International Journal of Research in Medical Sciences
Kamaraj KSJ et al. Int J Res Med Sci. 2026 Jul;14(7):2945-2948
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012
DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20262185

Original Research Article

Role of thymosin alpha-1 in improving pregnancy outcomes in patients with implantation failure

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Received: 18 April 2026
Revised: 11 May 2026
Accepted: 03 June 2026

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ABSTRACT

Background: Implantation failure remains a significant challenge in assisted reproductive technology, with nearly 10–15% of couples experiencing recurrent issues despite multiple treatment attempts. Immune dysregulation is believed to contribute substantially to this condition. Thymosin Alpha-1, an immunomodulatory agent, may improve reproductive outcomes. This study evaluated its effectiveness as an adjunct therapy in patients with implantation failure in an Indian clinical setting.
Methods: This retrospective study analyzed a prospectively maintained database of patients diagnosed with recurrent implantation failure (RIF) who received thymosin alpha-1 therapy. Demographic details, clinical characteristics, infertility profile, prior treatment history, dosing regimen and pregnancy outcomes were evaluated
Results: A total of 102 participants were included. The mean age was 34.62±5.80 years and the mean BMI was 30.59±1.80 kg/m². The mean duration of infertility was 9.06±5.73 years. Pregnancy was achieved in 62 (60.8%) women following thymosin alpha-1 therapy, while 40 (39.2%) did not conceive. Most participants received 12 doses (58.8%), with a mean dose of 11.18 and median of 12 doses. The most common infertility etiology was diminished ovarian reserve (58.0%), followed by male factor (40.0%).
Conclusions: Thymosin alpha-1 was associated with encouraging pregnancy outcomes, with 60.8% achieving conception. These findings suggest a potential benefit of immunomodulatory therapy in implantation failure; however, larger controlled studies are needed to confirm its efficacy.

Keywords: Implantation failure, Infertility, Recurrent, Thymosin

INTRODUCTION

A dynamic interaction between the embryo and the endometrium drives the process of implantation.[1,2] This "cross-talk" is an extremely complex process that is essential to both the success of normal placentation and implantation.[1,3] The attachment, which is a stable adhesion of the embryo to the endometrial cells mediated by cell adhesion molecules like integrins, selectins and cadherins, is facilitated by a coordinated exchange of molecular signals between a competent blastocyst and a receptive endometrium.[1,4] A step forward is the invasion, in which trophoblast cells penetrate the mother's tissue to connect with her blood vessels, guaranteeing the supply of nutrients and oxygen.[1,5] Implantation failure may result from dysregulation of this cross-talk.[1] Technological developments in assisted reproductive technology (ART) have improved implantation and pregnancy outcomes.

Even with these notable advancements in reproductive outcomes, recurrent implantation failure (RIF) has become a new clinical challenge in few subsets.[6,7] Although the precise cause of RIF is still unknown, a number of factors, such as uterine abnormalities, sperm quality, genetic and hormonal imbalances, metabolic disorders, thrombophilia,

immune dysregulation, impaired endometrial receptivity and embryo-related factors, can affect the condition.[8-11] Maternal-foetal immune tolerance, which is mediated by intricate molecular and cellular interactions, is necessary for successful implantation. Recently, immunomodulatory adjuvant therapy with thymosin has been shown to improve implantation outcomes in patients with RIF, However, there is still little data available in Indian literature on the beneficial effects.[9,10] Therefore, the purpose of this retrospective study was to investigate the pregnancy outcomes in infertile women who were treated with thymosin in Indian setting.

METHODS

TA retrospective analytical study was conducted on a prospectively maintained clinical data of women diagnosed with infertility and implantation failure from April 2024 to March 2026. The objective was to evaluate the pregnancy outcome in individuals who had received thymosin therapy

This study was conducted out at a Aakash Fertility Centre & Hospital, a fertility and reproductive IVF Centre. Hospital ethics committee approval was obtained. The records of clinical data maintained in electronic medical records and registers were reviewed. 120 Women with history of infertility/implantation failures who received thymosin as part of treatment protocol were included in this study.

Inclusion criteria

Adult women diagnosed with infertility or history of implantation failure. Women who had received thymosin therapy at least 10 doses. Availability of complete clinical data and pregnancy outcomes

Exclusion criteria

Incomplete or missing medical data. Missing or lack of documented pregnancy outcomes. Lost to follow-up. Data were extracted from the prospectively maintained database and registers for baseline characteristics, clinical history, reproductive profile (diagnosis, duration of infertility), prior IVF/ICSI cycles, associated comorbid conditions/surgery undergone, treatment details and pregnancy outcomes. Data was compiled and analyzed using SPSS software. Data was expressed in descriptive statistics. Continuous variables were expressed in mean, standard deviation (SD), median and interquartile range (IQR). Categorical variables were expressed as frequency and percentage. Association of the doses with outcome was assessed with chi-square test. A p value less than 0.05 was considered statistically significant.

RESULTS

A total of 102 women were included in the analysis. The mean age was 34.62±5.80 years, with a median age of 33.5 years (IQR: 30–38). The mean BMI was 30.59±1.80 kg/m² and the median BMI was 30.40 kg/m2 (IQR: 29.40–31.60). The average duration of infertility was 9.06±5.73 years (Table 1). Regarding underlying diagnosis, diminished ovarian reserve was the most common etiology (58.0%), followed by male factor infertility (40.0%). Pulmonary tuberculosis was documented in one patient (2.0%). Most women had one (47.5%) or two (38.4%) prior embryo transfer failures. Thyroid disorder was present in 33 patients (47.1%). A history of tonsillectomy was noted in 9 patients (12.9%). Dermoid cyst, fibroid, asthma, appendicitis, chronic cervical pathology, myomectomy and tuberculosis were each observed in 1 patient (1.4%). Twenty-seven percent of patients had no documented comorbid condition (Figure 1).

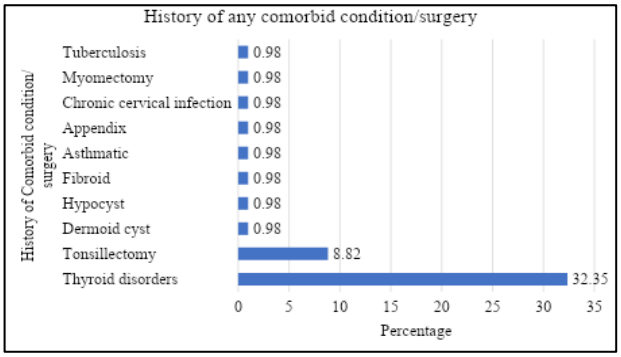

Figure 1: History of any comorbid condition/surgery.

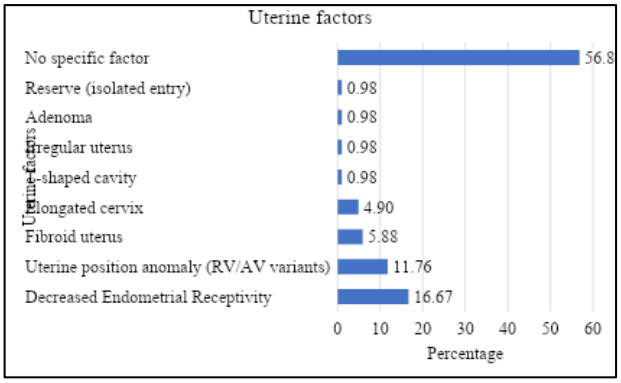

Figure 2: Uterine factors identified.

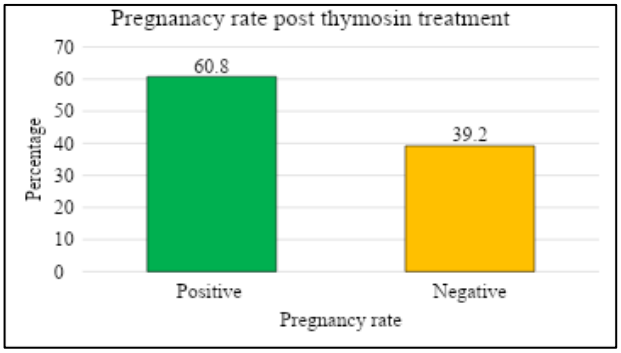

Figure 3: Outcome/pregnancy rate post treatment with Thymosin therapy.

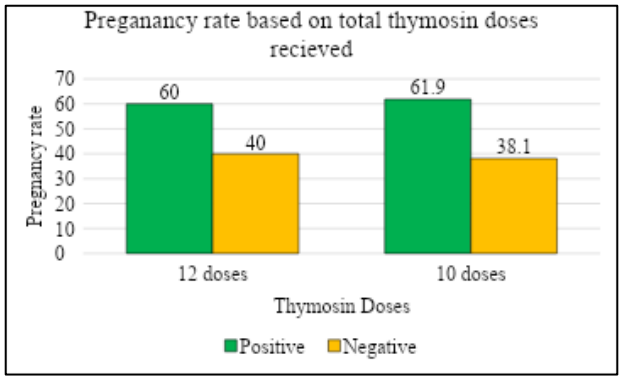

Figure 4: Outcome of pregnancy rate based on the total Thymosin doses of received.

With regards to uterine factors, decreased endometrial receptivity was identified in 17 patients (23.6%). Uterine position abnormalities were noted in 12 patients (16.7%). Fibroid uterus was present in 5 patients (6.9%) and elongated cervix in 6 patients (8.3%). T-shaped cavity, irregular uterine contour and adenoma were each observed in 1 patient (1.4%). No uterine abnormality was documented in 28 patients (38.9%) (Figure 2).

Overall, 62 women (60.8%) achieved pregnancy following thymosin alpha-1 therapy, whereas 40 (39.2%) did not conceive. Most participants received 12 doses (n=60, 58.8%), while 42 (41.2%) received 10 doses (Figure 3). The mean administered dose was 11.18, with a median of 12 doses.

Pregnancy rates were comparable between individuals who received 12 doses and those who received 10 doses of thymosin alpha-1. Sixty individuals (58.8%) received 12 doses and 42 (41.2%) received 10 doses of thymosin. Pregnancy occurred in 36 (60.0%) individuals who received 12 doses and in 26 (61.9%) individuals who received 10 doses (Figure 4). There was no statistically significant difference in pregnancy rates between the two dosing schedules (χ^2=0.038, p=0.846).

Table 1: Baseline characteristics of the patients.

Parameters		Value
Total patients		102 (100%)
Mean age±SD in years		34.62±5.80
Median age (IQR) in years		33.5 (IQR: 30–38).
Mean BMI, kg/m²		30.59±1.80
Median BMI, kg/m²		30.40 (IQR: 29.40–31.60)
Mean duration of infertility (in years)		9.06±5.73
Underlying diagnosis	Diminished ovarian reserve	58.0%
	Male factor infertility	40.0%
	Others	2.0%

DISCUSSION

Implantation failures have become a major clinical challenge despite advancements in ART, impacting ART couples. The results of this study showed promising outcomes in pregnancy rates, indicating that thymosin alpha-1 is a useful immunomodulatory adjuvant for patients who have failed implantations.

In this cohort of 102 women with previous embryo transfer failures, the average age and prolonged duration of infertility reflect a group at increased reproductive risk, consistent with observations that advanced maternal age and long-standing infertility are associated with reduced implantation potential. Diminished ovarian reserve was the predominant diagnosis in our study sample, a factor recognized in reproductive medicine as one that negatively impacts embryo quality and endometrial-embryo interaction.[1,6-8]

Immunological factors have been increasingly implicated in recurrent implantation failure, with a disrupted maternal immune environment hypothesized to impair endometrial receptivity during the window of implantation.[6,7,9-11] This immune dysregulation model is discussed in the literature, where altered Th1/Th2 balance and abnormal inflammatory responses at the endometrium are considered key contributors to RIF pathophysiology. Immunomodulatory strategies aimed at correcting these imbalances have been explored, albeit with variable success in clinical outcomes.[6,7,9]

In the present study, 60.8% of women conceived following thymosin alpha-1 therapy, suggesting a potentially favorable impact on implantation and pregnancy outcomes even in a population with multiple etiological challenges. Thymosin alpha-1 is a thymic peptide with well-documented immunomodulatory effects, including enhancement of T-cell function, modulation of cytokine production and regulation of immune tolerance, which are biologically relevant to early pregnancy and implantation.[9-14]

Although high-quality randomized controlled trials specifically evaluating thymosin alpha-1 in RIF are limited, observational and case reports support its potential benefit.[9,10,13,14] The efficacy of thymosin alpha 1 as an immunomodulatory treatment for patients with RIF is also highlighted by new data in the Indian context. Hirachan et al conducted an observational study in the real world.[9] Alpha thymosin has the potential to improve implantation success because it produced a positive β hCG response in 64.3% of patients, most of whom had confirmed fetal cardiac activity. Similarly, Rajan et al reported a successful pregnancy in a woman with unexplained RIF after receiving thymosin alpha 1, indicating that implantation can be directly facilitated by immune modulation at the maternal-foetal interface.[10] The analysis also compared dosing regimens, finding no statistically significant difference in pregnancy rates between women

receiving 10 and 12 doses of thymosin alpha-1. This suggests that beyond a certain threshold, increasing doses may not further improve outcomes, an important consideration for optimizing clinical protocols while minimizing treatment burden.

Overall, the pregnancy rates observed in this study align with emerging evidence that targeted immunomodulation may improve implantation outcomes in women with implantation failures, but further research is needed to strengthen the evidence base and guide individualized treatment.

CONCLUSION

Thymosin alpha-1 was associated with encouraging pregnancy outcomes, with 60.8% achieving conception. These findings suggest a potential benefit of immunomodulatory therapy in implantation failure; however, larger controlled studies are needed to confirm its efficacy.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Kamaraj KSJ, Parekh P, Agarwal R. Role of thymosin alpha-1 in improving pregnancy outcomes in patients with implantation failure. Int J Res Med Sci 2026;14:2945-8.