



## METHOTREXATE TREATMENT FOR ECTOPIC PREGNANCIES: SUCCESS RATES, FACTORS, AND SIDE-EFFECTS

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### Abstract

**Background:** Methotrexate presently finds application in the domain of gynecology for the therapeutic management of ailments stemming from trophoblastic tissue, notably encompassing ectopic pregnancy and gestational trophoblastic disease. This study is poised to fill a critical lacuna in medical literature, fostering a deeper understanding of Methotrexate's therapeutic potential and limitations when addressing ectopic pregnancies.

**Methods:** The present prospective observational design was meticulously executed within the esteemed confines of the Postgraduate Department of Obstetrics and Gynecology, ensconced within the esteemed premises of LallaDed Hospital, Government Medical College, Srinagar. A total of 120 patients were included in the study which spanned from 2020 to 2021.

**Results:** The success rate of methotrexate treatment for ectopic pregnancies was 82.5%. The success rate decreased with increasing maternal age, with a success rate of 86.4% in the 25-29 age group, 82.8% in the 30-34 age group, and 75.0% in the 35-39 age group. Success rates varied by age, gravidity, ectopic pregnancy size, and initial  $\beta$ -hcg levels, with no statistically significant differences except for the size of ectopic pregnancies. Patients with 1-2 cm ectopic pregnancies achieved a remarkable 90.3% success rate, while those with 2-3 cm ectopic pregnancies had a lower 74.1% success rate. However, the overall success rate for all ectopic pregnancy sizes was 82.5%, with a significant difference based on size ( $P=0.019^*$ ). Patients with initial  $\beta$ -hcg levels of 1000-3000 had a 90.4% success rate, whereas those with levels of 3000-5000 had a 76.5% success rate. The overall study success rate was 82.5%, with a significant difference based on  $\beta$ -hcg levels ( $P=0.047^*$ ). Additionally, 19.2% of patients experienced side effects from Methotrexate treatment. The single dose methotrexate treatment was associated with mild side-effects, including fever, stomatitis, gastroenteritis, and deranged liver function tests, affecting 19.2% of the study population, but no severe side-effects were reported.

**Conclusion:** Our findings emphasize that methotrexate serves as an effective medical management option for ectopic pregnancy, particularly in societies where preserving tubal function holds utmost importance. Its favorable success rate and relatively mild side-effect profile make it a valuable therapeutic approach, offering hope for successful outcomes in the management of this complex obstetric condition

**Keywords:** Ectopic pregnancy; Methotrexate; Tubal rupture; Human chorionic gonadotropin.

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## **1. Introduction**

In the annals of contemporary medical research, the management of ectopic pregnancy with the therapeutic agent Methotrexate has emerged as an imperative and captivating subject of investigation. Ectopic pregnancy, a pathophysiological condition characterized by the implantation of a fertilized ovum outside the uterine cavity, presents a formidable challenge to the field of obstetrics, necessitating the advent of efficacious and patient-tailored treatment modalities.<sup>1</sup> In this context, Methotrexate, a versatile chemotherapeutic agent historically employed for malignancies, has garnered considerable attention for its potential as a non-invasive, pharmacological solution to this obstetric predicament.<sup>2</sup> Methotrexate presently finds application in the domain of gynecology for the therapeutic management of ailments stemming from trophoblastic tissue, notably encompassing ectopic pregnancy and gestational trophoblastic disease. Despite the relatively infrequent occurrence of these pathologies during pregnancy, with incidences ranging from 0.7% for gestational trophoblastic disease (GTD) to 1-2% for ectopic pregnancy, the ramifications of these conditions on the lives of young women within their reproductive prime yield profound implications in terms of both mortality and morbidity, particularly entailing the jeopardization of their fecundity and reproductive potential.<sup>3,4</sup> The clinical manifestation of ectopic pregnancy has undergone a discernible metamorphosis, evolving from a perilous affliction fraught with life-threatening implications to a comparatively less menacing state, wherein non-surgical therapeutic alternatives, such as systemic methotrexate (MTX) administration or expectant management, have become viable options.<sup>5</sup>

Methotrexate, an esteemed antimetabolic agent, exerts its profound influence upon the dynamic landscape of viable trophoblastic cells. As an avid antagonist of folate, its modus operandi revolves around the precise blockade of DNA synthesis through the inactivation of the pivotal enzyme dihydrofolate reductase. Notably, its primary sphere of activity unfurls during the S-phase of

the cell cycle, yet its ambit extends to encompass the potential to perturb cellular progression across all stages of this intricate mitotic cascade. Emanating its pronounced effects on the site of implantation, this pharmacological titan selectively targets the proliferative fervor of rapidly dividing cells, notably manifesting its inimitable efficacy within the domain of trophoblast cells, heralding its unequivocal prominence in the therapeutic armamentarium.<sup>6</sup> In view of the dearth of comprehensive and contemporary investigations in this domain, this study is poised to fill a critical lacuna in medical literature, fostering a deeper understanding of Methotrexate's therapeutic potential and limitations when addressing ectopic pregnancy. It is envisaged that the findings of this study will not only inform and refine current clinical practices but also stimulate further research avenues, potentially unveiling novel strategies for optimizing ectopic pregnancy management and further honing the delicate balance between therapeutic potency and patient safety.

## **Methods**

This scholarly investigation embodies a prospective observational design, meticulously executed within the esteemed confines of the Postgraduate Department of Obstetrics and Gynecology, ensconced within the esteemed premises of LallaDed Hospital, Government Medical College, Srinagar. The temporal trajectory of this study spanned the expanse of 18 months, precisely from 2020 to 2021, effectively encapsulating a substantial period for in-depth data collection and analysis.

## **Sample Size and Ethical Considerations:**

A meticulously discerned cohort of 120 patients, presenting at LallaDed Hospital with a diagnosis of ectopic pregnancy and satisfying the stringent criteria necessitated for the application of methotrexate treatment, were seamlessly integrated into this empirical exploration. A paramount emphasis on ethical prerogatives was steadfastly upheld, with scrupulous adherence to the Helsinki Declaration and ethical clearance procured from the institutional ethical committee. All participants, upon cognizance of comprehensive information, offered their

informed written consent to partake in this seminal inquiry.

***Inclusion and Exclusion Criteria:***

A judiciously curated set of inclusion criteria acted as the fulcrum for participant selection, encompassing salient attributes such as hemodynamic stability, B-hcg levels below 5000 mIU/ml, ectopic size less than 3.5 cm, the absence of embryonic cardiac activity, exclusion of intrauterine pregnancy, an absence of known methotrexate sensitivity, and the willingness to adhere to diligent follow-up. Conversely, a well-considered array of exclusion criteria diligently disqualified patients grappling with hemodynamic instability, suspected ruptured ectopic pregnancy, methotrexate sensitivity, intrauterine pregnancy, breastfeeding, anemia, active pulmonary disease, renal disease, chronic liver disease, peptic ulcer disease, and those unable to comply with scheduled visits and follow-up regimens.

***Methodology and Investigations:***

Employing the rubric of "medical management of ectopic pregnancy with single dose methotrexate and its outcome," this study orchestrates an intricate interplay of diagnostic precision and therapeutic efficacy. Patient enrollment was predicated on meeting the stipulated inclusion criteria, with ectopic pregnancy diagnoses confirmed through serum B-hcg levels and transvaginal ultrasound (TVS) examinations. The temporal canvas stretched across 1 year and 6 months, a temporal expanse conducive to thorough data acquisition and analysis. A meticulously curated data repository comprising pertinent patient information was assembled, encompassing demographic attributes, medical and obstetric history, past medical and surgical encounters, family history, and personal details. A comprehensive physical examination was conducted, appraising general parameters such as pulse, blood pressure, pallor, cyanosis, icterus, and edema, in tandem with systemic and local examinations encompassing pertinent anatomical domains.

Unraveling the intricacies of ectopic pregnancy, an array of investigative endeavors was diligently pursued, encompassing

Complete Blood Count (CBC), blood group typing, Liver Function Tests (LFT), Kidney Function Tests (KFT), serum B-hcg measurements, and Transvaginal Ultrasound (TVS) evaluations. Treatment ensued, with patients adhering to a single dose of 50 mg/m<sup>2</sup> of methotrexate intramuscularly (I/M), and serial B-hcg monitoring at designated intervals, particularly on day 4 and day 7. A substantive reduction of B-hcg levels by >15% from day 4 to day 7 was indicative of successful treatment, while instances of inadequate decline or stagnation prompted surgical intervention. Throughout this pioneering inquiry, a steadfast commitment to methodological precision and ethical principles underpins the scientific integrity, allowing for nuanced insights into the treatment outcomes and adverse effects of methotrexate in the management of ectopic pregnancies. By illuminating this multifaceted therapeutic terrain, this study strives to contribute substantively to the advancement of medical knowledge and the refinement of clinical practices, ultimately fortifying the edifice of patient-centered care in this intricate domain.

***Statistical Methods***

The data was compiled and entered into a Microsoft Excel spreadsheet and then exported to the data editor of SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA). Continuous variables were presented as Mean±SD, and categorical variables were summarized as frequencies and percentages. Graphical representation included bar and pie diagrams. The comparison of Methotrexate treatment success rates with demographic factors was performed using Chi-square test or Fisher's exact test as appropriate. A P-value < 0.05 was considered statistically significant.

**2. Results**

In this section, the results of the study will be described:

When age distribution of study patients was assessed, we found that 44 (36.7%) fell within the age group of 25-29 years, 64 (53.3%) were aged between 30-34 years, and 12 (10.0%) belonged to the age group of 35-39 years. The mean age of the participants was 30.8 years with a standard deviation (SD) of 2.91, and the

age range spanned from 25 to 38 years. Among the 120 studied patients, 42 (35.0%) were primigravida, 51 (42.5%) were second gravida, and 27 (22.5%) were multi gravida. Out of a total of 120 patients, 18 (15.0%) had a present history of ectopic pregnancy, while

the majority, 102 (85.0%), had no previous history of ectopic pregnancy. The data revealed that 62 cases (51.7%) had ectopic pregnancies sized between 1-2 cm, while 58 cases (48.3%) exhibited ectopic pregnancies sized between 2-3 cm

**Table 1: Distribution as per initial  $\beta$ -hcg among study patients**

Initial $\beta$ -hcg	Number	Percentage
1000-3000	52	43.3
3000-5000	68	56.7
Total	120	100

Table 1 presents the distribution of initial  $\beta$ -hcg levels among the study patients. Among the 120 cases analyzed, 52 patients (43.3%) exhibited  $\beta$ -hcg levels ranging from 1000 to 3000, while 68 patients (56.7%) showed levels

ranging from 3000 to 5000. The table provides a comprehensive representation of the entire study population in terms of their initial  $\beta$ -hcg values.

**Table 2: Success rate of Methotrexate treatment among study patients**

Outcome	Number	Percentage
Success	99	82.5
Failure	21	17.5
Total	120	100

Table 2 presents the success rate of Methotrexate treatment among the study patients. Of the total 120 cases analyzed, 99

cases (82.5%) achieved a successful outcome with Methotrexate treatment, while 21 cases (17.5%) were deemed as treatment failures.

**Table 3: Success rate according to age in study patients**

Age (Years)	N	Success Rate		P-value
		No.	%age	
25-29	44	38	86.4	0.637
30-34	64	53	82.8	
35-39	12	9	75.0	
Total	120	100	83.3	

Table 3 presents the success rate of Methotrexate treatment in study patients categorized by age. Among patients aged 25-29 years (n=44), 38 individuals achieved

treatment success, yielding a success rate of 86.4%. For the age group 30-34 years (n=64), 53 patients attained treatment success, resulting in a success rate of 82.8%. In the 35-

39 age group (n=12), 9 patients achieved treatment success, yielding a success rate of 75.0%. Overall, the study encompassed 120 patients, with a total treatment success rate of 83.3%. The P-value for the comparison of

success rates among different age groups was found to be 0.637, indicating no statistically significant difference in success rates based on age.

**Table 4: Success rate according to gravidity in Study patients**

Gravidity	N	Success Rate		P-value
		No.	%age	
Primi gravida	42	36	85.7	0.169
Second gravida	51	44	86.3	
Multi gravida	27	19	70.4	
Total	120	99	82.5	

Table 4 depicts the success rate of Methotrexate treatment in study patients stratified by gravidity. Among primigravidas (n=42), 36 individuals experienced treatment success, resulting in a success rate of 85.7%. For second gravidas (n=51), 44 patients achieved treatment success, yielding a success rate of 86.3%. Among multigravidas (n=27), 19 patients attained treatment success,

resulting in a success rate of 70.4%. The overall study cohort comprised 120 patients, with a total treatment success rate of 82.5%. The P-value for comparing success rates among different gravidity categories was found to be 0.169, indicating no statistically significant difference in success rates based on gravidity.

**Table 5 : Success rate according to previous history of ectopic pregnancy**

Previous history of ectopic pregnancy	N	Success Rate		P-value
		No.	%age	
Present	18	13	72.2	0.213
Absent	102	86	84.3	
Total	120	99	82.5	

Table 5 exhibits the success rate of Methotrexate treatment in study patients categorized by their previous history of ectopic pregnancy. Among patients with a present history of ectopic pregnancy (n=18), 13 individuals achieved treatment success, resulting in a success rate of 72.2%. For patients without a previous history of ectopic pregnancy (n=102), 86 individuals attained treatment success, yielding a success rate of

84.3%. The overall study cohort comprised 120 patients, with a total treatment success rate of 82.5%. The P-value for comparing success rates between patients with a present history of ectopic pregnancy and those without such history was found to be 0.213, indicating no statistically significant difference in success rates based on their previous ectopic pregnancy history.

Size of Ectopic (cm)	N	Success Rate		P-value
		No.	%age	
1-2 cm	62	56	90.3	0.019*
2-3 cm	58	43	74.1	
Total	120	99	82.5	

Table 6 displays the success rate of Methotrexate treatment in study patients based on the size of their ectopic pregnancies. Among patients with ectopic pregnancies sized between 1-2 cm (n=62), 56 individuals achieved treatment success, resulted in an impressive success rate of 90.3%. For patients with ectopic pregnancies sized between 2-3 cm (n=58), 43 individuals attained treatment

success, yielding a success rate of 74.1%. The overall study cohort comprised 120 patients, with a total treatment success rate of 82.5%. The P-value for comparing success rates between patients with ectopic pregnancies of sizes 1-2 cm and 2-3 cm was found to be 0.019\*, signifying a statistically significant difference in success rates based on the size of the ectopic pregnancy.

Initial $\beta$ -hcg	N	Success Rate		P-value
		No.	%age	
1000-3000	52	47	90.4	0.047*
3000-5000	68	52	76.5	
Total	120	99	82.5	

Table 7 delineates the success rate of Methotrexate treatment among study patients, classified by their initial  $\beta$ -hcg levels. Among patients with initial  $\beta$ -hcg levels ranging from 1000 to 3000 (n=52), 47 individuals achieved treatment success, resulting in a success rate of 90.4%. For patients with initial  $\beta$ -hcg levels between 3000 and 5000 (n=68), 52 individuals

attained treatment success, yielding a success rate of 76.5%. The overall study cohort comprised 120 patients, with a total treatment success rate of 82.5%. The P-value for comparing success rates based on initial  $\beta$ -hcg levels was found to be 0.047\*, indicating a statistically significant difference in success rates between the two groups.

Side-effects	Numberofpatientswhoexperiencedit	Percentage
Liver involvement (Derranged LFT's)	7	5.8%
Stomatitis	6	5%
Gastroenteritis(nausea, vomiting, diarrhoea)	5	4.2%
Fever	5	4.2%
Total patients who developed side-effects	23	19.2%



Table 8 delineates the side effects encountered by patients who received a single dose of Methotrexate in our study. Among the observed side effects, liver involvement with deranged liver function tests (LFT's) was reported in 7 patients, representing 5.8% of the study cohort. Stomatitis was experienced by 6 patients, accounting for 5% of the participants. Gastroenteritis, characterized by symptoms of nausea, vomiting, and diarrhea, was encountered by 5 patients, constituting 4.2% of the study population. Additionally, 5 patients (4.2%) experienced fever as a side effect. In total, 23 patients (19.2%) developed side effects following the administration of Methotrexate in our study. These observations offer valuable insights into the prevalence and spectrum of adverse effects associated with this therapeutic modality further informing clinicians of potential challenges that may arise during the course of treatment.

### **3. Discussion**

Our study comprised 120 patients diagnosed with ectopic pregnancy, and its core objectives were to assess the efficacy of single dose methotrexate in the treatment of ectopic pregnancy while concurrently investigating the potential adverse effects of this therapeutic intervention. Among the participants, 44 patients fell within the age bracket of 25-29 years, 64 patients were in the 30-34 age group, and 12 patients were in the 35-39 age group. The mean age of the cases was calculated to be  $30.8 \pm 2.91$  years. When comparing our findings with relevant literature, we observe remarkable consistency in the mean age of patients across different studies. In a study conducted by Emre et al, the mean age of cases was reported as  $30.9 \pm 4.9$  years, with the age range spanning from 18 to 41 years.<sup>7</sup> Similarly, Dharet al. study yielded a mean age of 30 years among their study participants, with ages ranging from 15 to 45 years.<sup>8</sup> In Sindiani et al.'s study, the mean age of patients was documented as  $30.74 \pm 5.244$  years, with an age range of 25.5 to 36 years, which is compatible with our study.<sup>9</sup> Our study comprised 42 patients (45%) who were primigravida, 51 patients (42.5%) as second gravida, and 27 patients (22.5%) classified as multigravida, encompassing gravidity between

one and five. Notably, other studies reviewed in the literature also reported similar patterns of gravidity ranges. Sumant et al encountered cases with gravidity spanning between one and six, while Dhar et al reported cases with gravidity between one and seven.<sup>8,10</sup> Additionally, Taset al observed cases with gravidity ranging from one to eight, and Sindiani et al study encompassed cases with gravidity between one and twelve.<sup>7,9</sup> Concerning the previous history of ectopic pregnancy, our study documented a presence of 18 patients (15%) with such history, while 102 patients (85%) had no previous history of ectopic pregnancy. Similarly, the reviewed literature also revealed varying percentages of previous ectopic pregnancy histories. Taset al, study recorded a 15.5% incidence of previous history, while as Dharet al study noted an 8.3% occurrence.<sup>7,8</sup> Sindiani et al study identified a 7.27% prevalence of previous ectopic pregnancy cases.<sup>9</sup> These concurrences in findings among our study and the cited literature underscore the consistency of demographic characteristics and previous history patterns in patients with ectopic pregnancies. The convergence of these results across various studies reinforces the generalizability and relevance of such observations in the broader context of ectopic pregnancy research.

Our study demonstrated a favorable success rate of 82.5% in treating ectopic pregnancies with Methotrexate. This finding aligns with several prior investigations, including Srivichai et al's study, which reported a success rate of 90.6% with single-dose Methotrexate treatment in 96 out of 106 patients, though 4 patients required a second dose.<sup>11</sup> Mahboob's et al study also observed a success rate of 80% with single-dose Methotrexate while as Henry and Gentry reported a success rate of 85.2%, which is consistent with our study.<sup>12,13</sup> Lee and colleagues study reported an impressive success rate of 96% in patients with  $\beta$ -hCG levels below 6000 mIU/ml, which is slightly higher compared to 82.5% observed in the present study. In line with our findings, Taset al study recorded a success rate of 72.4% with single-dose Methotrexate.<sup>7</sup> Other studies, such

as Lipscomb et al, and Thoen and Creinin, reported success rates of 91.5%, and 91.5%, respectively.<sup>14,15</sup> Our study revealed a decreasing success rate of Methotrexate with increasing maternal age, with the highest success rate observed in the age group of 25-29 years (86.4%), followed by 30-34 years (82.8%), and 35-39 years (75%). This trend mirrored the findings of Dhar et al study, where success rates decreased with maternal age, with 72.7% success rate in the 15-25 years age group, 67.5% in the 25-35 years age group, and 44.4% in the 35-45 years age group.<sup>8</sup> Similarly, Sumant et al study also observed a decline in success rate with increasing maternal age, further reinforcing the relevance and significance of our findings.<sup>10</sup>

In our study, we observed that the success rate of Methotrexate treatment varied significantly based on certain patient-related factors. Specifically, we found that the success rate was highest among second gravidas, with 86.3%, followed closely by primigravidas with 85.7%, and relatively lower among multigravidas with 70.4%. These findings are in concurrence with the study conducted by Dharet al where they reported the highest success rate of 75% in patients with gravidity 2-5, followed by 61.1% in primigravidas, and 50% in patients with gravidity greater than 5.<sup>8</sup> Regarding the size of the ectopic pregnancy, our study showed a decreasing trend in the success rate with an increase in ectopic size. The highest success rate of 90.3% was observed in patients with ectopic size between 1-2 cm, followed by 70.1% in patients with ectopic size between 2-3 cm. This is consistent with the findings of Sumant et al, where they also reported a decrease in the success rate with an increase in ectopic size, observing a success rate of 82.1% in patients with ectopic size between 2-3 cm.<sup>10</sup> In contrast to our study, Dhar et al observed a lower success rate of 55.5% in patients with ectopic size between 0-2cm, 64.2% for size between 2-3cm, and 50% for size 3-4cm.<sup>8</sup> This disparity in success rates between the studies highlights the potential variability in treatment outcomes based on ectopic size, warranting further investigation to identify the contributing factors.

Regarding initial  $\beta$ -hCG levels, our study demonstrated a decline in the success rate of Methotrexate treatment with increasing  $\beta$ -hCG levels. The highest success rate of 90.4% was observed in patients with initial  $\beta$ -hCG levels between 1000-3000 mIU/ml, followed by 76.5% in patients with initial  $\beta$ -hCG levels between 3000-5000 mIU/ml. These findings align with the observations made by Cho et al, who reported a success rate of 96% when  $\beta$ -hCG levels were less than 6000 mIU/ml, and 58% when  $\beta$ -hCG levels were greater than 6000 mIU/ml.<sup>16</sup> Cho et al noted that initial  $\beta$ -hCG levels were the sole predictor of success for repeated injections of Methotrexate in a single-dose regimen.<sup>16</sup> Furthermore, the studies conducted by Sumant et al, and Taset et al also revealed a decrease in the success rate of Methotrexate treatment with increasing initial  $\beta$ -hCG levels.<sup>7,10</sup> These collective findings underscore the importance of careful patient selection and the consideration of crucial factors, such as gravidity, ectopic size, and initial  $\beta$ -hCG levels, in tailoring the most appropriate treatment approach for ectopic pregnancies. Understanding these associations aids in optimizing therapeutic decisions and improving treatment outcomes in this complex clinical scenario.

In our study, we observed that 19.16% of patients experienced side-effects following Methotrexate treatment, with the most common side-effects being deranged liver function tests (LFT's), stomatitis, gastroenteritis, and fever. These side-effects were resolved within 4-5 days through symptomatic treatment. Specifically, 5.84% of patients had deranged LFT's (transaminitis), 5% developed stomatitis, 4.16% developed gastroenteritis, and 4.16% developed fever. Interestingly, our findings are comparable to a study conducted by Parker et al from 1968 to 1997, investigating the efficacy, side-effects, and complications of single dose intramuscular Methotrexate for primary treatment of ectopic pregnancy. In that study, they reported that 24% of patients developed side-effects, which encompassed symptoms such as nausea, vomiting, diarrhea, stomatitis, elevated LFT's, dehydration, and fatigue. The resemblance in the incidence of side-effects between our study and Parker et al.'s study implies that the observed adverse events following



Methotrexate treatment are consistent across different cohorts and time frames.<sup>17</sup> Both studies highlight the importance of monitoring patients closely during the post-treatment period, as most side-effects were transient and resolved with supportive care. Such comparative analysis reinforces the significance of our research findings and contributes to the growing body of evidence surrounding the safety profile of Methotrexate as a therapeutic option for managing ectopic pregnancies.

#### 4. Conclusion

Our study on the treatment of ectopic pregnancy with a single dose of methotrexate yielded a success rate of 82.5%. Importantly, we observed that the success rate decreased with increasing maternal age, size of the ectopic pregnancy, and initial  $\beta$ -hCG levels. Despite these factors, methotrexate's medical management showcased several advantages, including its non-invasiveness, cost-effectiveness, and independence from specialized expertise like laparoscopy. Notably, the single dose methotrexate treatment was associated with mild side-effects, such as fever, stomatitis, gastroenteritis, and deranged liver function tests, which typically resolved within 4-5 days or required only symptomatic treatment. Crucially, no severe side-effects were reported in association with single dose methotrexate treatment. Overall, our findings emphasize that methotrexate serves as an effective medical management option for ectopic pregnancy, particularly in societies where preserving tubal function holds utmost importance. Its favorable success rate and relatively mild side-effect profile make it a valuable therapeutic approach, offering hope for successful outcomes in the management of this complex obstetric condition.

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