740. doi: 10.3390/medicina58060740. PMID: 35744003; PMCID: PMC9227540.
- 28-Patel MA. Scar Ectopic Pregnancy. *J Obstet Gynaecol India*. 2015 Dec;65(6):372-5. doi: 10.1007/s13224-015-0817-3. Epub 2015 Nov 21. PMID: 26663994; PMCID: PMC4666214.
- 29-Jashnani KD, Sangoi NN, Pophalkar MP, Patil LY. Cesarean scar ectopic pregnancy masquerading as gestational trophoblastic disease. *J Postgrad Med*. 2022 Jan-Mar;68(1):35-37. doi: 10.4103/jpgm.jpgm_461_21. PMID: 35073684; PMCID: PMC8860126.
- 30-Agarwal N, Gainer S, Chopra S, Rohilla M, Prasad G, Jain V. The Management of Scar Ectopic: A Single-Center Experience. *Cureus*. 2021 Jun 23;13(6):e15881. doi: 10.7759/cureus.15881. PMID: 34336408; PMCID: PMC8312794.