

# **AIM OF THE WORK**

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The aim of this work is to evaluate the role of the 5-fluorouracil in the treatment of problematic scars.

**PATIENTS**

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This work was carried out in plastic surgery unit of the Alexandria University Faculty of Medicine in the period from June 2013 to July 2014.

The study included twenty patients of both sex and of adult age group, complaining of Keloid, Recurrent keloid, Extensive dermal scars (widened scars) and scars resistance to medical treatment (Hypertrophic scars).

**Group 1;** Include (9) patients whose Keloids were surgically excised and thereafter treated by intrascar injections of 5floururacil at special intervals according to a proposed protocol.

**Group 2;** Include (8) patients whose Hypertrophic scars were surgically excised and thereafter treated by intrascar injections of 5floururacil at special intervals according to a proposed protocol except one patient the scar injected without surgical excision.

**Group 3;** Include (3) patients whose extensive dermal scars were surgically excised and thereafter treated by intrascar injections of 5floururacil at special intervals according to a proposed protocol.

# **METHODS**

# METHODS

The study was divided into two parts:

1. Clinical study.
2. Histopathological study.

## 1) Clinical study

### A) History taking

1. Personal data; name, age, sex, sex, residence and occupation.
2. Complaint.
3. Present history of the lesion.
  - a) Cause (burn, trauma, surgery,.....etc).
  - b) Duration of the scar (scar age).
  - c) Clinical course (change in size, colour, consistency,
  - d) Associated symptoms, aggravating and alleviating factors).
4. Family history of similar condition.
5. Past history of.
  - a) Similar previous conditions.
  - b) Previous treatment of the lesion.

### B) Clinical examination; this include.

1. Anatomical site.
2. Number.
3. Size.
4. Colour.
5. Thickness.
6. Consistency.
7. Telangectasia.
8. Signs of skin irritation (e.g. scratches).

Pretreatment documentation with colour digital photography was included.

## Treatment protocol

Number of patient: 20

- Surgical excision.
- Direct closure.
- Injection of 5floururacil intrascar after healing.

## Anesthesia

Local infiltration using 0.5%lidocaine, with epinephrine 1; 200,000 in a dose enough to provide 60- 90minutes anesthesia or general anesthesia.

## Preparation of the scar site

The scar and the surrounding area were carefully swabbed and sterilized using Betadine. Skin incisions were planned and marked with methylene blue in the form of ellipse just outside the limits of the scar.

## **Excision of the scar**

Incision were made using a number 15 scalpel blade. Excision was carried out in elliptical fashion or z plasty or w plasty. The blade should always be applied perpendicular to the skin surface, and the incision should be made completely through skin and subcutaneous tissue for the entire length of the cut. The wound was carefully undermined to effect a tension free closure after homeostasis.

## **Excision of earlobe keloids**

Earlobe keloids were excised flush with the keloid border taking care to spare every bit of normal tissue to allow for reconstruction of the new earlobe.

## **Wound closure**

The wound was closed in layers; the inverted interrupted subcutaneous 4/0 polyglactin (vicryl) sutures were carefully applied to provide strength to the closure and to relieve the tension on the wound edges prior to insertion of the skin sutures.

The skin was closed using was closed using simple interrupted 5/0 or 6/0 or subcuticular polypropylene (proline) sutures. The thicker stitch was used in area of possible tension. Care was taken to ensure that the suture were:

1. Placed at the same depth on each side of the incision of the wound.
2. Not tight.
3. Placed approximately 5-7mm apart and 2-3mm from the skin edge.
4. Knots were placed on one side of the wound.
5. Wound edge should be vertical and well apposed to avoid epidermal inversion.

In some cases we excise keloid and put split thickness skin graft

## **Wound dressing**

Adequate dressing was carried out using antibiotic ointment, a non adhesive gauze. And gamgee tissue. Or cotton gauze, followed by adhesive tape. Wound was checked 48 hours post-operatively then the dressing was left undisturbed until the time of stitches removal.

## **Post-operative medications**

- Proper antibiotic for one week.
- Vitamin C.
- Analgesics particularly during first post-operative day.

## **Suture removal**

In area with minimal tension all the stitches were removed on the 5th post-operative day. Alternative stitches were removed on the 5th and 7th post-operative days in areas with greater tension.

## **Protocol of 5flourouracil injections**

The excised scar will be halved and biopsies will be taken from each one for histopathological examination.

Injection of 5- fluorouracil will be done in the site of half of the scar after healing then every month in the same half for ten months at concentration of 50 mg/mL for a total of 10 treatments, Injection may be painful, Purpura and ulcer may occur.

The patients were assessed followed up for six to ten months, a standard photography was taken at every patient visit for injection.

### The types of scars

**Keloids** manifest as exaggerated growths of scar tissue, usually in areas of previous trauma. Keloids extend past the areas of trauma, projecting above the level of the surrounding skin, but they rarely extend into underlying subcutaneous tissue.

**Hypertrophic scars** remain limited to the traumatized area and regress spontaneously within 12-24 months, although regression may not necessarily be complete.<sup>(117)</sup>

**Widened scars** are flat and sometimes depressed. With adequate wound maturation, these wounds fade to the pigment of the surrounding uninjured skin. Widened scars are not usually red or pruritic.<sup>(120)</sup>

### Clinical assessment of the results

- The results were assessed at every monthly and then 10 months post-operatively according to the following parameter.

#### a- Scar grading according to Vancouver scar scale

Every item of the scar was considered to be improved if its grade return to normal or changed in the direction of normality (Table 5).

**Table (5): Vancouver scar scale.**

Vascularisation	Pigmentation	Pliability	Thickness
Normal	Normal	Normal	Flat
Pink	Hypo pigmentation	Supple	<2mm
Red	Mixed	Yielding	Between 2-5 mm
Purple	Hyper pigmentation	Firm	>5 mm
		Ropes	
		Contracture	

#### b- Scoring of the scar

The difference between the number of positive items present in every scar at the start and the number of items that improved according to above grading system, after 10 times of injection, was made .If for example, 4 items had been noted before treatment and three of them were improved after treatment, the scar would be scored 3/4.

### ***c- Correlation of positive improvements to total***

Overall evaluation of the effect of the drug was graded as "good", "average" and "poor" according to the degree of improvement of elevation, Pigmentation, Pliability and vascularity.

For example if 3 or 4 of these 4 clinical findings have improved with treatment, this was evaluated as " good", 2 improvements were graded " average", 1 or non improvement was evaluated as "poor" response.

## **2) Histopathological study**

The excised scar were halved and biopsy will be taken from each one for histopathological examination.

Other incisional biopsies about 2-3 mm were taken from the site of the already excised halves after 3 months.

Tissue specimens were fixed in 10 % solution of formalin, embedded in parrafin and subsequently stained with Hematoxylin-eosin stain for assessment of degree of fibrosis.

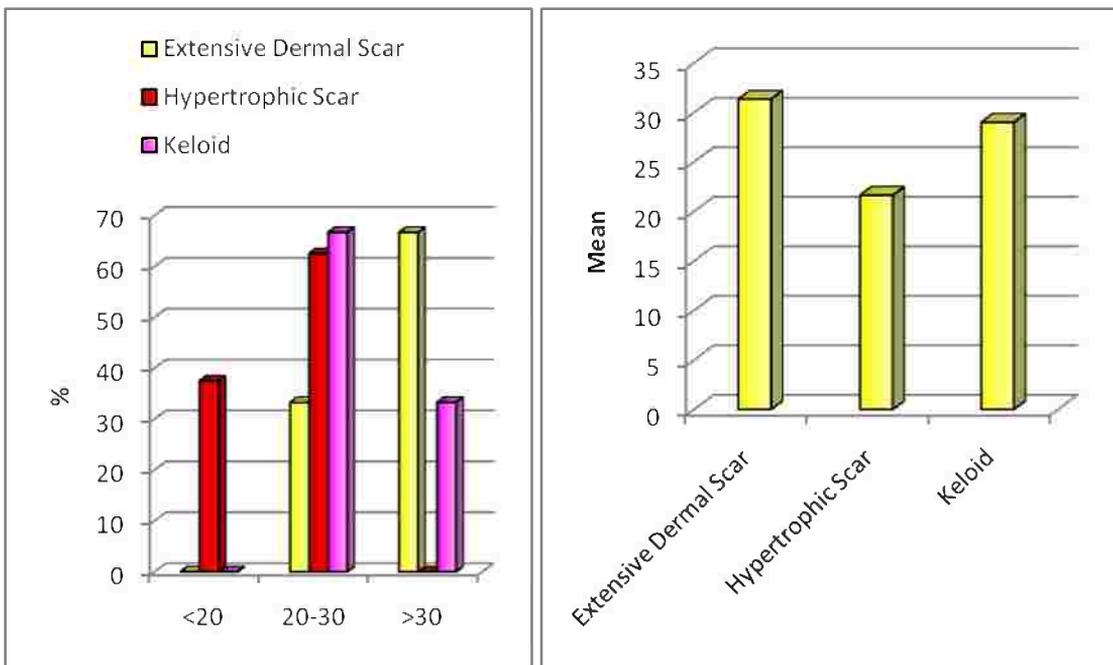
# **RESULTS**

## RESULTS

As regard to patients ages, in the Extensive Dermal Scar lesion group one patient (33.3%) out of the three patients his age 26 year and two patients (66.7%) out of the patients their ages were over 30 years; patients ages in the Extensive dermal scar lesion group were between 21-37 years with mean±S.D. 31.33±8.963 years. In the hypertrophic scar lesion group three patients (37.5%) out of the eight patients their ages under 20 years and five patients (62.5%) out of the patients their ages were from 20 years to 30 years; patients ages in the hypertrophic lesion group were between 18-26 years with mean±S.D. 21.63±2.875 years. in the keloid lesion group six patients (66.7%) out of the nine patients their ages were from 20 years to 30 years and three patients (33.3%) out of the patients their ages were over 30 years; patients ages in the keloid lesion group were between 23-39 years with mean±S.D. 29±5.679 years. (Table 6, Figure 5).

**Table (6): Comparison between the lesion groups as regard to patient's age.**

Age	Lesion						Total	
	Extensive Dermal Scar		Hypertrophic Scar		Keloid			
	No.	%	No.	%	No.	%	No.	%
<20	0	0	3	37.5	0	0	3	15
20-30	1	33.3	5	62.5	6	66.7	12	60
>30	2	66.7	0	0	3	33.3	5	25
<b>Total</b>	3	100	8	100	9	100	20	100
<b>Min.</b>	21		18		23		18	
<b>Max.</b>	37		26		39		39	
<b>Mean</b>	31.33		21.63		29.00		26.40	
<b>S.D.</b>	8.963		2.875		5.679		6.460	

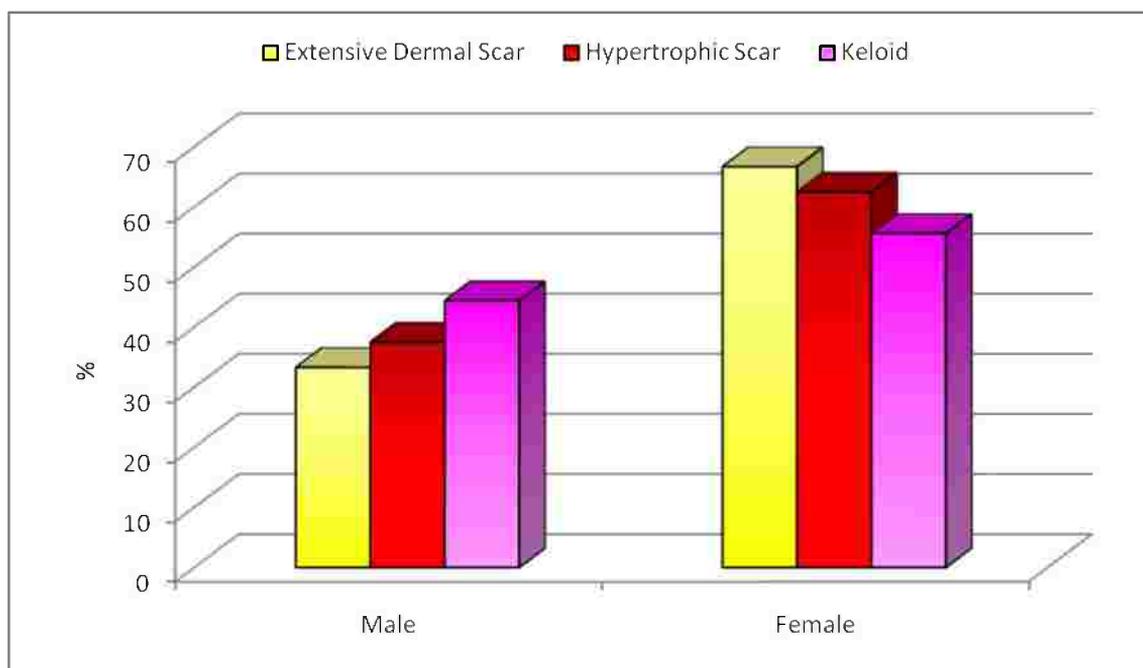


**Figure (5):** Comparison between the lesion groups as regard to patient's age.

As regard to patients sex, in the Extensive Dermal Scar lesion group one patient (33.3%) out of the three patients was male and two patients (66.7%) out of the patients were females while in the hypertrophic scar lesion group three patients (37.5%) out of the eight patients were males and five patients (62.5%) out of the patients were females and in the keloid lesion group four patients (44.4%) out of the nine patients were males and five patients (55.6%) out of the patients were females.(Table 7, Figure 6).

**Table (7): Comparison between the lesion groups as regard to patient’s sex.**

Sex	Lesion						Total	
	Extensive Dermal Scar		Hypertrophic Scar		Keloid			
	No.	%	No.	%	No.	%	No.	%
<b>Male</b>	1	33.3	3	37.5	4	44.4	8	40
<b>Female</b>	2	66.7	5	62.5	5	55.6	12	60
<b>Total</b>	3	100	8	100	9	100	20	100

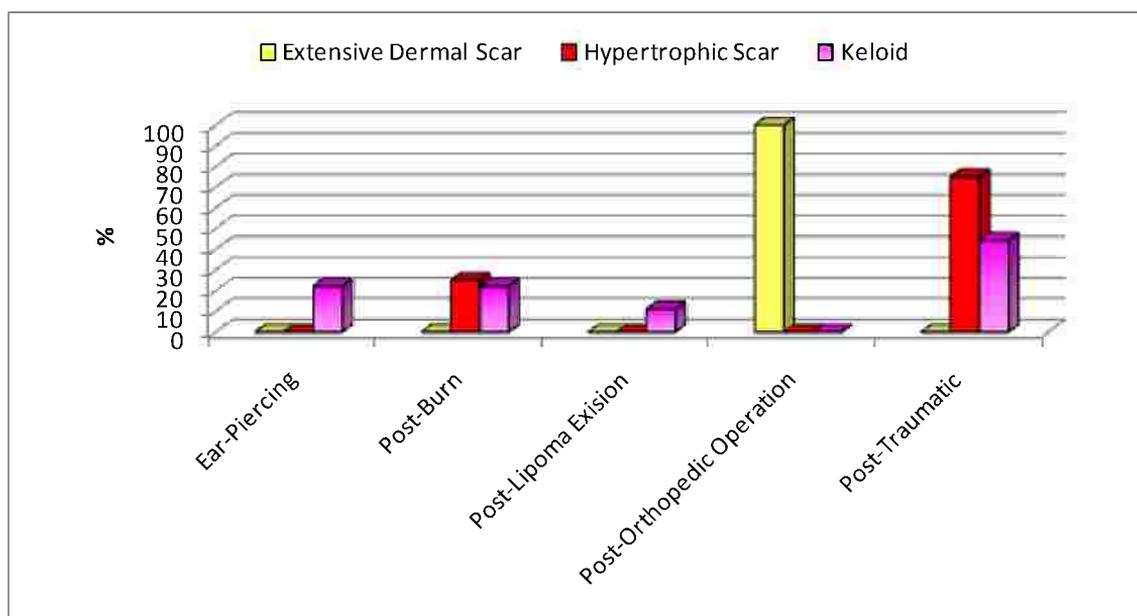


**Figure (6): Comparison between the lesion groups as regard to patient’s sex.**

As regard to the causes of lesions , in the Extensive Dermal Scar lesion group all patients (100%) had post-orthopedic operations causes while in the hypertrophic scar lesion group two patients (25%) out of the eight patients had post-burn causes and six patients (75%) out of the patients had post traumatic causes and in the keloid lesion group two patients (22.3%) out of the patients had ear-piercing causes, two patients (22.3%) out of the patients had post-burn causes , one patient (11.1%) out of the patients had post-lipoma excision cause and four patients (44.4%) out of the patients had post-traumatic causes. (Table 8, Figure 7).

**Table (8): Comparison between the lesion groups as regard to causes of lesions.**

Cause	Lesion						Total	
	Extensive Dermal Scar		Hypertrophic Scar		Keloid			
	No.	%	No.	%	No.	%	No.	%
Ear-Piercing	0	0	0	0	2	22.2	2	10
Post-Burn	0	0	2	25	2	22.2	4	20
Post-Lipoma Exision	0	0	0	0	1	11.1	1	5
Post-Orthopedic Operation	3	100	0	0	0	0	3	15
Post-Traumatic	0	0	6	75	4	44.4	10	50
<b>Total</b>	<b>3</b>	<b>100</b>	<b>8</b>	<b>100</b>	<b>9</b>	<b>100</b>	<b>20</b>	<b>100</b>

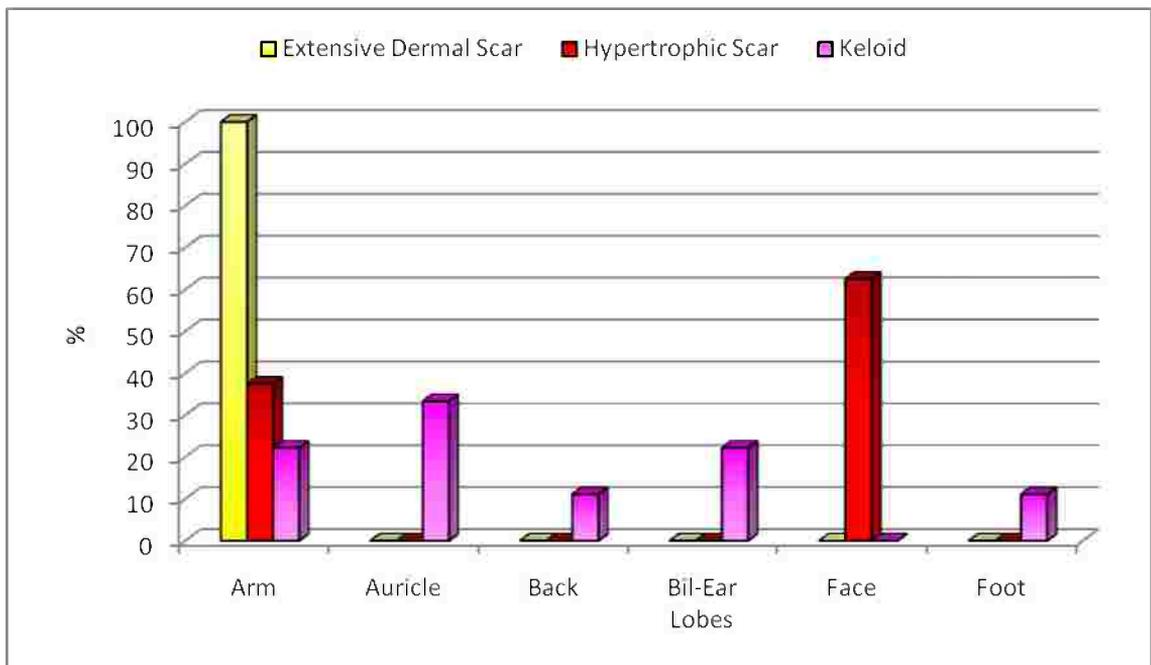


**Figure (7): Comparison between the lesion groups as regard to causes of lesions.**

As regard to the site of lesion, in the Extensive Dermal Scar lesion group all patients (100%) were in arms while in the hypertrophic scar lesion group three patients (37.5%) out of the patients were in arms , five patients (62.5%) out of the patients were in different sites of the face (mandibular area, cheek and forehead). In the keloid lesion group two patients (22.3%) out of the patients were in arms, three patients (33.3%) out of the patients were in auricles , one patient (11.1%) out of the patients was in the back of the shoulder, two patients (22.2%) out of the patients were in bilateral-ear lobes and one patient (11.1%) out of the patients was in foot.(Table 9, Figure 8).

**Table (9): Comparison between the lesion groups as regard to site.**

Site	Lesion						Total	
	Extensive Dermal Scar		Hypertrophic Scar		Keloid			
	No.	%	No.	%	No.	%	No.	%
Arm	3	100	3	37.5	2	22.2	8	40
Auricle	0	0	0	0	3	33.3	3	15
Back of the shoulder	0	0	0	0	1	11.1	1	5
Bil-Ear Lobes	0	0	0	0	2	22.2	2	10
Other sites in the face	0	0	5	62.5	0	0	5	25
Foot	0	0	0	0	1	11.1	1	5
<b>Total</b>	3	100	8	100	9	100	20	100

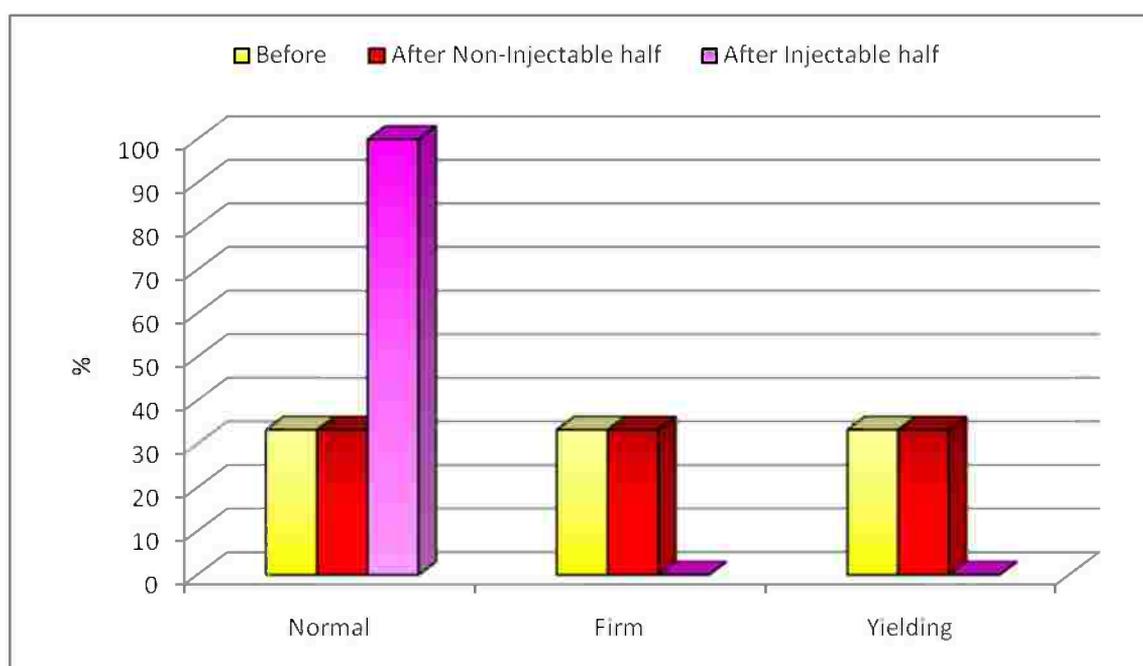


**Figure (8):** Comparison between the lesion groups as regard to site.

As regard to the Pliability in Extensive Dermal Scar lesion patients, before treatment one patient (33.3%) out of the three patients was normal, one patient (33.3%) out of the patients was firm and one patient (33.3%) out of the patients was yielding while after treatment in non-injectable halves one patient (33.3%) out of the patients was normal, one patient (33.3%) out of the patients was firm and one patient (33.3%) out of the patients was yielding and in the injectable halves all patients (100%) were normal. (Table 10, Figure 9)

**Table (10): Comparison between injectable and non injectable halves before and after treatment as regard to Pliability in Extensive Dermal Scar lesion patients.**

Pliability	Before		Non-Injectable halves		Injectable half	
	No.	%	No.	%	No.	%
Normal	1	33.3	1	33.3	3	100
Firm	1	33.3	1	33.3	0	0
Yielding	1	33.3	1	33.3	0	0
Total	3	100	3	100	3	100
P Value	0.463					

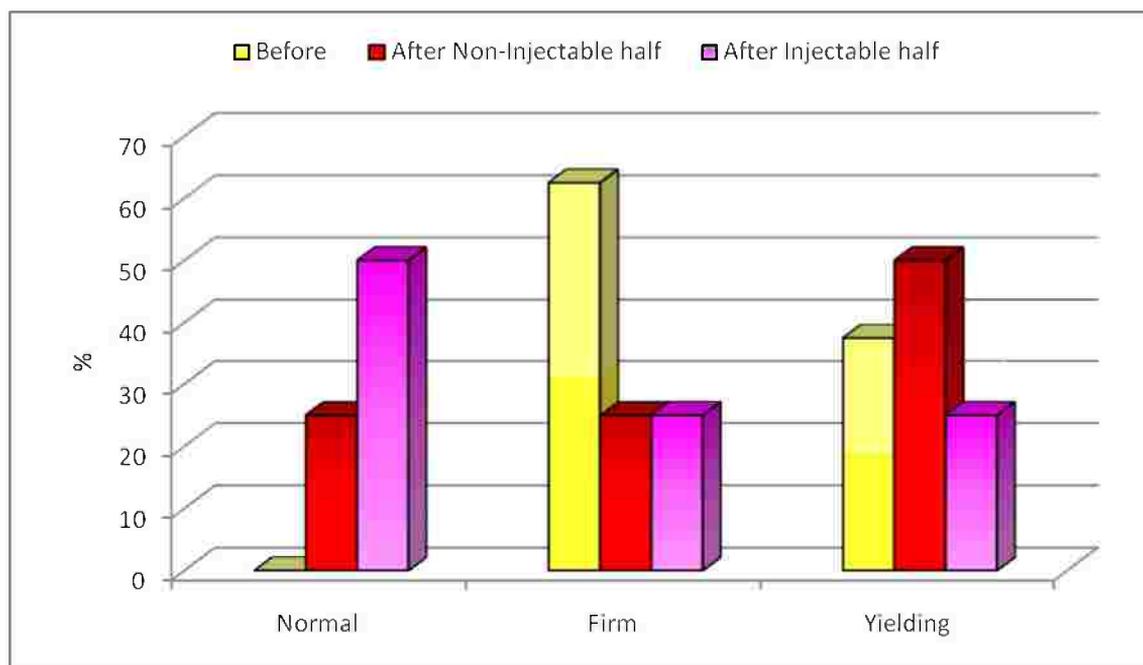


**Figure (9): Comparison between injectable and non injectable halves before and after treatment as regard to Pliability in Extensive Dermal Scar lesion patients.**

As regard to the Pliability in Hypertrophic Scar lesion patients, before treatment five patients (62.5%) out of the eight patients were firm and three patients (37.5%) out of the patients were yielding while after treatment in non-injectable halves two patients (25%) out of the patients were normal, two patients (25%) out of the patients were firm and four patients (50%) out of the patients were yielding and in the injectable halves group four patients (50%) out of the patients were normal, two patients (25%) out of the patients were firm and two patients (25%) out of the patients were yielding. (Table 11, Figure 10)

**Table (11): Comparison between injectable and non injectable halves before and after treatment as regard to Pliability in Hypertrophic Scar lesion patients.**

Pliability	Before		Non-Injectable halves		Injectable halves	
	No.	%	No.	%	No.	%
Normal	0	0	2	25	4	50
Yielding	3	37.5	4	50	2	25
Firm	5	62.5	2	25	2	25
Total	8	100	8	100	8	100
P Value	0.155					

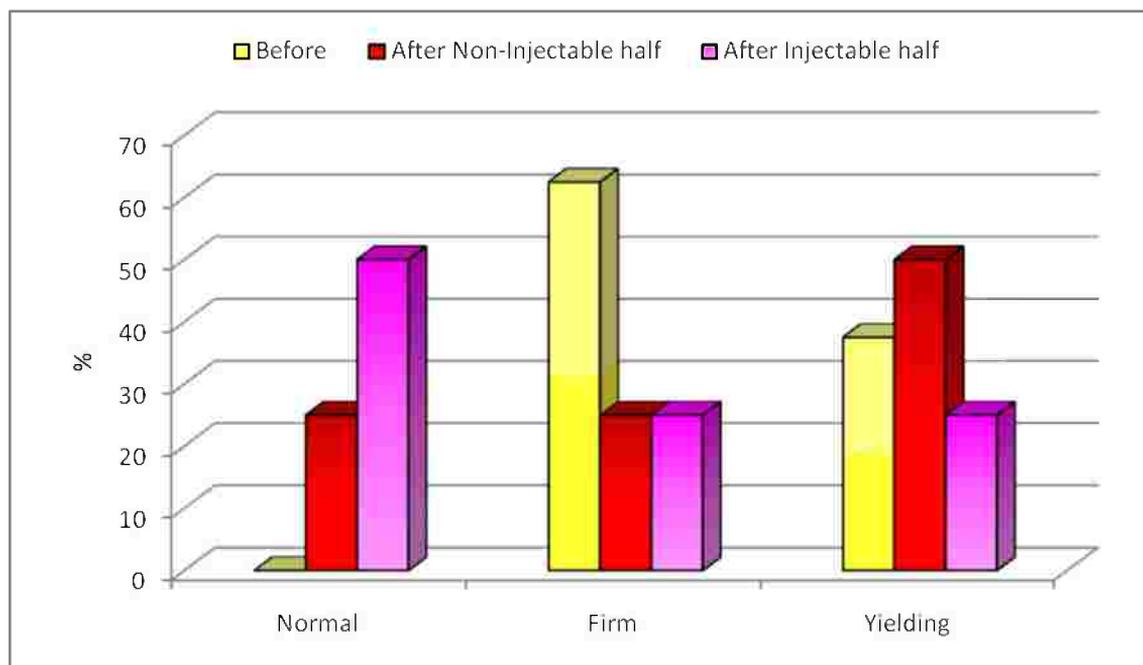


**Figure (10): Comparison between injectable and non injectable halves before and after treatment as regard to Pliability in Hypertrophic Scar lesion patients.**

As regard to the Pliability in Keloid lesion patients, before treatment five patients (62.5%) out of the nine patients were firm and three patients (37.5%) out of the patients were yielding while after treatment in non-injectable halves group two patients (25%) out of the patients were normal, two patients (25%) out of the patients were firm and four patients (50%) out of the patients were yielding and in the injectable halves four patients (50%) out of the patients were normal, two patients (25%) out of the patients were firm and two patients (25%) out of the patients were yielding. (Table 12, Figure 11)

**Table (12): Comparison between injectable and non injectable halves before and after as regard to Pliability in Keloid lesion patients.**

Pliability	Before		Non-Injectable halves		Injectable halves	
	No.	%	No.	%	No.	%
Normal	0	0	2	25	4	50
Yielding	3	37.5	4	50	2	25
Firm	5	62.5	2	25	2	25
Total	8	100	8	100	8	100
P Value	0.155					



**Figure (11): Comparison between injectable and non injectable halves before and after as regard to Pliability in Keloid lesion patients.**

As regard to the thickness in Extensive Dermal Scar lesion patients, all patients in the three groups were flat. (Table 13, Figure 12)

**Table (13): Comparison between the injectable and non injectable halves before and after as regard to Thickness in Extensive Dermal Scar lesion patients.**

Thickness	Before		After Non-Injectable half		After Injectable half	
	No.	%	No.	%	No.	%
Flat	3	100	3	100	3	100
Total	3	100	3	100	3	100

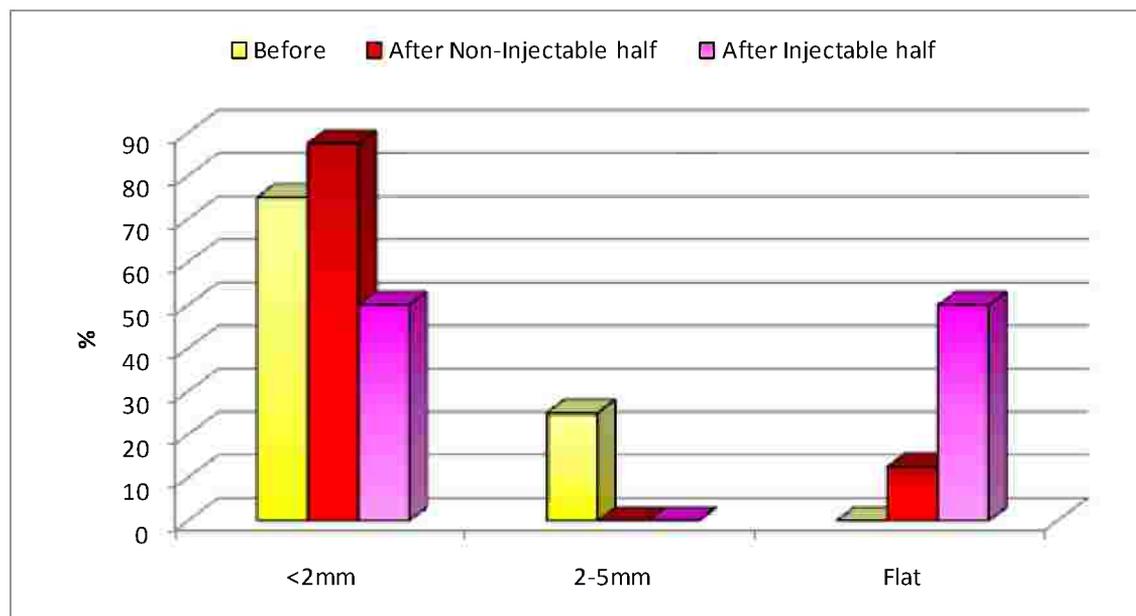


**Figure (12): Comparison between the injectable and non injectable halves before and after as regard to Thickness in Extensive Dermal Scar lesion patients.**

As regard to the Thickness in Hypertrophic Scar lesion patients, before treatment six patients (75%) out of the eight patients the thickness was less than 2mm and two patients (25%) out of the patients the thickness was between 2-5mm while after treatment in non-Injectable halves seven patients (87.5%) out of the patients the thickness was less than 2mm and one patient (12.5%) out of the patients was flat and in the Injectable halves four patients (50%) out of the patients the thickness was less than 2mm and four patients (50%) out of the patients was flat. There was statistically significant differences between injectable and non injectable halves before and after treatment while  $P=0.040$  ( $P$  significant level at  $P$  less than 0.05). (Table 14, Figure 13)

**Table (14): Comparison between the injectable and non injectable halves before and after s as regard to Thickness in Hypertrophic Scar lesion patients.**

Thickness	Before		Non-Injectable halves		Injectable halves	
	No.	%	No.	%	No.	%
Flat	0	0	1	12.5	4	50
<2mm	6	75	7	87.5	4	50
2-5mm	2	25	0	0	0	0
Total	8	100	8	100	8	100
P Value	0.040*					

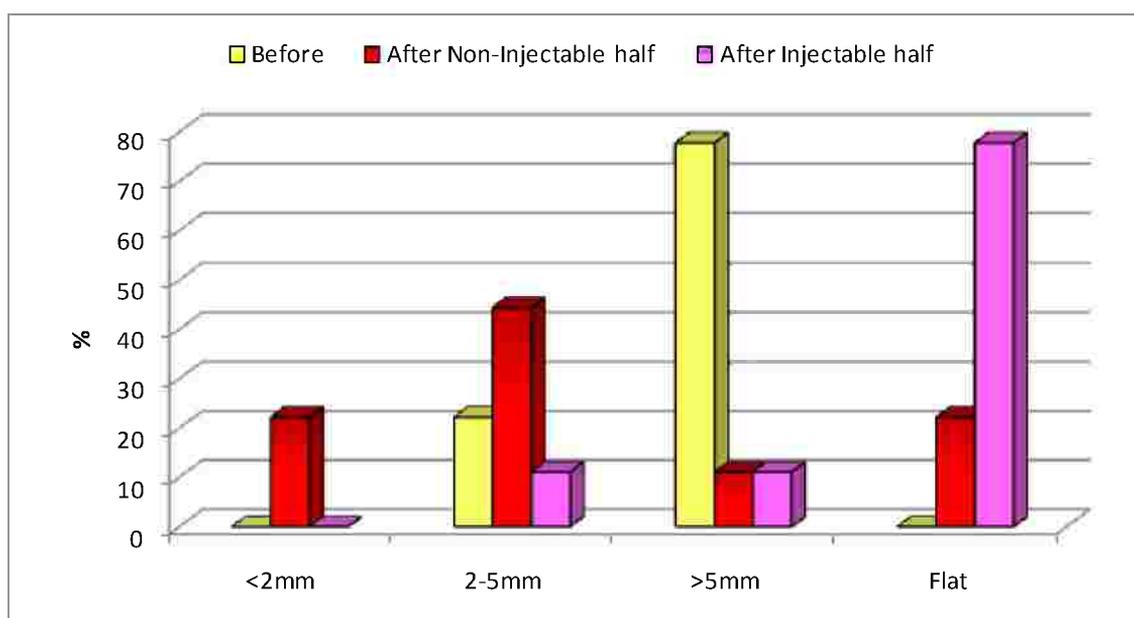


**Figure (13): Comparison between the injectable and non injectable halves before and after as regard to Thickness in Hypertrophic Scar lesion patients.**

As regard to the Thickness in keloid lesion patients, before treatment two patients (22.2%) out of the nine patients the thickness was between 2-5mm and seven patients (77.8%) out of the patients the thickness was more than 5mm while After treatment in non-Injectable half group 2(22.2%) out of the patients the thickness was less than 2mm, four patients (44.4%) out of the patients the thickness was between 2-5mm, one patient (11.1%) out of the patients the thickness was more than 5mm and two patients (22.2%) out of the patients the thickness was flat and in the Injectable halves one patient (11.1%) out of the patients the thickness was between 2-5mm, one patient (11.1%) out of the patients the thickness was more than 5mm and seven patients (77.8%) out of the patients the thickness was flat. There was statistically significant differences between injectable and non injectable halves before and after treatment while  $P=0.001$  (P significant level at P less than 0.05). (Table 15, Figure 14)

**Table (15): Comparison between the injectable and non injectable halves before and after as regard to Thickness in keloid lesion patients.**

Thickness	Before		Non-Injectable halves		Injectable halves	
	No.	%	No.	%	No.	%
Flat	0	0	2	22.2	7	77.8
<2mm	0	0	2	22.2	0	0
2-5mm	2	22.2	4	44.4	1	11.1
>5mm	7	77.8	1	11.1	1	11.1
<b>Total</b>	9	100	9	100	9	100
<b>P Value</b>	0.001*					

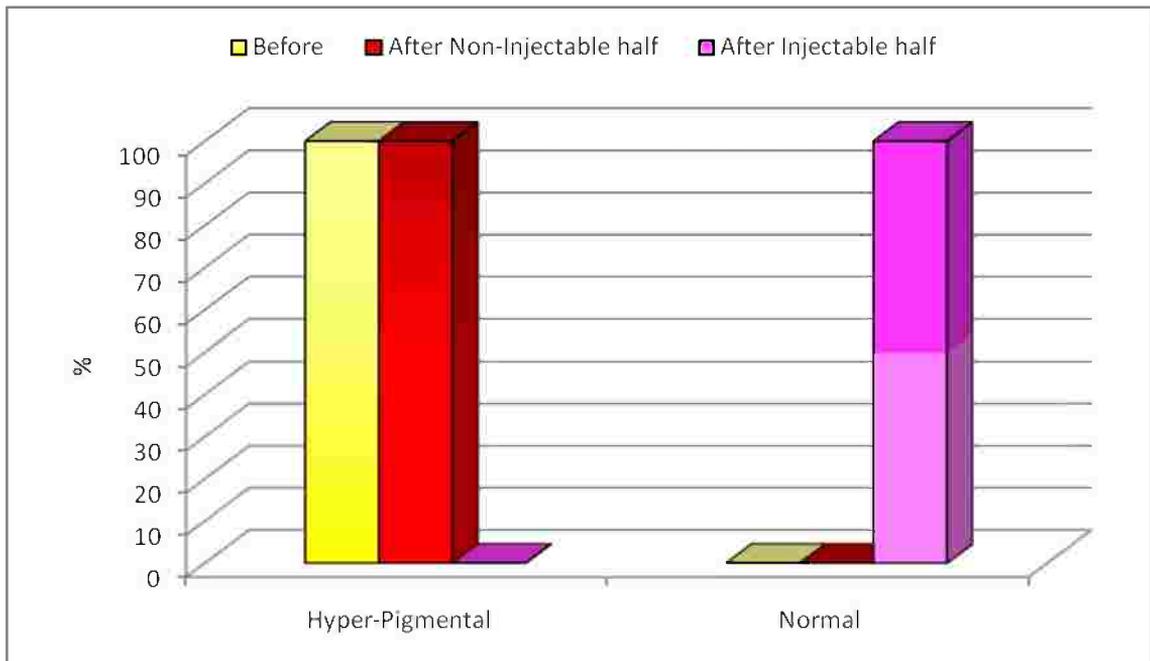


**Figure (14): Comparison between the injectable and non injectable halves before and after as regard to Thickness in keloid lesion patients.**

As regard to the Pigmentation in Extensive Dermal Scar lesion patients, before treatment in all patients (100%) the lesions were Hyper-Pigmented while. After treatment in non-Injectable halves in all patients the lesions were Hyper-Pigmented and in the Injectable half in all patients the lesions were normal. There was statistically significant differences between injectable and non injectable halves before and after treatment while  $P=0.011$  ( $P$  significant level at  $P$  less than 0.05). (Table 16, Figure 15)

**Table (16): Comparison between the injectable and non injectable halves before and after as regard to Pigmentation in Extensive Dermal Scar lesion patients.**

Pigmentation	Before		Non-Injectable half		Injectable half	
	No.	%	No.	%	No.	%
Hyper-Pigmental	3	100	3	100	0	0
Normal	0	0	0	0	3	100
Total	3	100	3	100	3	100
P Value	0.011*					

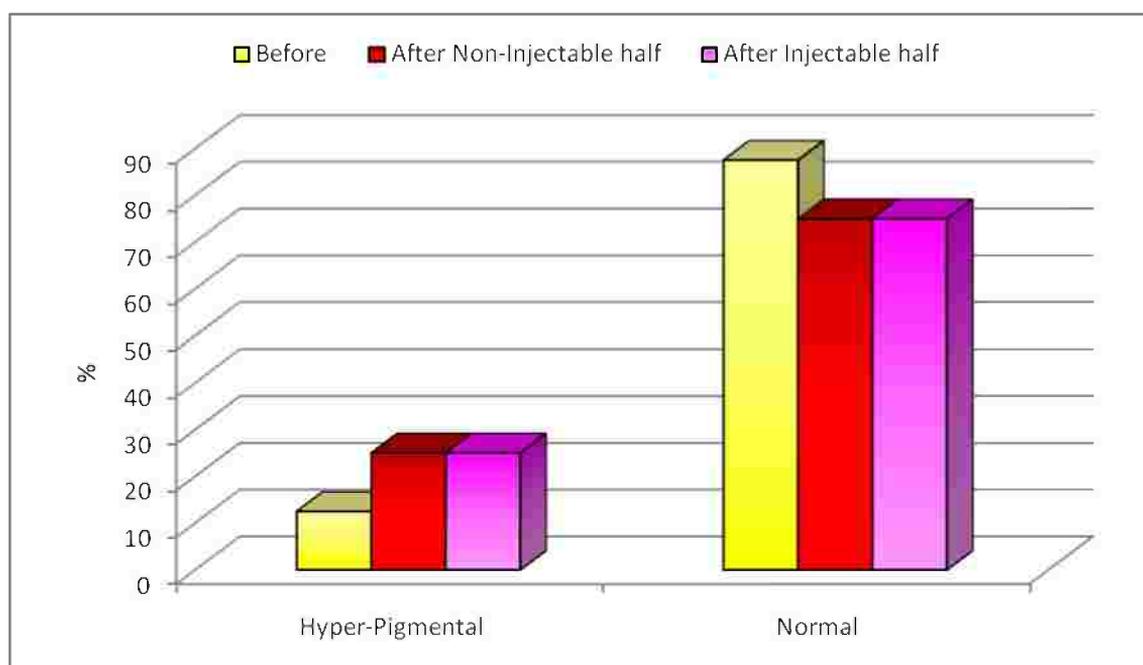


**Figure (15): Comparison between the injectable and non injectable halves before and after as regard to Pigmentation in Extensive Dermal Scar lesion patients.**

As regard to the Pigmentation in Hypertrophic Scar lesion patients, before treatment in one patient (12.5%) out of the eight patients the lesion was Hyper-Pigmented and in seven patients (87.5%) out of the patients the lesions were normal while after treatment in non-Injectable halves in two patients (25%) out of the patients the lesions were Hyper-Pigmented and in six patients (75%) out of the patients the lesions were normal and in the Injectable halves in two patients (25%) out of the patients the lesions were Hyper-Pigmented and in six patients (75%) out of the patients the lesions were normal. (Table 17, Figure 16)

**Table (17): Comparison between the injectable and non injectable halves before and after treatment as regard to Pigmentation in Hypertrophic Scar lesion patients.**

Pigmentation	Before		Non-Injectable halves		Injectable halves	
	No.	%	No.	%	No.	%
Hyper-Pigmental	1	12.5	2	25	2	25
Normal	7	87.5	6	75	6	75
Total	8	100	8	100	8	100
P Value	0.777					

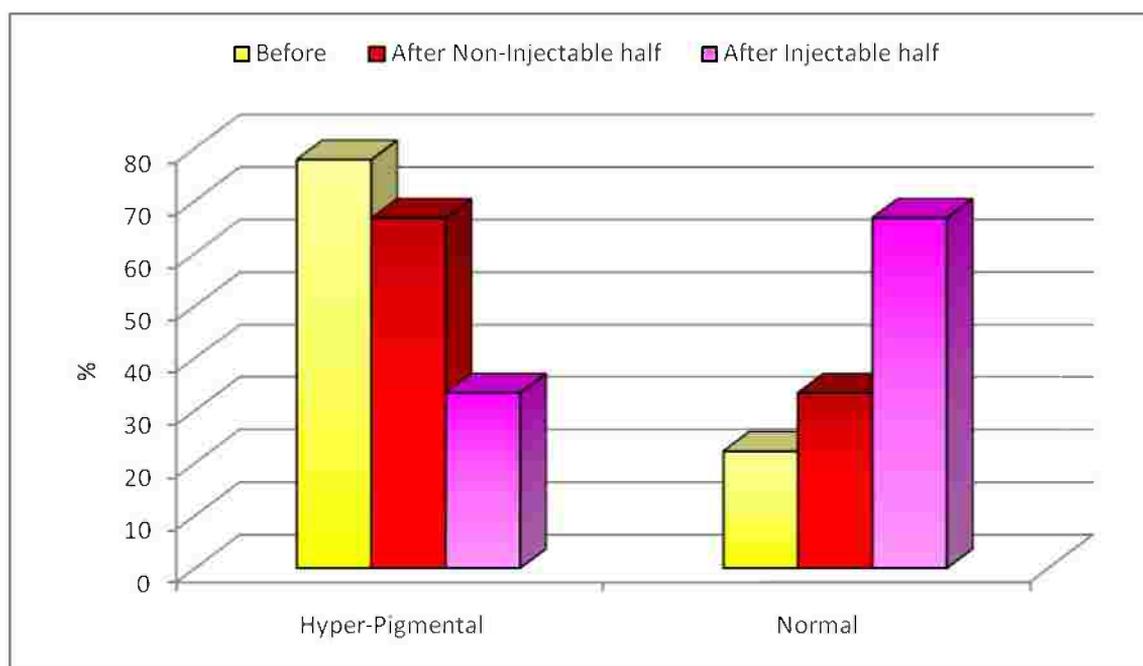


**Figure (16): Comparison between the injectable and non injectable halves before and after as regard to Pigmentation in Hypertrophic Scar lesion patients**

As regard to the Pigmentation in keloid lesion patients, before treatment in seven patients (77.8%) out of the nine patients the lesions were Hyper-Pigmented and in two patients (22.2%) out of the patients the lesions were normal while after treatment in non-Injectable halves in six patients (66.7%) out of the patients the lesions were Hyper-Pigmented and in three patients (33.3%) out of the patients the lesions were normal and in the Injectable halves in three patients (33.3%) out of the patients the lesions were Hyper-Pigmented and in six patients (66.7%) out of the patients the lesions were normal. (Table 18, Figure 17)

**Table (18): Comparison between the injectable and non injectable halves before and after as regard to Pigmentation in keloid lesion patients.**

Pigmentation	Before		Non-Injectable halves		Injectable halves	
	No.	%	No.	%	No.	%
Hyper-Pigmental	7	77.8	6	66.7	3	33.3
Normal	2	22.2	3	33.3	6	66.7
Total	9	100	9	100	9	100
P Value	0.136					



**Figure (17): Comparison between the injectable and non injectable halves before and after as regard to Pigmentation in keloid lesion patients.**

As regard to the Vascularity in Extensive Dermal Scar lesion patients, in all patients in the three groups the lesions were normal. (Table 19, Figure 18).

**Table (19): Comparison between the injectable and non injectable hal before and after as regard to Vascularity in Extensive Dermal Scar lesion patients.**

Vascularity	Before		Non-Injectable halves		Injectable halves	
	No.	%	No.	%	No.	%
Normal	3	100	3	100	3	100
Total	3	100	3	100	3	100

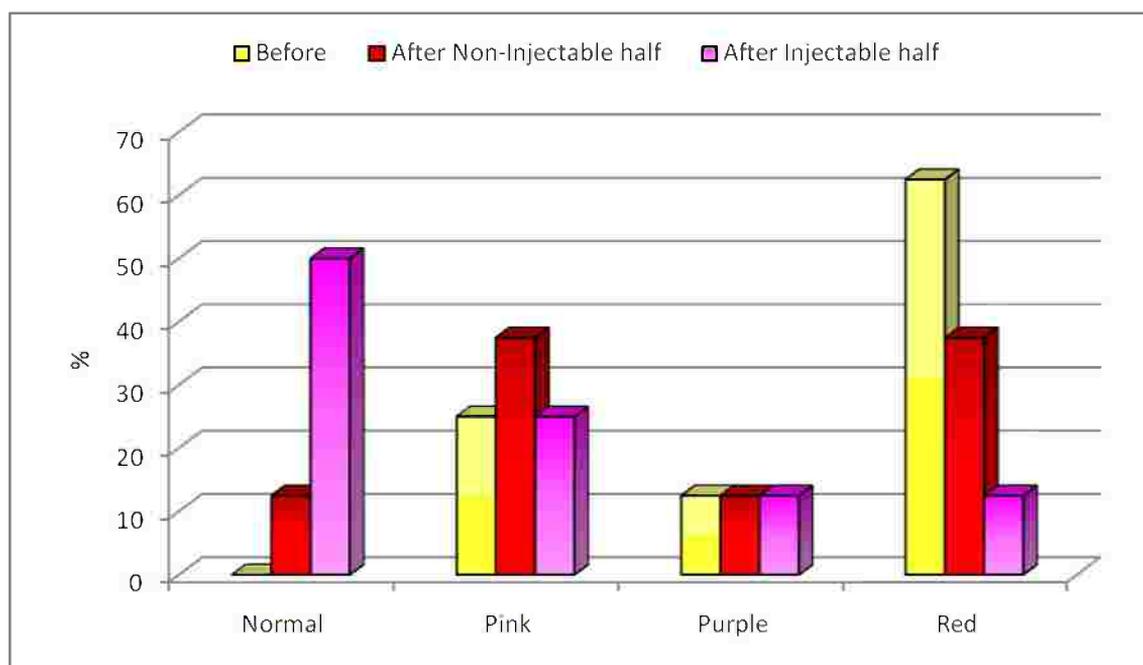


**Figure (18): Comparison between the injectable and non injectable halves before and after as regard to Vascularity in Extensive Dermal Scar lesion patients.**

As regard to the Vascularity in Hypertrophic Scar lesion patients, before treatment in two patients (25%) out of the eight patients the lesions were pink, in one patient (12.5%) out of the patients the lesion was purple and in five patients (62.5%) out of the patients the lesions were red while after treatment in non-Injectable halves in one patient (12.5%) out of the patients the lesion was normal, in three patients (37.5%) out of the patients the lesions were pink, in one patient (12.5%) out of the patients the lesion was purple and in three patients (37.5%) out of the patients the lesions were red and in the Injectable halves in four patients (50%) out of the patients the lesions were normal, in two patients (25%) out of the patients the lesions were pink, in one patient (12.5%) out of the patients the lesion was purple and in one patient (12.5%) out of the patients the lesion was red. (Table (20), figure (19))

**Table (20): Comparison between the injectable and non injectable halves before and after as regard to Vascularity in Hypertrophic Scar lesion patients.**

Vascularity	Before		Non-Injectable halves		Injectable halves	
	No.	%	No.	%	No.	%
Normal	0	0	1	12.5	4	50
Pink	2	25	3	37.5	2	25
Red	5	62.5	3	37.5	1	12.5
Purple	1	12.5	1	12.5	1	12.5
Total	8	100	8	100	8	100
P Value	0.227					

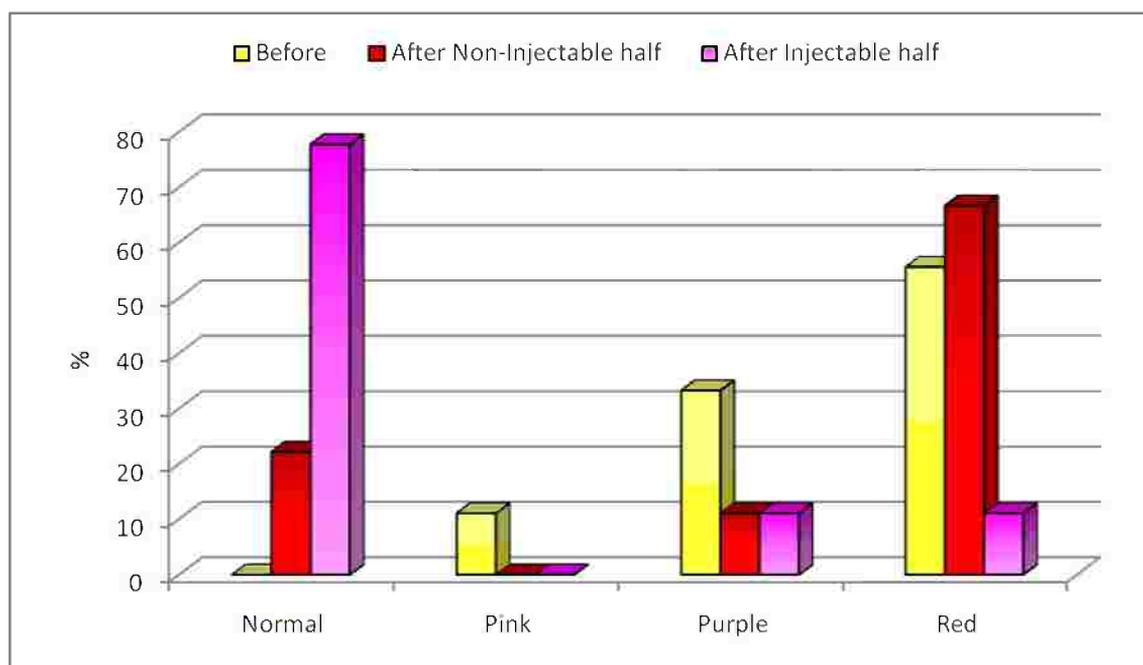


**Figure (19): Comparison between the injectable and non injectable halves before and after as regard to Vascularity in Hypertrophic Scar lesion patients.**

As regard to the Vascularity in keloid lesion patients, before treatment in one patient (11.1%) out of the nine patients the lesion was pink, in three patients (33.3%) out of the patients the lesions were purple and in five patients (55.6%) out of the patients the lesions were red while after treatment in non-Injectable halves in two patients (22.2%) out of the patients the lesions were normal, in one patient (11.1%) out of the patients the lesion was purple and in six patients (66.7%) out of the patients the lesions were red and in the Injectable halves in seven patients (77.8%) out of the patients the lesions were normal, in one patient (11.1%) out of the patients the lesion was purple and in one patient (11.1%) out of the patients the lesion was red. There was statistically significant differences between injectable and non injectable halves before and after while  $P=0.015$  ( $P$  significant level at  $P$  less than 0.05). (Table 21, Figure 20)

**Table (21): Comparison between the injectable and non injectable halves before and after as regard to Vascularity in keloid lesion patients.**

Vascularity	Before		Non-Injectable half		Injectable half	
	No.	%	No.	%	No.	%
Normal	0	0	2	22.2	7	77.8
Pink	1	11.1	0	0	0	0
Red	5	55.6	6	66.7	1	11.1
Purple	3	33.3	1	11.1	1	11.1
Total	9	100	9	100	9	100
P Value	0.015*					

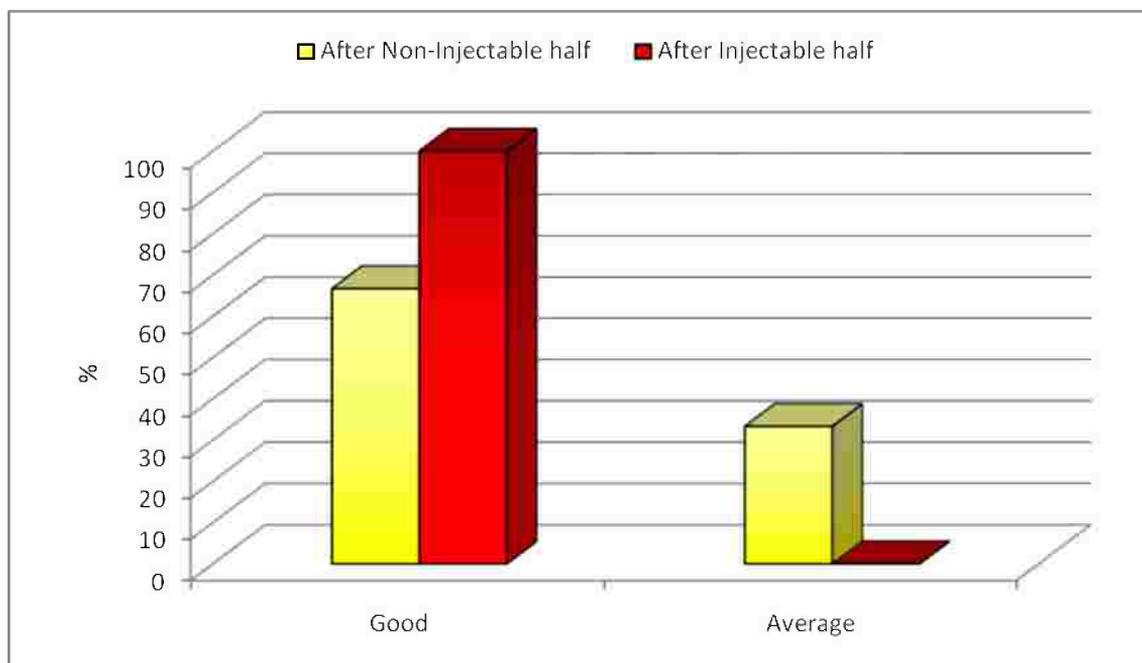


**Figure (20): Comparison between the injectable and non injectable halves before and after as regard to Vascularity in keloid lesion patients.**

As regard to the response in Extensive Dermal Scar lesion group, in the non-Injectable halves two patients (66.7%) out of the three patients had good results and one patient (33.3%) out of the patients had average result while in the Injectable halves all patients (100%) had good results. (Table 22, Figure 21)

**Table (22): Comparison between the injectable and non-injectable halves as regard to patient’s response in Extensive Dermal Scar lesion patients.**

Response	After Non-Injectable half		After Injectable half	
	No.	%	No.	%
Good	2	66.7	3	100
Average	1	33.3	0	0
Total	3	100	3	100
P Value	0.500			

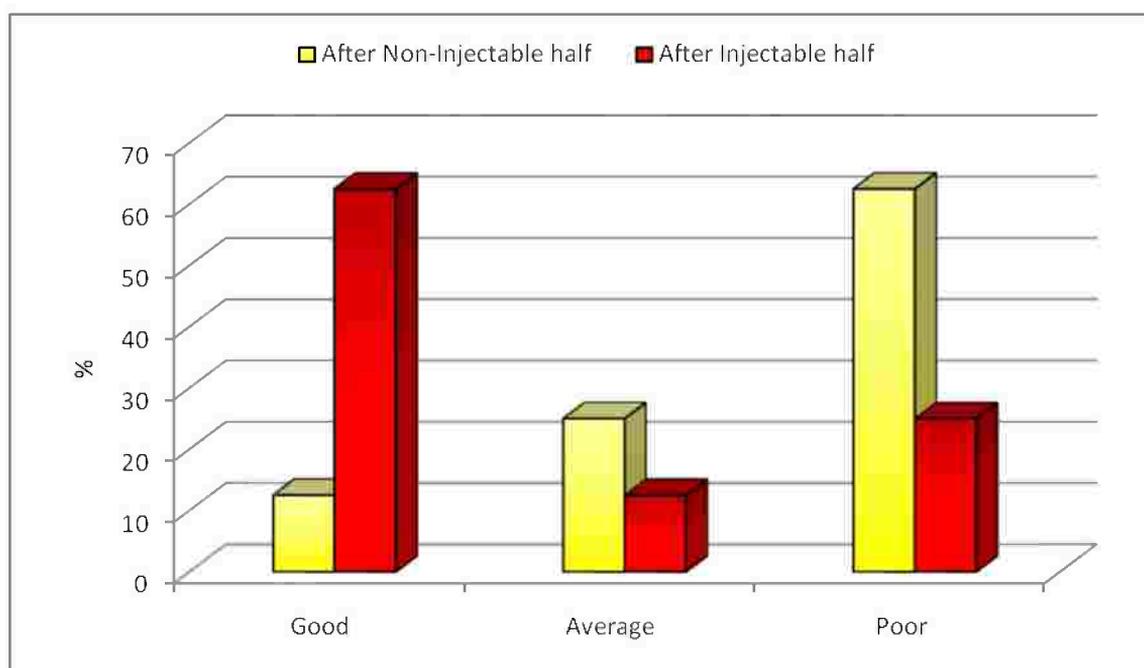


**Figure (21): Comparison between the injectable and non-injectable halves as regard to patient’s response in Extensive Dermal Scar lesion patients.**

As regard to the Response in Hypertrophic Scar lesion group, in the non-Injectable halves one patient (12.5%) out of the eight patients had good result, two patients (25%) out of the patients had average results and five patients (62.5%) out of the patients had poor results while in the Injectable halves five patients (62.5%) out of the patients had good results , one patient (12.5%) out of the patients had average result and two patients (25%) out of the patients had poor results. (Table 23, Figure 22)

**Table (23): Comparison between the injectable and non-injectable halves as regard to patient’s response in Hypertrophic Scar lesion patients.**

Response	After Non-Injectable half		After Injectable half	
	No.	%	No.	%
Good	1	12.5	5	62.5
Average	2	25	1	12.5
Poor	5	62.5	2	25
Total	8	100	8	100
P Value	0.117			

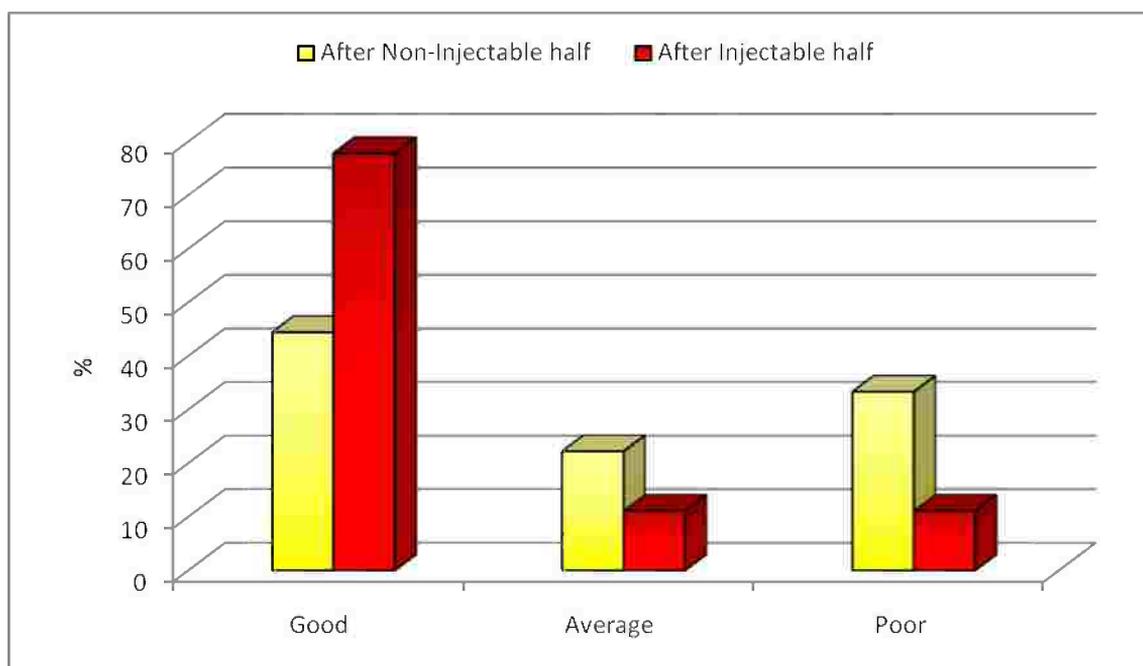


**Figure (22): Comparison between the injectable and non-injectable halves as regard to patient’s response in Hypertrophic Scar lesion patients.**

As regard to the Response in keloid lesion group, in the non-Injectable halves four patients (44.4%) out of the patients had good results, two patients (22.2%) out of the patients had average results and three patients (33.3%) out of the patients had poor results while in the Injectable halves seven patients (77.8%) out of the patients had good results , one patient (11.1%) out of the patients had average result and one patient (11.1%) out of the patients had poor result. (Table 24, Figure 23)

**Table (24): Comparison between the injectable and non-injectable halves as regard to patient’s response in keloid lesion patients.**

Response	After Non-Injectable half		After Injectable half	
	No.	%	No.	%
Good	4	44.4	7	77.8
Average	2	22.2	1	11.1
Poor	3	33.3	1	11.1
Total	9	100	9	100
P Value	0.341			

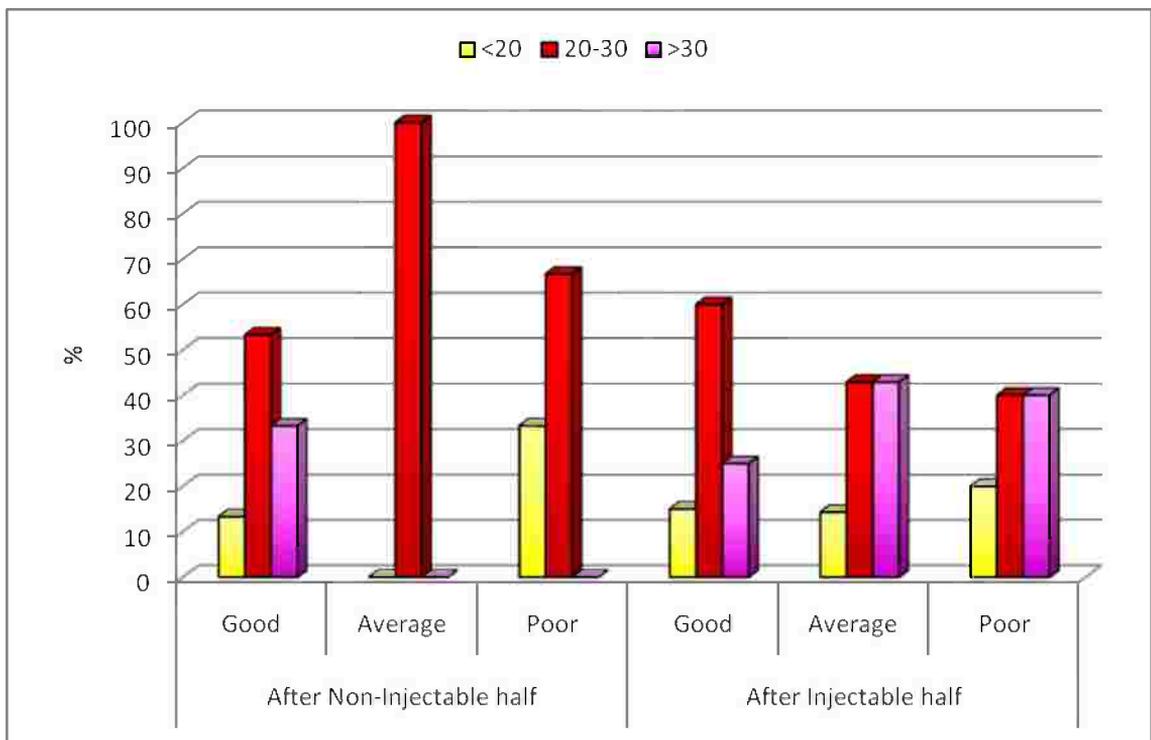


**Figure (23): Comparison between the injectable and non-injectable halves as regard to patient’s response in keloid lesion patients.**

As regard to results according to patients ages, after treatment in injectable halves the patients with good results show that two patients (13.3%) out of the fifteen patients their ages were less than 20 years, eight patients (53.3%) out of the patients their age were from 20 years to 30 years and five patients (33.3%) out of the patients their ages were over 30 years; the patients with average results show that two patients (100%) out of the patients their ages were from 20 years to 30 years and the patients with poor results show that one patient (33.3%) out of the three patients his age was less than 20 years and two patients (66.7%) out of the patients their ages were from 20 years to 30 years while after treatment in non injectable halves the patients with good results show that one patient(13%) out of the eight patients his age was less than 20 years, and six patients (87%) out of the patients their ages were from 20 years to 30 years; the patients with average results show that one patient (20%) out of the five patients his age was less than 20 years, two patients (40%) out of the patients their ages were from 20 years to 30 years and two patients (40%) out of the patients their ages were over 30 years and the patients with poor results show that one patient (12.5%) out of the eight patients his age was less than 20 years, four patients (50%) out of the patients their age ranged from 20 years to 30 years and three patients (37.5%) out of the patients their ages was over 30 years. (Table 25, Figure 24)

**Table (25): Comparison between patients response as regard to patient’s age.**

Age	After treatment in injectable halves						After treatment in non Injectable halves					
	Good		Average		Poor		Good		Average		Poor	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
<20	2	13.3	0	0	1	33.3	1	13	1	20	1	12.5
20-30	8	53.3	2	100	2	66.7	6	87	2	40	4	50
>30	5	33.3	0	0	0	0	0	0	2	40	3	37.5
<b>Total</b>	15	100	2	100	3	100	7	100	5	100	8	100

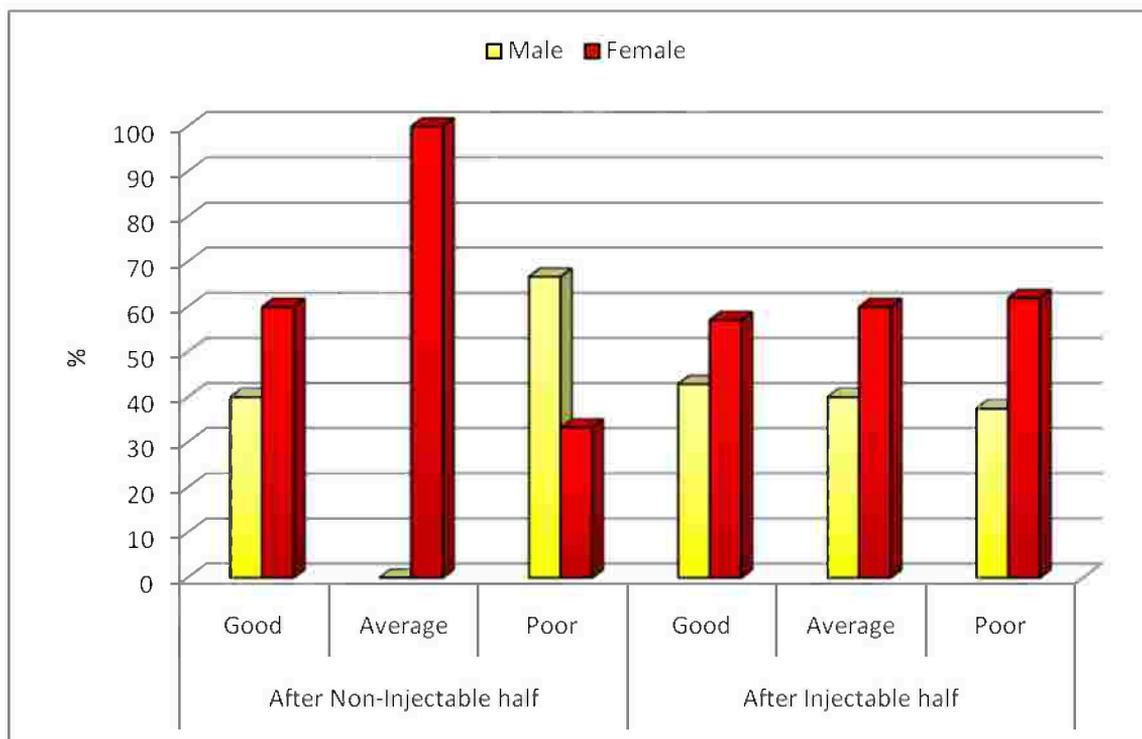


**Figure (24):** Comparison between patients response as regard to patient's age.

As regard to patients results according to patients sex, after treatment in injectable halves the patients with good results show that six patients (40%) out of the fifteen patients were males and nine patients (60%) out of the patients were females; the patients with average results show that two patients (100%) out of the patients were females and the patients with poor results show that two patients (66.7%) out of the three patients were males and one patient (33.3%) out of the patients was female while after treatment in non injectable halves the patients with good results show that three patients (42.9%) out of the seven patients were males and four patients (57.1%) out of the patients were females; the patients with average results show that two patients (40%) out of the five patients were males and three patients (60%) out of the patients were females and the patients with poor results show that three patients (37.5%) out of the eight patients were males and five patients (62%) out of the patients were females. (Table (26), figure (25))

**Table (26): Comparison between patients response as regard to patient’s sex.**

Gender	After treatment in Injectable halves						After treatment in non Injectable halves					
	Good		Average		Poor		Good		Average		Poor	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Male	6	40	0	0	2	66.7	3	42.9	2	40	3	37.5
Female	9	60	2	100	1	33.3	4	57.1	3	60	5	62
<b>Total</b>	15	100	2	100	3	100	7	100	5	100	8	100

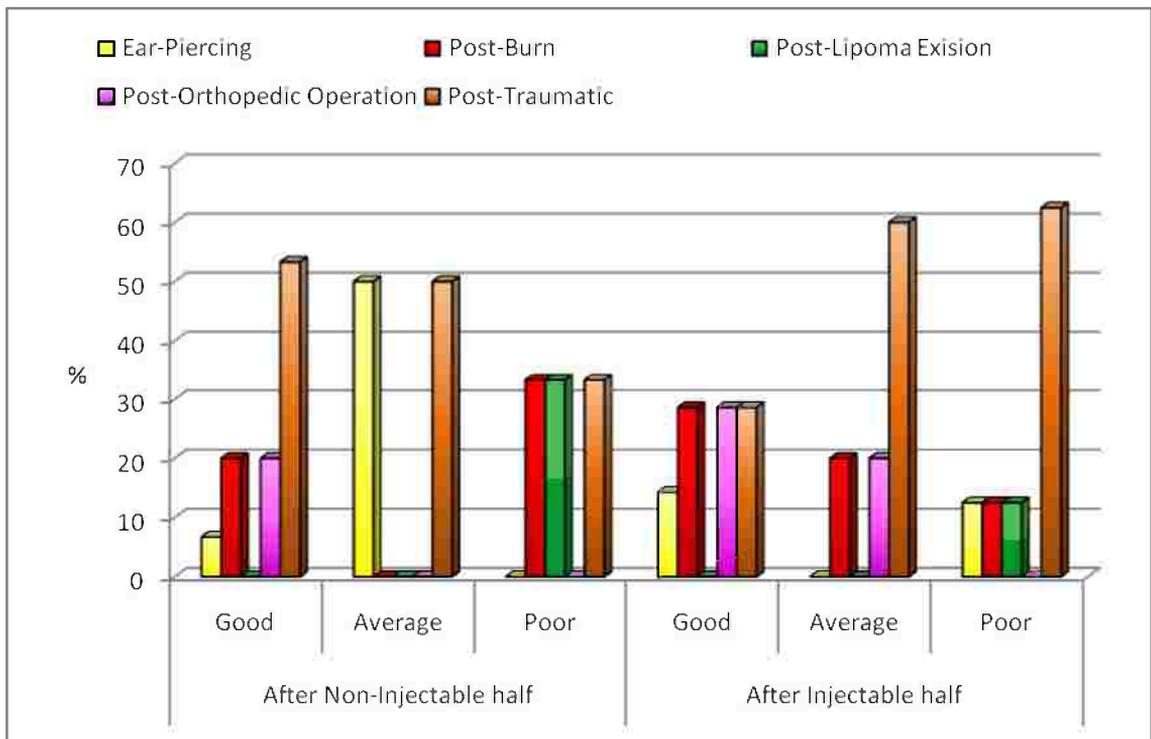


**Figure (25): Comparison between patients response as regard to patient’s sex.**

As regard to cause of lesion in a comparison with patients response, after treatment in injectable halves the patients with good results show that one patient (6.7%) out of the fifteen patients had ear-piercing cause, three patients (20%) out of the patients had post-burn causes, three patients (20%) out of the patients had post-Orthopedic Operations and eight patients (53.3%) out of the patients had post-traumatic causes, the patients with average results show that one patient (50%) out of the two patients had ear-piercing cause and one patient (50%) out of the patients had post-traumatic cause and the patients with poor results show that one patient (33.3) out of the three patients had post-burn cause, one patient (1%) out of the patients had post-lipoma excision cause and one patient (33.3%) out of the patients had post-traumatic cause while after treatment in non injectable halves the patients with good results show that one patient (14.3%) out of the seven patients had ear-piercing cause, two patients (28.6%) out of the patients had post-burn causes, two patients (28.6%) out of the patients had post-Orthopedic Operations and two patients (28.6%) out of the patients had post-traumatic causes, the patients with average results show that one patient (20%) out of the five patients had post-burn, one patient (20%) out of the patients had post-orthopedic operation and three patients (60%) out of the patients had post-traumatic cause and the patients with poor results show that one patient (12.5%) out of the eight patients had ear-piercing cause, one patient (12.5) out of the patients had post-burn cause, one patient (12.5%) out of the patients had post-lipoma excision cause and five patients (62.5%) out of the patients had post-traumatic causes.(Table 27, Figure 26)

**Table (27): Comparison between patients response as regard to patient’s causes of lesions**

Cause	After treatment in Injectable halves						After treatment in non Injectable halves					
	Good		Average		Poor		Good		Average		Poor	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
<b>Ear-Piercing</b>	1	6.7	1	50	0	0	1	14.3	0	0	1	12.5
<b>Post-Burn</b>	3	20	0	0	1	33.3	2	28.6	1	20	1	12.5
<b>Post-Lipoma Exision</b>	0	0	0	0	1	33.3	0	0	0	0	1	12.5
<b>Post-Orthopedic Operation</b>	3	20	0	0	0	0	2	28.6	1	20	0	0
<b>Post-Traumatic</b>	8	53.3	1	50	1	33.3	2	28.6	3	60	5	62.5
<b>Total</b>	15	100	2	100	3	100	7	100	5	100	8	100

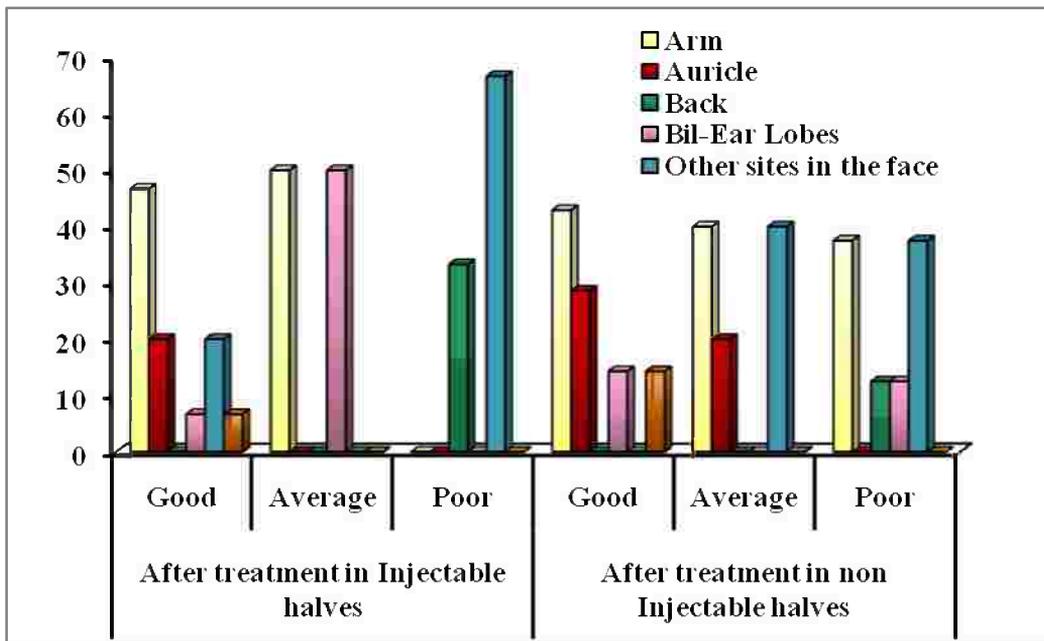


**Figure (26):** Comparison between patients response as regard to patient's causes of lesions.

As regard to lesion site in a comparison with patients results, after treatment in injectable halves the patients with good results show that seven patients (46.7%) out of the fifteen patients had lesions in arms, three patient (20%) out of the patients had lesions in auricles, one patient (6.7%) out of the patients had lesion in bilateral-ear lobes, three patients (20%) out of the patients had lesions in different sites of the face and one patient (6.7%) out of the patients had lesion in foot, the patients with average results show that one patient (50%) out of the two patients had lesion in arm and one patient (50%) out of the patients had lesion in bilateral-ear lobes and the patients with poor results show that one patient (33.3%) out of the three patients had lesion in the back of the shoulder and two patients (66.7%) out of the patients had lesions in different sites of the face while after treatment in non injectable halves the patients with good results show that three patients (42.9%) out of the seven patients had lesions in arms, two patients (28.6%) out of the patients had lesions in auricles, one patient (14.3%) out of the patients had lesion in bilateral-ear lobes and one patient (14.3%) out of the patients had lesion in foot, the patients with average results show that two patients (40%) out of the five patients had lesions in arms, one patient (20%) out of the patients had lesion in auricle and two patients (40%) out of the patients had lesions in different sites of the face and the patients with poor results show that three patients (37.5%) out of the eight patients had lesions in arms, one patient (12.5%) out of the patients had lesion in the back of the shoulder, one patient (12.5%) out of the patients had lesion in bilateral-ear lobes and three patients (37.5%) out of the patients had lesions in different sites of the face. (Table 28, Figure 27)

**Table (28): Comparison between patients response as regard to patient’s lesions sites.**

Site	After treatment in Injectable halves						After treatment in non Injectable halves					
	Good		Average		Poor		Good		Average		Poor	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Arm	7	46.7	1	50	0	0	3	42.9	2	40	3	37.5
Auricle	3	20	0	0	0	0	2	28.6	1	20	0	0
Back	0	0	0	0	1	33.3	0	0	0	0	1	12.5
Bil-Ear Lobes	1	6.7	1	50	0	0	1	14.3	0	0	1	12.5
Other sites in the face	3	20	0	0	2	66.7	0	0	2	40	3	37.5
Foot	1	6.7	0	0	0	0	1	14.3	0	0	0	0
<b>Total</b>	15	100	2	100	3	100	7	100	5	100	8	100



**Figure (27):** Comparison between patients response as regard to patient’s lesions sites.

## **Before injection of 5 fluorouracil**

The present work comprised 10 cases of abnormal scars subjected for histopathologic examination. The cases include four keloid, four hypertrophic scars and 2 extensive scars.

Keloid: H&E stain revealed scar tissue with thick broad glassy eosinophilic hyalinized collagen bundles arranged haphazardly. Few fibroblasts are noted. (Figure 28, 29). Numerous newly formed blood vessels are also seen in the dermis.

Hypertrophic scar: the examined cases exhibited whorls and nodules of fibrillary collagen with fairly regular thickness. The collagen fibrils are cigar shaped, and run parallel to the surface of the skin. Fibroblasts are more seen than in keloid. (Fig 30, 31, 32)

Masson trichrome stain was used to highlight the arrangement of the collagen. (Figure 33)

Extensive scar showed broad scar tissue made of collagen fibers parallel to the epidermis. Neither keloid collagen nor nodular collagen is noted.

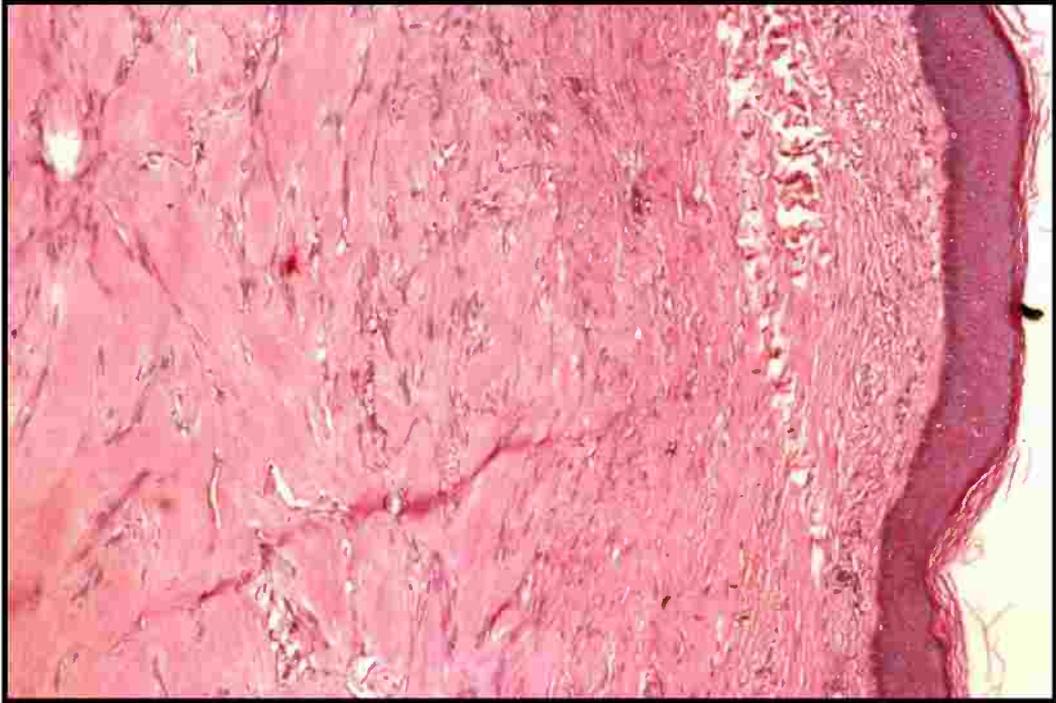
## **After injection of % fluorouracil**

Keloid cases showed decreased thickness of the scar, decreased size of collagen bundles, fragmentation and fraying of the collagen fibers as shown by H&E stain. (Figure 34, 35).

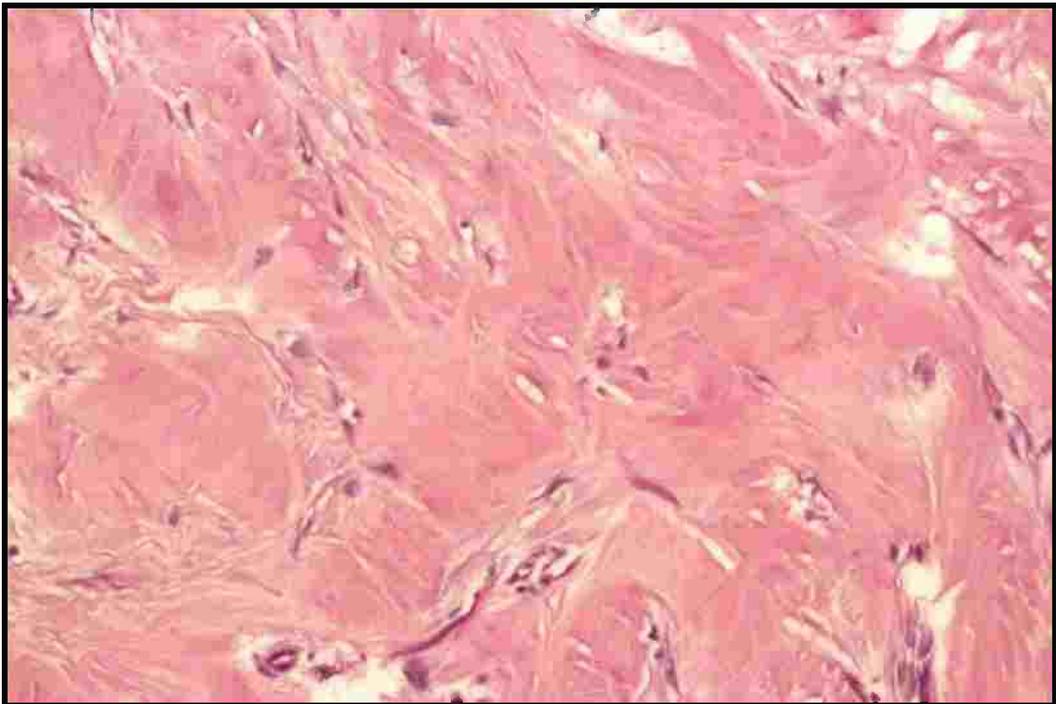
Vascularity is remarkably diminished after treatment as shown in (Figure 34, 36, 37, 38 and 39).

No remarkable difference is noted between non-injectable and injectable cases in extensive scar.

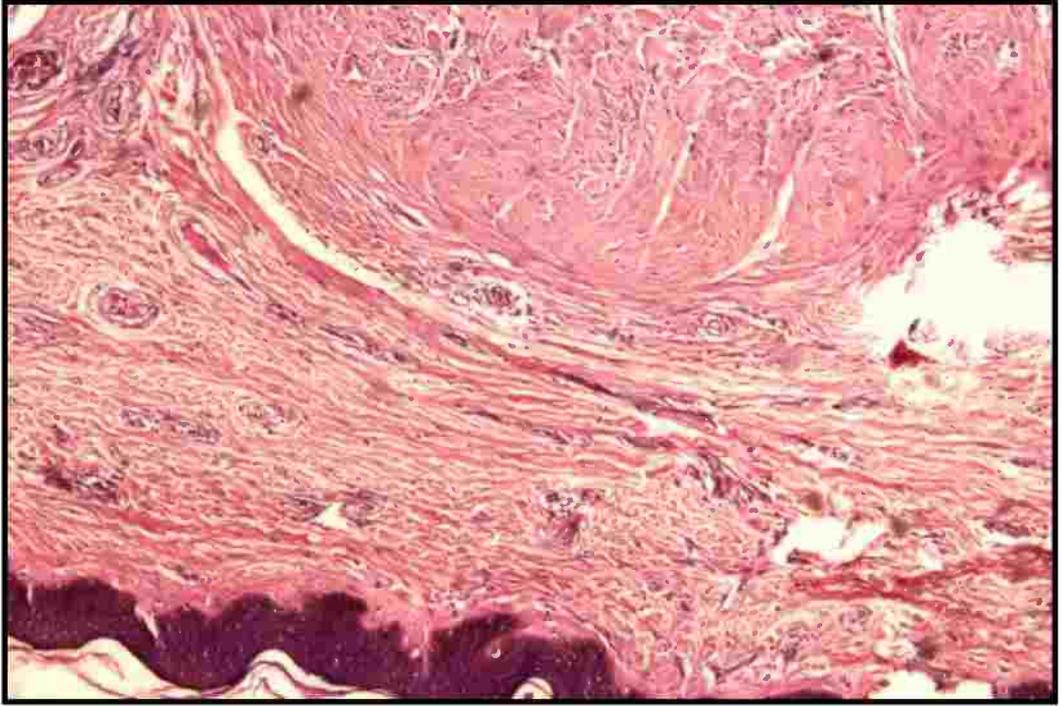
Immunohistochemical stain for Ki67 (a proliferating marker) showed mild positivity in the fibroblasts of keloid and hypertrophic scar before injection of 5 fluorouracil and absent staining after injection. (Figure 40, 41).



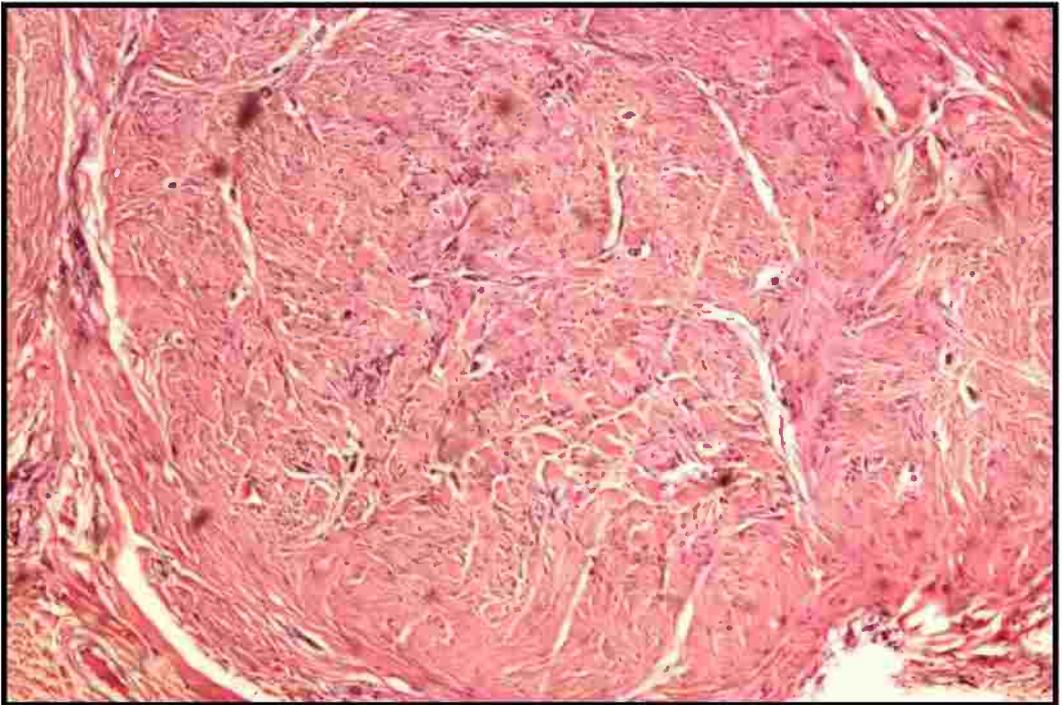
**Figure (28):** A case of keloid showing bundles of hyalinized collagen arranged haphazardly. (H&E stain x100).



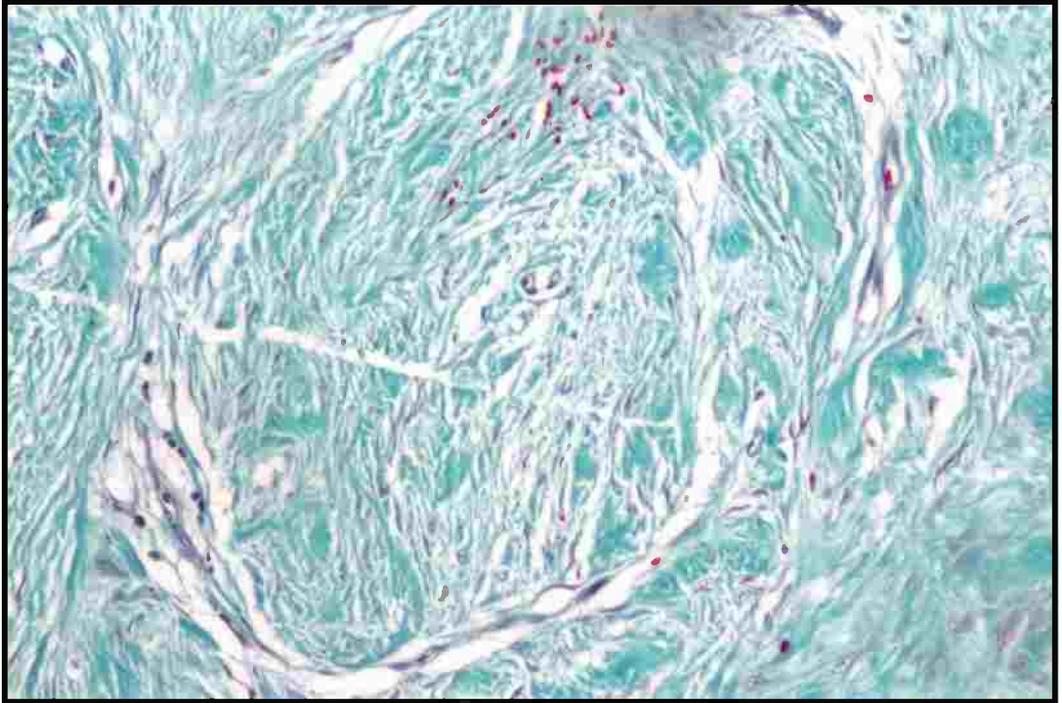
**Figure (29):** High power view of the previous case showing the broad glassy eosinophilic collagen (keloid Collagen), few fibroblasts H&E x200.



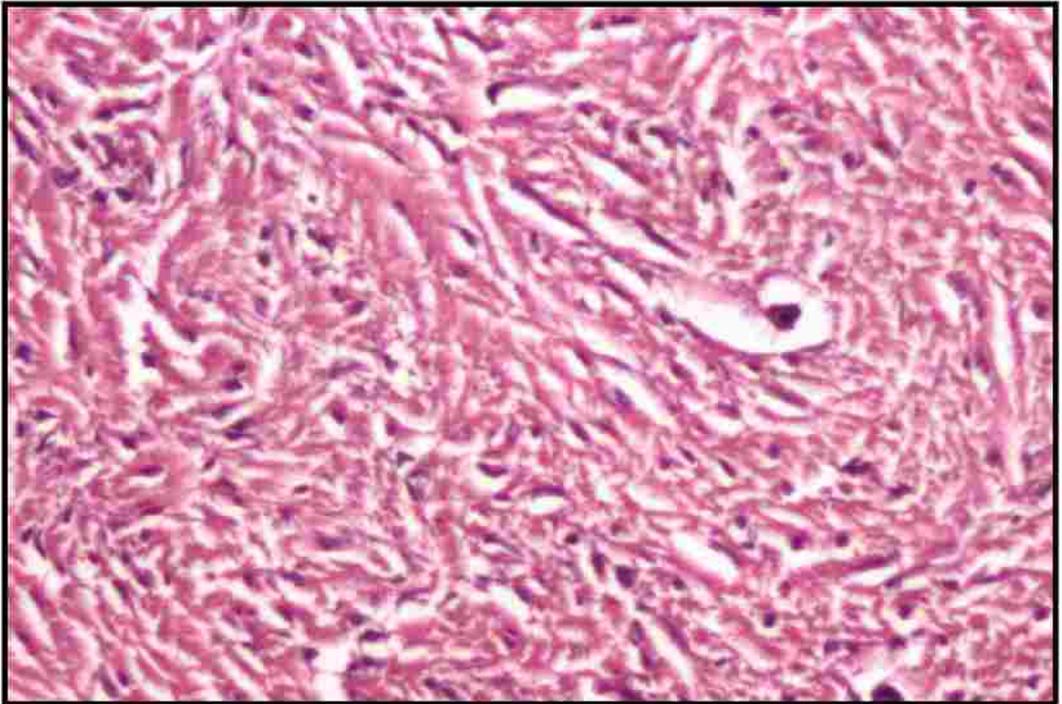
**Figure (30):** A case of hypertrophic scar exhibiting nodules of fibrillary collagen. H&E x100.



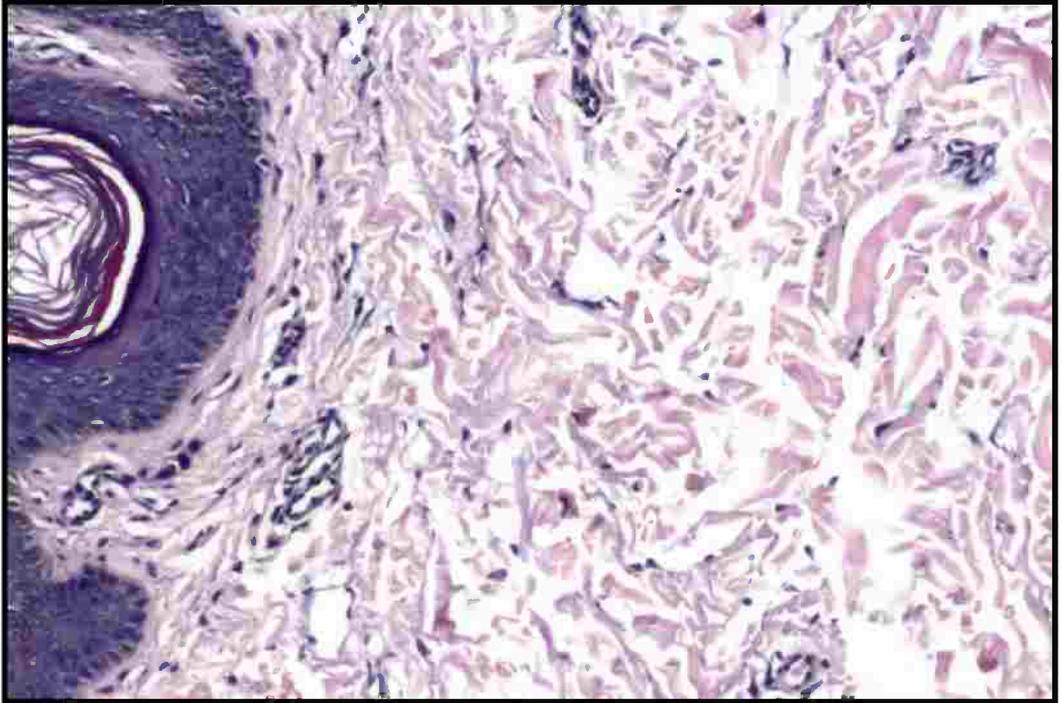
**Figure (31):** Another view of the previous case showing whorls of collagen with regular thickness. H&E stain x100.



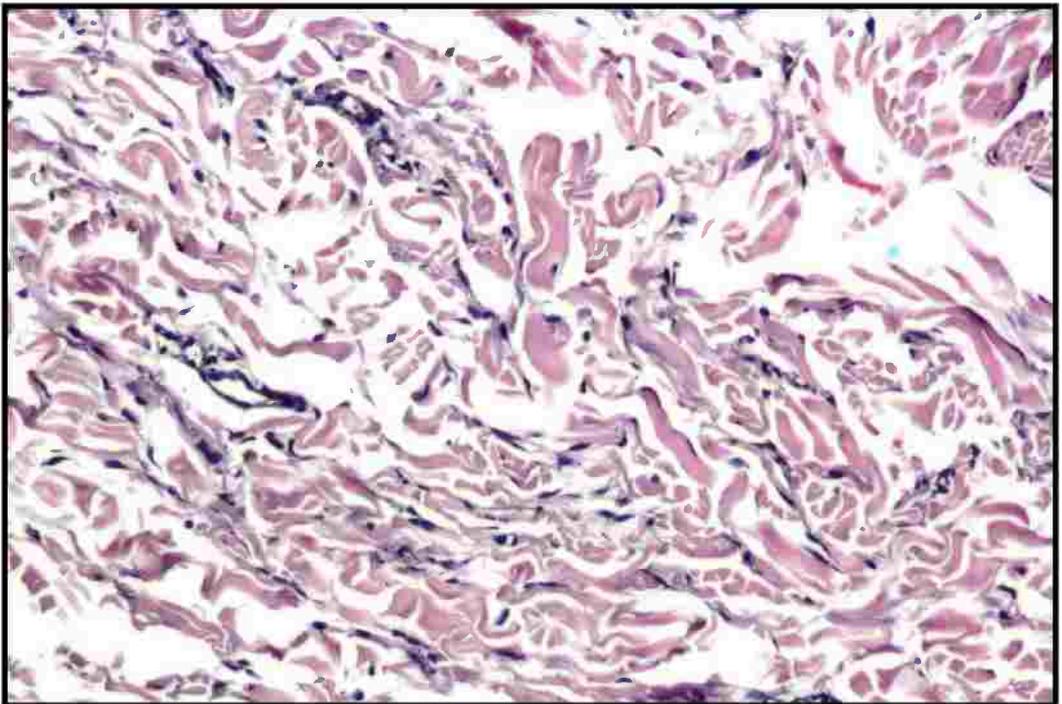
**Figure (32):** Masson trichrome stain of the previous case to highlight the whorls of collagen. X200.



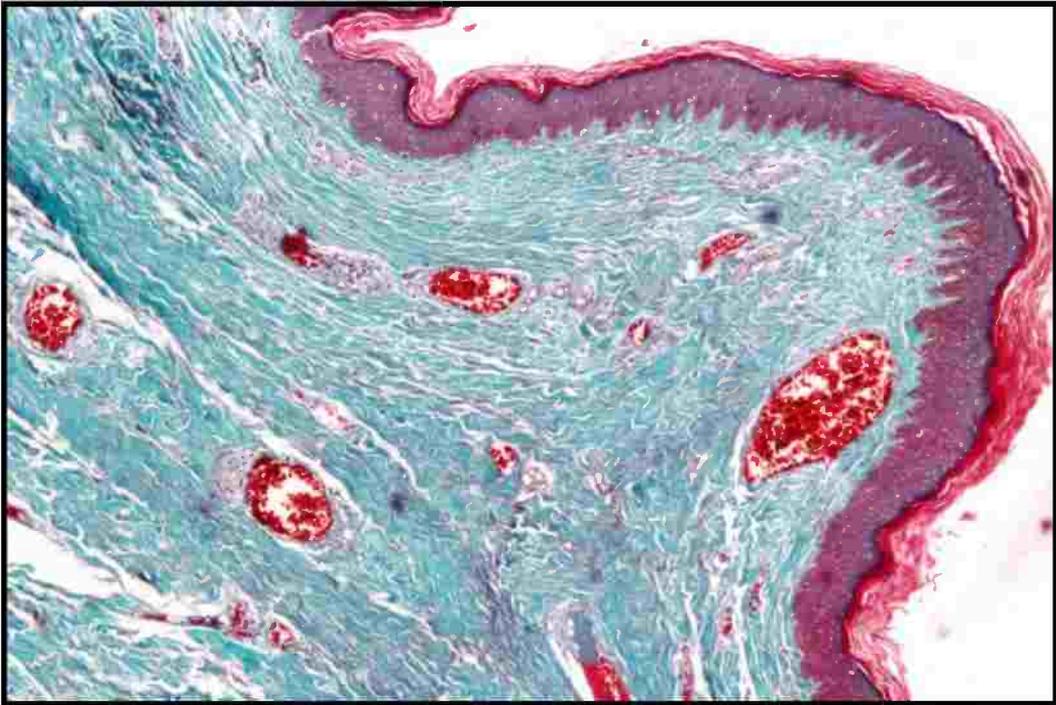
**Figure (33):** A closer view of the previous case showing numerous fibroblasts. H&Ex200.



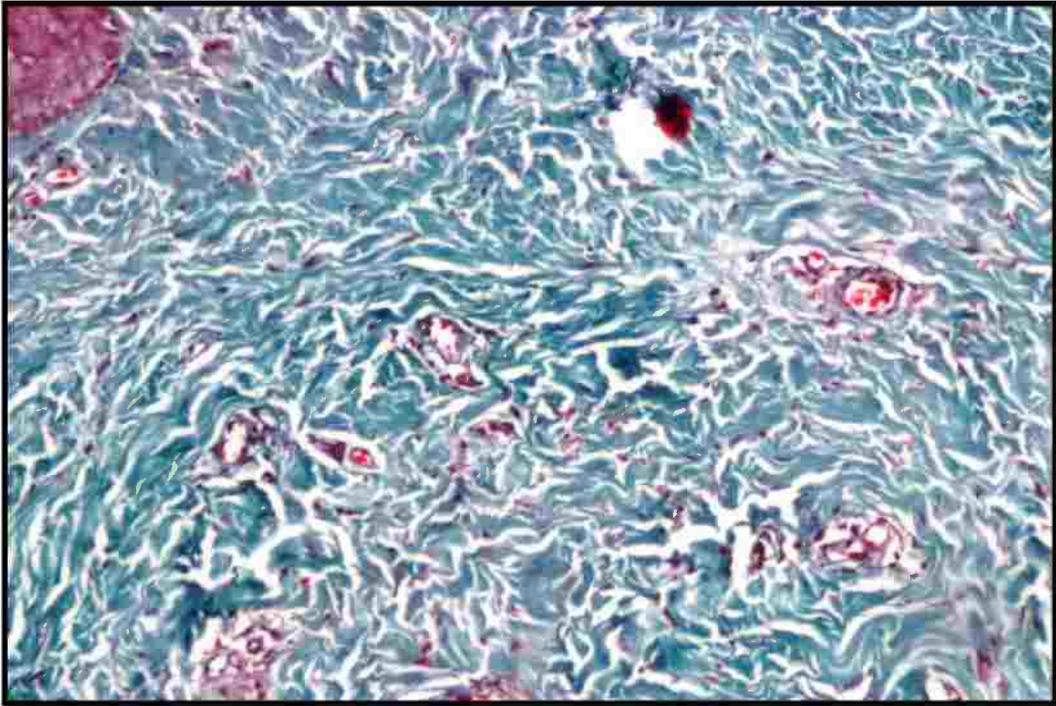
**Figure (34):** Case of keloid after injection of 5 fluorouracil. Notice the fragmentation of the collagen fibers. H&E x100.



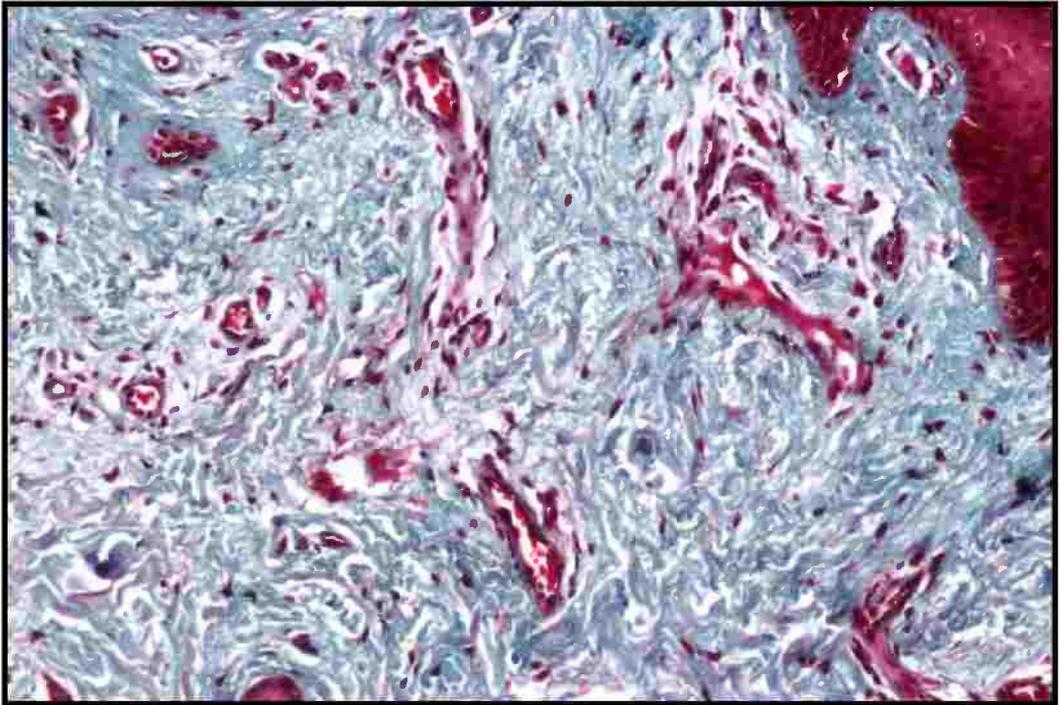
**Figure (35):** Another view for keloid after injection. H&E x100.



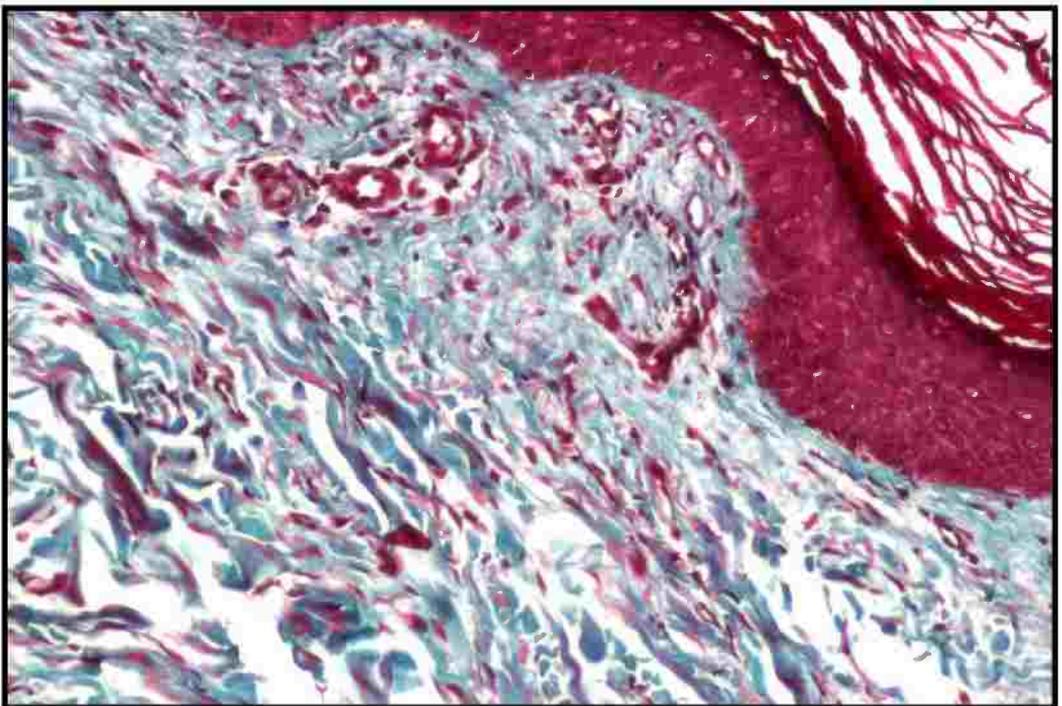
**Figure (36):** A case of keloid showing marked vascularity of the lesion before treatment. Masson trichrome stainx100.



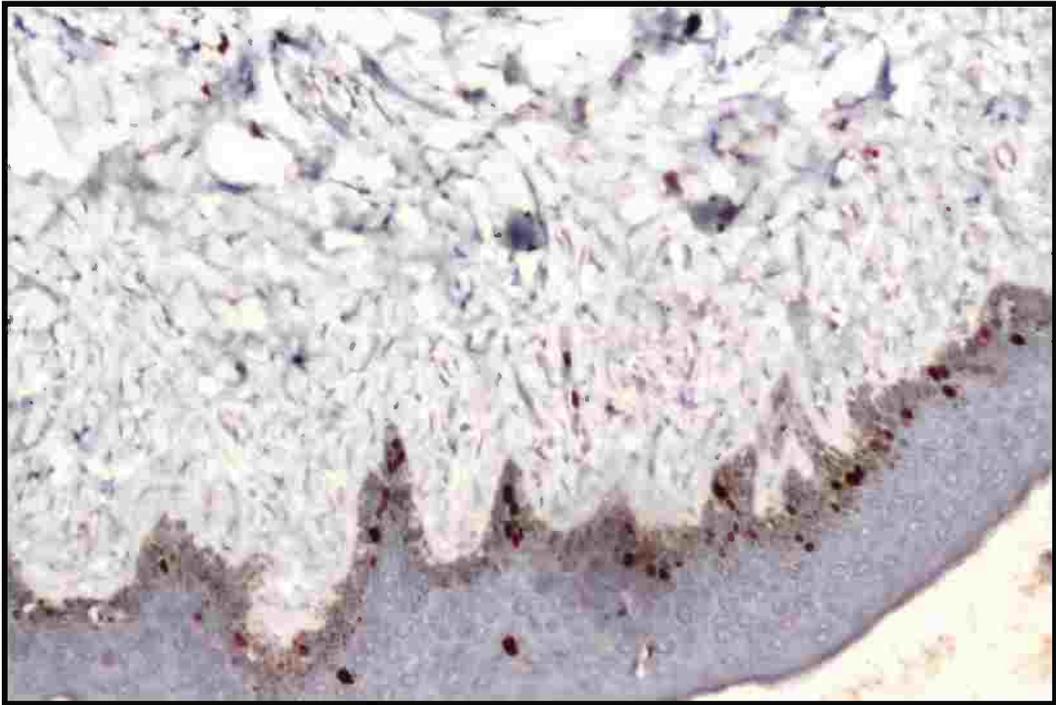
**Figure (37):** The same case after injection of 5 fluorouracil. Notice the decreased vascularity.masson trichrome stain. X100.



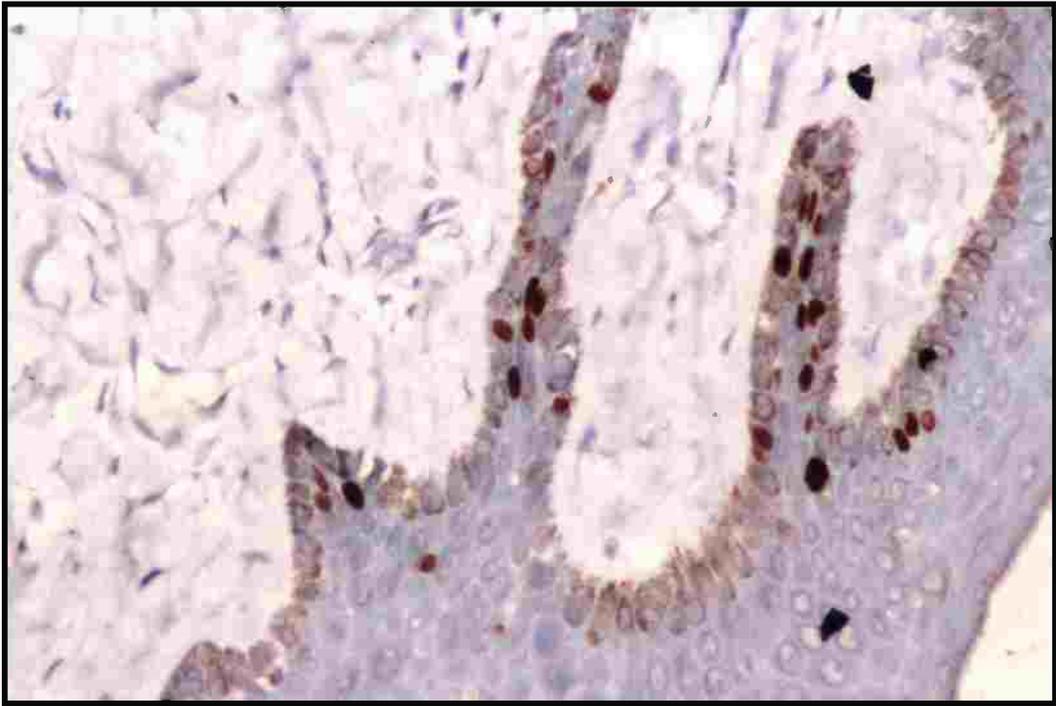
**Figure (38):** A case of hypertrophic scar exhibiting marked vascularity. Masson trichrome x200.



**Figure (39):** The same case after injection showing decreased vascularity. Masson trichrome x200.



**Figure (40):** Immunohistochemical staining from Ki67 antibody showing proliferation of basal layer of epidermis and few dermal fibroblasts. X200.



**Figure (41):** Immunohistochemical staining for ki67 of the same case after injection showing absent staining of fibroblasts for ki67.x400.



**Figure (42a):** A case of post auricular keloid



**Figure (42b):** After healing of wound.



**Figure (42c):** Show good result in upper half (injectable half) and bad result in lower half (non injectable half) after one year.



**Figure (43a):** A case of keloid in the back of the shoulder.



**Figure (43b):** After surgical excision.



**Figure (43c):** Show bad results in both halves after 10 months.



**Figure (44a):** A case keloid in the foot.



**Figure (44b):** Show good results in both halves after 6 months.



**Figure (45a):** A case of hypertrophic scar in the face



**Figure (45b):** After surgical excision.



**Figure (45c):** Show good result in injectable half and bad result in Non-injectable half after 1 year.



**Figure (46a):** A case of extensive dermal scar in the arm.



**Figure (46b):** Show diagram of lesion before excision.



**Figure (46c):** After surgical excision.



**Figure (46d):** Show good result in injectable half (upper half) and average result in non-injectable half (lower half) after 10 months.



**Figure (47a):** A Case of hypertrophic scar in the face and the neck.



**Figure (47b):** After surgical excision.



**Figure (47c):** Show good result injectable half toward mandible and bad result in non injectable half after 10 months