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RESEARCH ARTICLE
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A COMPARATIVE STUDY OF INTRALESIONAL TRIAMCINOLONE ACETONIDE, 5- FLUOROURACIL AND THEIR COMBINATION FOR TREATMENT OF KELOIDS

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Abstract:

Background: The benign fibrous tissue growth that develops from an aberrant healing process in response to cutaneous injuries extending beyond the primary site of trauma/lesion or inflammatory response is called keloid. Multiple treatments have been tried and it's still a concern for dermatologists to tell which the best modality for treating keloid. The current study evaluates the effect of intralesional triamcinolone acetonide and 5-FU either alone or in combination on various symptoms of keloid such as tenderness, pruritus, vascularity, telangiectasia, pliability, pigmentation, and dimensions.

Aim & Objectives: To study and compare the therapeutic efficacy of intralesional triamcinolone acetonide, 5- fluorouracil and their combination keloids treatment in terms of clearance of lesions, side effects due to therapy and recurrence, if any on follow up.

Material and Methods: This study was done among 60 patients of keloid in Muzaffarnagar Medical College & Hospital, Muzaffarnagar, Uttar Pradesh. Study was conducted for 12 months. Data was analysed statistically using mean, standard deviation and ANOVA test.

Results: The participants in this study ranged from 10-70 years old. TAA had adverse effects in 12 patients, 5- FU had adverse effects in 10 patients while TAA + 5 FU (combination treatment) had adverse effects only in 08 patients. There is difference between the treatment TAA and 5-FU & also between 5 FU and TAA + 5 FU at the end of 30th week. But there is no significant difference between TAA and TAA+ 5 FU which concludes that these both are superior to 5 FU. But between TAA and combined treatment (TAA+ 5 FU), combination treatment is better than TAA having less average mean.

Conclusion: So, we finally concluded that overall combination treatment was better than TAA and 5 FU alone in terms of both better result and less adverse effects.

Keywords: Keloid, Intralesional triamcinolone acetonide, 5- Fluorouracil.

Introduction:

A keloid is a benign fibrous tissue growth that develops from an aberrant healing process response to cutaneous injuries which extends beyond the primary site of trauma/lesion or inflammatory response. [1]Keloids are more clinically severe than hypertrophic scars, with frequent complaints of itching and pain. Traditionally, hypertrophic scars form over a period of weeks and remain confined to the initial wound borders, whereas keloid scars appear beyond the initial wound edges progressively over the period of months. [2]Keloids develop into rarely spontaneously healing thick and solid scars, as opposed to hypertrophic scars, which heal by their own after sometime. As keloids are painful for patients, there has been a significant deal of interest in understanding the key elements of keloid pathology. [3] Keloids have been known to develop secondary to various factors including genetic predisposition, skin trauma, excessive collagen production, skin tension and hormonal changes. [4] Genetic predisposition may increase the likelihood of developing keloids in persons with a family history. Skin trauma such as acne scars, burns, cuts or vaccinations can trigger the formation of keloids. Excessive collagen production, particularly during pregnancy or puberty, can also contribute to the development of keloids. [5] Keloids can develop on any part of the body, but there are certain areas where they tend to occur more frequently. Most common sites where keloids are often found include: Earlobes, upper chest and shoulder followed by back, neck and abdomen. [6]

Management of keloid is aimed at reducing symptoms, improving appearance, and preventing their recurrence. Current approaches to keloid management include intralesional steroids, oral antihistamines, cryotherapy, laser removal, radiotherapy, occlusive dressings, immunomodulators and in some exceptions surgical excision. [7] Intralesional TAA& 5-Fluorouracil (5-FU) are both commonly used treatments for keloids in the present study. This can be used either individually or in combination.

This study is aimed to assess effectiveness of intralesional triamcinolone acetonide and 5-FU either alone or in combination in treating patients of keloids. Also, the current study also evaluates the effect of TAA & 5-FU either alone or in combination on various symptoms of keloid such as tenderness, pruritus, vascularity, telangiectasia, pliability, pigmentation, and dimensions. It also aims to find the treatment which is best suited for the patient in terms of side effects and effective results.

Aim & Objectives:

1. To compare the therapeutic efficacy of intralesional triamcinolone acetonide, 5- fluorouracil and their combination for treatment of keloids.
2. To study the efficacy of TAA and 5- FU and combination of both in keloid patients in terms of clearance of lesions, side effects due to therapy and recurrence, if any on follow up.

Material and methods:

This was a hospital based prospective study done in the Department of Dermatology, Venereology and Leprology, Muzaffarnagar Medical College & Hospital, Muzaffarnagar. 60keloid patientswho presented to OPD for treatment of keloidin Muzaffarnagar Medical College & Hospital, Muzaffarnagar; were included in the study by simple random sampling.Study was done for a period of12 months i.e.June, 2023 toMay, 2024.

60 patients were divided into three groups at random. Group A (TAA) received intralesional TAA 10-40 mg/mL, Group B (5-FU) received intralesional 5-FU 50 mg/mL, and those in Group C (T+F) received intralesional injection of a combination of TAA (40 mg/mL) and 5FU (50 mg/ mL) in a ratio of 1:9. Until 24 weeks or, whichever came first, until the keloid healed, injections were given every 3 weeks. When a patient had a total score of two or fewer on the Vancouver Scar Scale

(VSS), the condition was considered "resolved."Every patient was assessed prior to each injection, and a follow-up assessment was carried out 30 weeks following the initial dosage.

Inclusion criteria:

- Newly diagnosed cases of keloid.
- Patient aged 18 to 60 years irrespective of gender
- Keloid size within 1-10 cm in greatest dimension.
- Patients who gave consent.

Exclusion criteria:

- Previously diagnosed cases of the keloid or patient with the history of treatment for keloid in past 1 year.
- Pregnant and lactating females.
- Patients with bleeding or coagulation disorder, immunosuppressive/chronic inflammatory disorders, renal or liver failure history.
- Patients having active infection, inflammation or ulcer in or around the keloid, allergy or sensitivity to drugs used in treatment in study.

Ethical approval was taken from the institute's ethical committee and written informed consent was taken from all the participants.Data was expressed in percentages. Qualitative data was reported as mean and standard deviation and the ANOVA test was used for comparison. A *p- value* equals to or less than 0.*05* was considered statistically significant.

Results:

The participants in this study ranged in age from 10-70 years old. 62% participants were male and only 38% were female.Maximum participants were residents of rural area i.e. 76.7% and 23.3% study participants were residents of urban area. **(Table 1)**

Table 1: Socio-demographic profile of participants:

Variables	Number	Percentage
Age group		
10-20	10	16.66%
21-30	25	41.66%
31-40	14	23.3%
41-50	4	6.6%
51-60	3	5%
61-70	4	6.6%
Gender		
Male	37	61.66%
Female	23	38.33%
Residence		
Urban	14	23.33%
Rural	46	76.6%

Maximum patients (48.3%) had trauma as their etiology followed by 26.7% having infective etiology, 13.3% having inflammatory etiology and minimum had spontaneous etiology i.e. 11.7%. On the basis of duration of keloid, 81.7% patients had duration of keloid from 3 months to 1 year, forming the maximum percentage.**(Figure 1)**

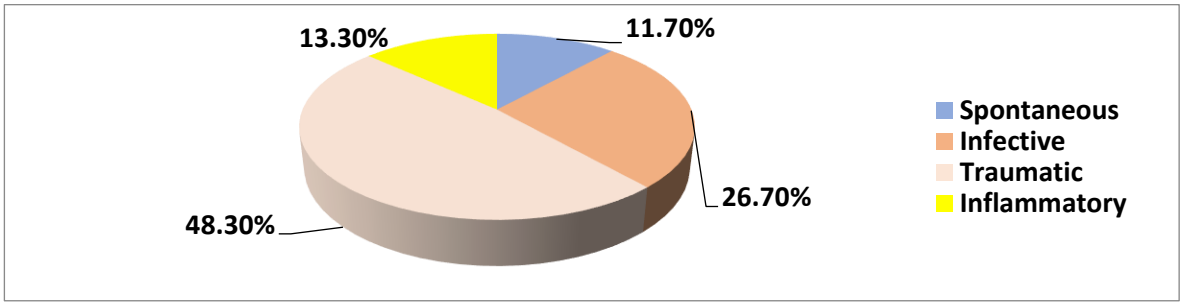

Figure 1: Pie chart showing participants according to etiology of keloid

TAA had adverse effects in 12 patients, out of which, 5 had telangiectasia, 4 had skin atrophy and 3 had skin ulceration. 5- FU had adverse effects in 10 patients, out of which, only 1 patient had telangiectasia, 2 had skin atrophy and 5 had skin ulceration and 2 had infection. TAA + 5 FU (combination treatment) had adverse effects only in 08 patients, out of which, 3 had telangiectasia, 1 had skin atrophy and 1 had infection.**(Figure 2)**

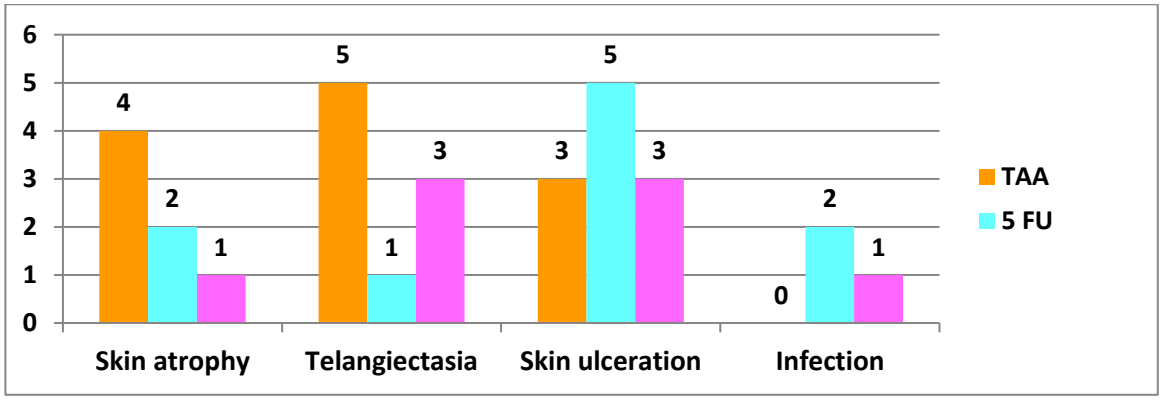

Figure 2: Figure showing participants according to adverse effects with different treatments

For vascularity, pruritis and pain, p value is <0.05 (statistically significant), so there is difference in treatments. Combination treatment is the best treatment for these variables i.e. TAA+ 5- FU; having the lowest mean. For pliability and height, the difference is borderline statistically significant; but still combination treatment is best for pliability and height also having the lowest mean. For pigmentation, the difference between the treatments is not significant having p value more than 0.05.**(Table 2)**

Table 2: Comparison of different variables in terms of mean, F ratio and p value in different treatment groups at 30 weeks:

Variable		TAA	5-FU	TAA + 5FU
Vascularity	**Mean**	0.35	0.90	0.45
	F ratio	3.58		
	P value	**0.03**		
Pigmentation	**Mean**	0.35	0.85	0.60
	F ratio	2.55		
	P value	0.09		
Pliability	**Mean**	0.60	0.65	0.30
	F ratio	3.01		
	P value	0.057		
Height	**Mean**	0.60	0.55	0.25
	F ratio	3.03		
	P value	0.056		
Pruritis	**Mean**	1.05	1.70	1.20
	F ratio	3.27		

	P value	**0.04**		
Pain	**Mean**	0.85	1.25	0.55
	F ratio	3.25		
	P value	**0.04**		

There is difference between the treatment TAA and 5-FU & also between 5 FU and TAA + 5 FU at the end of 30th week. But there is no significant difference between TAA and TAA+ 5 FU which concludes that these both are superior to 5 FU. But between TAA and combined treatment (TAA+ 5 FU), combination treatment is better than TAA having less average mean.**(Table 3)**

Table 3: Pairwise comparison between different treatment groups according to p- value (at 30th week):

Pairwise comparison	**P value**
Between TAA and 5-FU	**0.005**
Between TAA and TAA+5-FU	**0.96**
Between 5 FU and TAA+5-FU	**0.002**

Clinical Response in Group A(TAA alone) at week 0 & week 30th

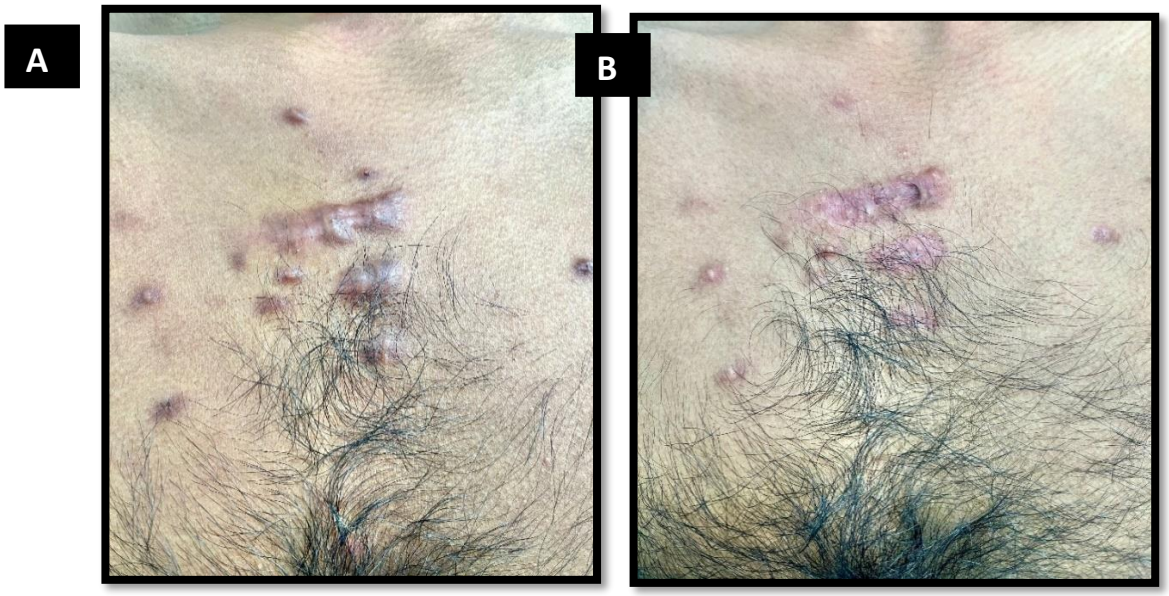

IMAGE 1 -(A) Pre-Sternal Keloid Before Treatment (Week 0)
(B) Pre-Sternal Keloid After Intralesional Taa (4 Sessions) At Week 30th

Clinical Response in Group B (5-FU alone) at week 0 & week 30th

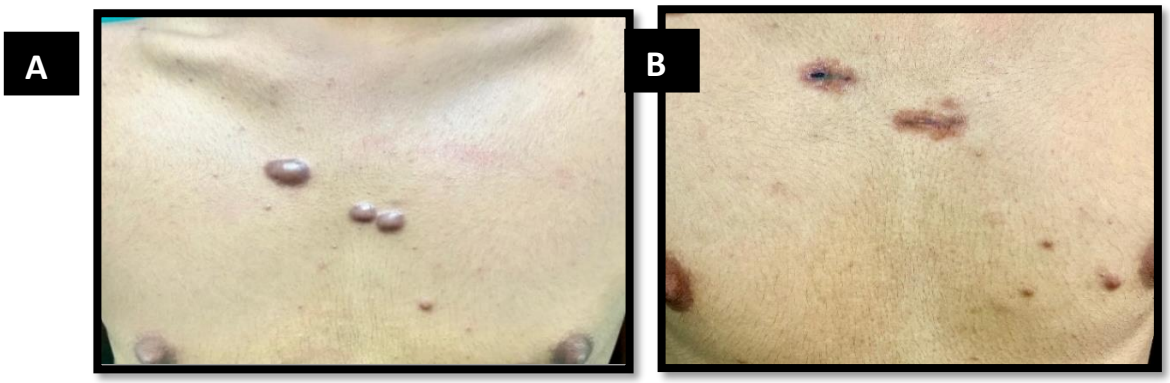

Image 2 - (A)Pre-Sternal Keloid Before Treatment (Week 0)
(B) Pre-Sternal Keloid After Intralesional 5-Fu (4 Sessions) At Week 30th

Clinical Response in Group C (TAA + 5-FU) at week 0 & week 30th

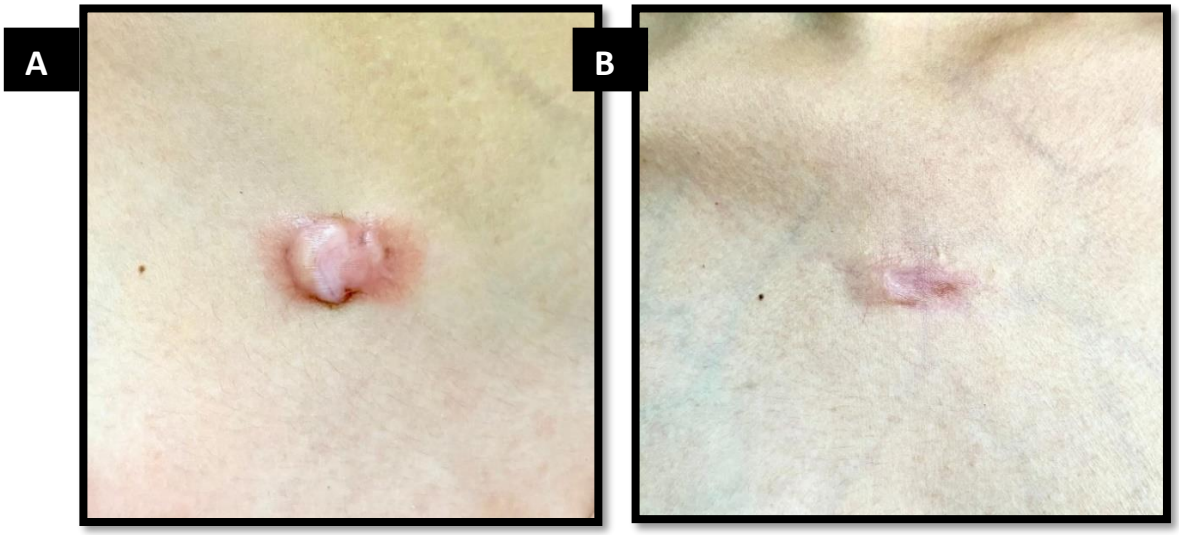

Image 3 - (A)Pre-Sternal Keloid Before Treatment (Week 0)
(B) Pre-Sternal Keloid After Intralesional Taa+5-Fu (4 Sessions) At Week 30th

Discussion:

In present study, majority of patients were of 21- 30 years i.e. 25 patients (41.7%) and minimum patients were of 51-60 years i.e. 3 patients (5%). A study done by **Raja ravi kumar PS et al (2023)** included patients between 26- 30 years of age. About half patients were of 21-30 years (51.7%) and minimum in the age group 31-40 years i.e. 15%. [8]In a research done by **Rana PPet al (2024),**age range was 11-50 years. Maximum patients were of 21-30 years i.e. 50% and minimum were in 41-50 years age group (5%).[9] These findings were comparable to the finding of our study.

In our study, 62% were male and only 38% were female. In a study done by **Shah V.Vet al (2016)**, 65.2% were female and only 34.8% were male. [10] In a study done by **Raja ravi kumar PSet al (2023)**, 43.3% study participants were male and 56.7% were female. [8]In a study done by **Rana PP et al (2024),**45% participants were male and 55% were female.[9] In contrast to other studies, we noted a male predominance among the cases of the keloids.

In the present study, maximum participants were residents of rural area i.e. 76.7% and 23.3% study participants were residents of urban area. In a study done by **Shah V.V et al (2016)**, 52.5% were from rural area and 47.5% were from urban area.[10]This was similar to the present study as majority of population was form rural area.In our study, majority of patients (48.3%) had trauma as the precipitating factor for keloids followed by 26.7% having infective etiology, 13.3% having inflammatory etiology and minimum had spontaneous etiology i.e. 11.7%.

In the present study, TAA had adverse effects in 12 patients, out of which, 5 had telangiectasia, 4 had skin atrophy and 3 had skin ulceration. 5- FU had adverse effects in 10 patients, out of which, only 1 patient had telangiectasia, 2 had skin atrophy and 5 had skin ulceration and 2 had infection. TAA + 5 FU (combination treatment) had adverse effects only in 08 patients, out of which, 3 had telangiectasia, 3 had skin atrophy and 2 had skin ulceration. In a study done by **Srivastava S et al (2018)**, telangiectasia and skin atrophy were maximum in TAA group. 5 FU group had a common problem of pain at injection site (84%). [11] In a research done by **Raja ravi kumar PS et al (2023)**, TAA had adverse effects in 10 patients, out of which, 5 had telangiectasia, 4 had skin atrophy and 3 had skin ulceration. TAA + 5 FU (combination treatment) had adverse effects only in 06 patients, out of which, 4 had skin ulceration, 1 had telangiectasia and 1 had skin atrophy. [8]These findings were almost same as our study.

At 30th week, combination treatment is the best treatment for these variables i.e. TAA+ 5- FU; having the lowest mean. For pliability and height, the difference is borderline statistically significant; but still combination treatment is best for pliability and height also having the lowest

mean. For pigmentation, the difference between the treatments is not significant having p value is more than 0.05. In a study done by **Srivastava S et al (2018),** combination of TAA+5FU gives the faster and more efficacious response with less side effects as compared to single drugs.[11]In a study done by **Morelli Coppola M in 2018,** combination of 5-FU and TAA was more effective and showed less side effects compared to TAA or 5-FU alone. [12]In a research done by **Raja ravi kumar P.S. et al. in 2023**, it was found that the combination was better to treat keloids as compared to Triamcinolone Acetonide (TAA) alone. [8]In a study done by **PP Rana et al in 2024,** it was found thatcombining 5-fluorouracil with triamcinolone acetonide had a better result than 5-fluorouracil alone. There was no recurrence in both groups. [9] These findings were same as our study.

Conclusion:
So, we finally concluded that overall combination treatment was better than TAA and 5 FU alone in terms of both better result and less adverse effects.

Limitations of the study:
Our study included patients only with a single keloid. Also, patientswere included only from one hospital that represented a sample from a single geographical area.

Relevance of the study:
This study is very helpful as it will help the dermatologists to treat keloid patients with best treatment having maximum efficacy and minimum adverse effects.

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Conflict of interest: None declared.

Authors Contribution: The study was done under the continuous and expert guidance of Dr. Swati Gupta (Assistant Professor).

References:
1. Limandjaja GC, Niessen FB, Scheper RJ, Gibbs S. The keloid disorder: heterogeneity, histopathology, mechanisms and models. Frontiers in cell and developmental biology. 2020 May 26;8:360.
2. Berman B, Maderal A, Raphael B. Keloids and hypertrophic scars: pathophysiology, classification, and treatment. Dermatologic Surgery. 2017 Jan 1;43:S3-18.
3. Huang C, Murphy GF, Akaishi S, Ogawa R. Keloids and hypertrophic scars: update and future directions. Plast Reconstr Surg Glob Open. 2013; 1(4):e25.
4. Shaheen A. Comprehensive review of keloid formation. Clin Res Dermatol Open Access. 2017 Oct;4(5):1-8.
5. Bran GM, Goessler UR, Hormann K, Riedel F, Sadick H. Keloids: current concepts of pathogenesis. International journal of molecular medicine. 2009 Sep 1;24(3):283-93.
6. Baldwin H. Keloids. InSkin of Color: A Practical Guide to Dermatologic Diagnosis and Treatment 2012 Jul 12 (pp. 181-210). New York, NY: Springer New York.
7. Ogawa R, Akita S, Akaishi S, Aramaki-Hattori N, Dohi T, Hayashi T, Kishi K, Kono T, Matsumura H, Muneuchi G, Murao N. Diagnosis and treatment of keloids and hypertrophic scars—Japan scar workshop consensus document 2018. Burns & trauma. 2019 Dec 1;7.
8. Raja Ravi Kumar PS, Vijaychandramouli, Bhargavi MS, Sindhu Priyanka. Comparison of Intralesional Triamcinolone Acetonide and Combination of 5- Fluorouracil and Triamcinolone in Ttreatment of Keloids. Int J Med Res Health Sci.2023;12(1):45-50.

9. Rana PP, Senapati D, Jena S, Mohanty P. Comparison of Intralesional 5-Fluorouracil and Intralesional 5-Fluorouracil with Triamcinolone Acetonide in treatment of Keloids: A Hospital Based Study. Int J Acad Med Pharm. 2024;6(1):1143-7.
10. Shah VV, Aldahan AS, Mlacker S, Alsaidan M, Samarkandy S, Nouri K. 5-fluorouracil in the treatment of keloids and hypertrophic scars: a comprehensive review of the literature. Dermatology and therapy. 2016 Jun;6:169-83.
11. Srivastava S, Patil A, Prakash C, Kumari H. Comparison of intralesional triamcinolone acetonide, 5-fluorouracil, and their combination in treatment of keloids. World Journal of Plastic Surgery. 2018 May;7(2):212.
12. Morelli Coppola M, Salzillo R, Segreto F, Persichetti P. Triamcinolone acetonide intralesional injection for the treatment of keloid scars: patient selection and perspectives. Clinical, cosmetic and investigational dermatology. 2018 Jul 24:387-96.