

East African Medical Journal Vol. 96 No. 1 January 2019

DETERMINATION OF THE PREVALENCE, CLINICAL CHARACTERISTICS AND HISTOPATHOLOGICAL FEATURES OF KELOIDS IN PATIENTS MANAGED AT THE KENYATTA NATIONAL HOSPITAL

Mahad Mohamud Ali, General Surgery resident, Department of Surgery, School of Medicine, University of Nairobi, P. O. Box 19676 – 00202, Nairobi, Faith Wanjiru Karanja, Consultant Plastic and Reconstructive Surgeon, Tutorial fellow, Department of Surgery, School of Medicine, University of Nairobi, P. O. Box 19676 – 00202, Nairobi, Ferdinand Wanjala Nang'ole, Consultant Plastic and Reconstructive Surgeon, Lecturer, Department of Surgery, School of Medicine, University of Nairobi, P. O. Box 19676 – 00202, Nairobi, Elly Oluoch Nyaim Opot, Consultant General Surgeon, Senior lecturer, Department of Surgery, School of Medicine, University of Nairobi, P. O. Box 19676 – 00202, Nairobi, Kennedy Ondede Mulehane, Consultant General and Hepatobiliary Surgeon, Department of Surgery, Kenyatta National Hospital, P. O. Box 20723 – 00202, Nairobi, Daniel Zuriel Mbithi, Consultant Pathologist, Lecturer, Department of Pathology, School of Medicine, University of Nairobi, P. O. Box 19676 – 00202, Nairobi.

Corresponding author: Faith Wanjiru Karanja, Consultant Plastic and Reconstructive Surgeon, Tutorial Fellow, Department of Surgery, School of Medicine, University of Nairobi, P. O. Box 19676 – 00202, Nairobi. Email: wanjiru.faith@uonbi.ac.ke, faithshiru@gmail.com.

DETERMINATION OF THE PREVALENCE, CLINICAL CHARACTERISTICS AND HISTOPATHOLOGICAL FEATURES OF KELOIDS IN PATIENTS MANAGED AT THE KENYATTA NATIONAL HOSPITAL

M. M. Ali, F. W. Karanja, F. W. Nang'ole, E. O. N. Opot, K. O. Mulehane and D. Z. Mbithi

ABSTRACT

Objectives Assess prevalence and clinical presentation, describe histopathology and determine association of clinical presentation with histopathological findings of keloids.

Design Cross-sectional study conducted over two months.

Setting Plastic surgery outpatient clinic at the Kenyatta National Hospital.

Subjects Patients undergoing keloid treatment.

Interventions Obtained clinical history based on a calibrated protocol and pain and pruritus scores based on a visual analog scale. Using numbers ranging from zero being no symptoms, to ten being unbearable symptoms of either pain or pruritus and registered as per the questionnaire. Excisional biopsy was performed, and specimen submitted to Kenyatta National Hospital histopathology department.

Main outcome measures Demographics: age, sex, religion, economic status; Presentation: pain, pruritus, location: parasternal, earlobe; and Histology: predominant cellularity: neutrophils, mast cells, macrophages, fibroblast density.

Results Most patients presented with a solitary keloid, trauma was a major trigger factor, with oval as the commonest shape, regular margins. Histologically mast

cells and lymphocytes were the majority of cells seen and a high keloid collagen. On correlation of clinical presentation with the histopathological findings of the keloids; we found a strong association between pain, pruritus and mast cells abundancy.

Conclusion Current approaches to keloid management are based on an algorithm including surgical excision, intralesional steroids, cryotherapy, laser removal, radiotherapy, occlusive dressings, and immunomodulators. From our findings, there could be further role of mast cell stabilizers or leukotriene receptor antagonist such as montelukast. We recommend that further studies be carried out on keloid immunocytochemistry and cytogenetics in correlation with clinical findings to support keloid management.

INTRODUCTION

A keloid is an enlargement of solid gristly tissue covering beyond the margins of the unusual injury. This can be due to unrestrained synthesis and deposition of dermal collagen. Keloids are generally described as either firm, raised, painful or pruritic and they don't regress spontaneously. Certain inflammatory skin disorder like lacerations, burns, tattoos, injections, surgery and local skin trauma may lead to keloids.

There is complex response to skin trauma in wound healing. Excessive formation of scar tissue may be due to deregulation of this process. Generally, keloids are not easy to treat with recorded high recurrence rate even with various modes of therapy. There are various treatments options widely used that include the use of intraregional corticosteroids, surgery, and topical applications, while radiation therapy is used for cases of recalcitrant keloids, recent developments have successfully used pulsed-dye laser to treat keloids. Treatment usually is individualized which is mostly dependent on the division, thickness, size, and steadiness of the lesions and alliance of inflammation, but mostly amalgamation advance to therapy is usually the best option.

There has been documentation of keloids in virtually all major ethnic groups, but majority of individuals are from African and Asian descent and to some extent to the Hispanic and Mediterranean decent. Individuals with dark skin are 15 times more likely to form keloids than their lighter-skinned counterparts ^[1]. Amongst the black and Hispanic populations, there has been a reported incidence as high as 16% of keloid formation, with highest frequencies observed during pregnancy and puberty ^[2]. Keloids affect the female population more than male counterpart partly due to ear piercing ^[3], though it affects both sexes equally. Keloids are mostly seen between the second and third decade ^[4], but they can also occur at any given age but are rarely found in new-borns or elderly persons.

A genetic component of the disease may explain the higher risk of keloid formation in some familial groups, as there have been documented as cases which may be due to autosomal dominance prototype of heritage with partial penetrance and variable appearance ^[5]. In one large familial study, chromosomes 6, 7 has been noted to predispose patients to keloid, and it was noted that patients with mutations of the loci may developed keloids ^[6], but it was however noted also that some cases were noted to be

sporadic and not necessarily due to inheritance patterns, and that it is unlikely that any single gene may play a role in majority of the keloids. Another study done at the KNH by Mwika also revealed that 22% of patients had a family narration and only 4 (8%) patients had developed keloids secondary to BCG immunization [7].

The incidence of keloids among the Kenyan population is not well documented but it accounts for a significant percentage of patients seen at plastic surgery outpatient clinic and cases seen at minor theatre at the KNH. Keloids accounted for 59% (2,489 out of 4218) cases seen at the KNH minor theatre from January 2010 to December 2014 according to its theatre register. In the 5-year period, an average of 14.6% of all excisions done was due to keloids and intralesional triamcinolone injections accounted for 44.8% of all cases done at the minor theatre. Keloids are difficult to treat as there are no set guidelines. An increase in awareness of keloid formation and further research, future targeted approaches shall progress keloid management.

MATERIALS AND METHODS

The study was approved by the KNH and University of Nairobi (UoN) Ethics Committee; P777/11/2018. Fifty-one patients presenting with keloids to the Kenyatta National Hospital (KNH) plastic surgical outpatient clinic (SOPC), in the month of December 2018 and January 2019, who met the inclusion criteria were enrolled for the study consecutively.

Data collected included patient demographics: age, sex, religion, economic status; clinical presentation: pain, pruritus, site of location: parasternal, earlobe; and histological type: predominant cellularity:

neutrophils, mast cells, macrophages, fibroblast density.

All patients were counselled about the study design and given the option to enrol, after which they provided consent to participate in the study. Inclusion criteria: Patients undergoing follow up for management of keloids at the KNH Plastic SOPC, who have consented were included in the study. Exclusion criteria: Patients who declined to consent for the study and patients with keloids who were not candidates for surgery but required other modes of treatment were excluded.

Data analysis was done with the use of Statistical Package for Social Sciences Software (Version 21.0, Chicago-Illinois). Associations amongst clinical findings were done with the Chi-square test, and a P value < 0.05 was considered vital.

RESULTS

The demographic characteristics show that out of the 51 patients, 33 (64.7%) were female, while 18 (35.5%) were male. The mean age of the participants was 26.3 (12.9) years, while the modal age 22 years.

Majority of the patients had one keloid which was seen in 26 (51.0%) patients, followed by 2 keloids seen in 20 (39.2%) patients. The commonest trigger factor was trauma, in 40 (78.4%) of our patients. 22 (43.1%) patients had their keloids for a duration of two years. Only 13 (25.5%) of the patients mentioned that their keloid was recurrent. As for previous treatment, only 10 (19.6%) had undergone prior treatment. Three (5.9%) patients had a family history of keloids. Most of the patients had no previous treatment 41 (80.4%), while the highest number of treatment mentioned was three in six (11.8%) patients, followed by two in two

(3.9%) patients, and lastly one treatment from one (2.0%) patient, table 1.

Table 1
Clinical Presentation

Number of Keloids	n (%)
1	26 (51.0)
2	20 (39.2)
3	2 (3.9)
5	2 (3.9)
6	1 (2.0)
Etiology/Trigger factors	
Infection	2 (3.9)
Trauma	40 (78.4)
Unknown	9 (17.6)
Duration of keloids (years)	
1	11 (21.6)
2	22 (43.1)
3	8 (15.7)
4	4 (7.8)
5	2 (3.9)
6	1 (2.0)
10	2 (3.9)
36	1 (2.0)
Recurrent/Previous history	
Yes	13 (25.5)
No	38 (74.5)
Previous treatment	
Yes	10 (19.6)
No	41 (80.4)
Family history	
Yes	3 (5.9)
No	48 (94.1)
Number of treatments	
None	42 (82.4)
One	1 (2.0)
Two	2 (3.9)
Three	6 (11.8)

Only 10 (19.6%) of the patients had an oval, in 39 (76.5%) patients. 39 (76.5%) infection. The commonest keloid shape was patients had regular margins, while 12

(23.5%) had irregular margins. Lymphocytes were seen in 43 (84.3%) patients, and 48 (94.1%) had mast cells present. Fibroblast were low in 37 (72.5%) patients, while neovascularization was seen in 48 (94.1%). Keloid consistency was rubbery in 28 (54.9%) patients, followed by a hard consistency in 15 (29.4%) patients, table 2.

Table 2
Patterns of Clinical Presentation

Infected	n (%)
Yes	10 (19.6)
No	41 (80.4)
Shape	
Oval	39 (76.5)
Oblong	8 (15.7)
Claw like	4 (7.8)
Margins	
Regular	39 (76.5)
Irregular	12 (23.5)
Lymphocytes	
Present	43 (84.3)
Absent	8 (15.7)
Mast cells	
Present	48 (94.1)
Absent	2 (3.9)
Minimal	1 (2.0)
Fibroblast	
High	2 (3.9)
Low	37 (72.5)
Minimal	1 (2.0)
Moderate	11 (21.6)
Neovascularization	
Present	3 (5.9)
Absent	48 (94.1)
Keloid consistency	
Soft/doughy	8 (15.7)
Rubbery	28 (54.9)
Hard	15 (29.4)

The score on pain, pruritus, tenderness and contracture were obtained from the patient using a VAS and the results are as seen in Table 3.

Table 3*Scores*

Score	Pain	Pruritus	Tender	Contracture
0			1 (2.0)	14 (27.5)
1	21 (41.2)	24 (47.1)	19 (37.3)	18 (35.3)
2	17 (33.3)	12 (23.5)	22 (43.1)	14 (27.5)
3	3 (5.9)	7 (13.7)	5 (9.8)	
4	2 (3.9)	3 (5.9)	2 (3.9)	4 (7.8)
5	4 (7.8)	3 (5.9)	1 (2.0)	1 (2.0)
6	3 (5.9)	1 (2.0)	1 (2.0)	
7		1 (2.0)		
8	1 (2.0)			

Most of the patients scored their pain at one with 21 (41.2%) patients, followed by a score of two by 17 (33.3%) patients. Pruritus had 24 (47.1%) patients giving a score of 1, followed by 12 (23.5%) patients giving it a score of 2. The tenderness score shows that 22 (43.1%) patients noted a score of 2, followed by 19

(37.3%) patients mentioning a score of 1. For contracture 18 (35.3%) patients rated it at 1, followed by 14 (27.5%) patients scoring it at zero and two. Most of the Keloid was caused by ear piercing as reported by 18 (35.3%) patients, followed by trauma reported by 13 (25.5%) patients, table 4.

Table 4*Cause(s) of Keloid*

	Frequency	Percent
Baker cyst	1	2.0
Burns	1	2.0
Contaminated shaving equipment	1	2.0
Dermal fibrosis	1	2.0
Ear piercing	18	35.3
Hair cut at a barber shop	1	2.0
Infection	5	9.8
Irmacnion	1	2.0
Papillomatosis	1	2.0
Post traumatic	1	2.0
Previous burns	1	2.0
Previous excision	1	2.0
Spontaneous	3	5.9
Superficial radiotherapy	1	2.0
Trauma	13	25.5
Traumatic hit	1	2.0

Most of the Keloids were observed on the ear (70.6%) patients. Other sites included the trunk in five (9.8%) patients, groin in four (7.8%) patients, face in three (5.9%) patients, table 5.

Table 5
Keloid Site

	Frequency	Percent of Cases
Arm	1	2.0
Ear	36	70.6
Face	3	5.9
Groin	4	7.8
Knee	1	2.0
Scalp	2	3.9
Shoulder	1	2.0
Sternal	2	3.9
Thigh	2	3.9
Trunk	5	9.8

The commonest size was 4cm in 14 (27.5%) patients, followed by 5cm seen in 13 (25.5%) patients, 3cm and 6cm in nine patients, 2cm in four patients, 8cm and 1cm in one patient each. Histological findings are as presented in table 6 below.

Table 6
Histopathological Findings

Margins	
Regular	13
Irregular	29
Inflammatory cell	
Mast cell	15 (high)
lymphocytes	16 (high)
neutrophils	0
Macrophage	0
Keloid collagen	42
Fibroblast density	7
Neovascularization	5

Only five patients had comorbidities, where 3 (5.9%) had human immunodeficiency virus (HIV), 1 (2.0%) had nodular capillary hyperplasia, while 1 (2.0%) did not specify. 25 (49.0%) patients had blood group O, followed by 13 (25.5%) patients with blood group B, 7

(13.7) patients with blood group A and 6 (11.8) patients with blood group AB. 36 (70.6%) patients were rhesus positive, while 15 (29.4%) patients were rhesus negative.

Results on county of birth of the patients were as follows 22 (43.1%) patients were born in Nairobi County, 4 (7.8%) patients in Kiambu, 3 (5.9%) patients in Nakuru and Meru, 2 (3.9%) Isiolo, Vihiga, Siaya, Murang'a

and Kajiado, 1 (2.0%) patient in Kitui, Kisii, Kisumu, Baringo, Embu, Narok, Kakamega, Machakos and Homabay. Correlation of patterns of clinical presentation with the histopathological findings of the keloids, revealed no significant differences between the patient groups with mild and moderate pain scores, table 7.

Table 7
Inflammatory Cells and Pain Score

	Pain Score		Total	P value
	Mild	Moderate		
<i>Lymphocytes</i>				
High	15 (78.9)	4 (21.1)	19	0.841
Low	23 (88.5)	3 (11.5)	26	0.139
Moderate	3 (50.0)	3 (50.0)	6	0.081
<i>Mast cells</i>				
High	15 (78.9)	4 (21.1)	19	0.841
Low	23 (88.5)	3 (11.5)	26	0.139
Moderate	3 (50.0)	3 (50.0)	6	0.081

There were significant differences between patient groups in the mild pruritus score and moderate pruritus score for the low and moderate lymphocytes and mast cells, table 8.

Table 8
Inflammatory Cells and Pruritus Score

	Pruritus Score		Total	P value
	Mild	Moderate		
<i>Lymphocytes</i>				
High	15 (78.9)	4 (21.1)	19	0.450
Low	25 (96.2)	1 (3.8)	26	0.024
Moderate	3 (50.0)	3 (50.0)	6	0.042
<i>Mast cells</i>				
High	15 (78.9)	4 (21.1)	19	0.450
Low	25 (96.2)	1 (3.8)	26	0.024
Moderate	3 (50.0)	3 (50.0)	6	0.042

DISCUSSION

Our study found that 26 (51.0%) patients presented with a single keloid, and this was consistent with a study conducted by Olabanji, where 40 (52.6%) patients were found to have a solitary keloid lesion [8]. Trauma was a major trigger factor in 40 (78.4%) patients. 22 (43.1%) patients had their keloids for 2 years. Our study showed that the ear was the most affected anatomical site with 36 (70.6%) patients found with keloids on the ear. This is consistent with other studies where it was observed the ear was the most common site for developing keloid scars, as well also the most common site for cases with either single or multiple site scars. Overall as an anatomical site, the ear has the highest number of keloid scars in contrast to the feet and the pubic mound [9]. Pruritus as well as pain were reported by all patients in this study, this is consistent with other studies such as that done by Lee et al [10] where 46% had pruritus and 86% reported that they experienced pain which is similar to this study where it was reported by majority of the patient who rated the pain on a VAS scale to be 1 and 2 respectively from 38 (74.5%) patients.

On patterns of clinical presentation of keloids among our patients, we found that the most presenting shape was oval as seen from 39 (76.5%) patients. 39 (76.5%) patients had regular margins, while 12 (23.5%) had irregular margins. Lymphocytes were seen in 43 (84.3%) patients, also 48 (94.1%) patients had mast cells.

The findings on anatomical region in our study concur with those of Mwika et al who conducted a study at the KNH on the occurrence and management of Keloids in surgical patients, where he found that majority of the keloids (74%) were in the head

and neck region, and trauma was the commonest underlying cause in 43 (86%) of the patients. All patients reported progressive growth and disfigurement from their keloids with pruritus being the second commonest presenting complaint in 72% of the patients [7].

Other significant histopathological findings of keloids among patients in our study, were that keloids demonstrate increased keloid collagen and glycosaminoglycan content with whorls of thickened hyalinized collagen bundles. In contrast, collagen bundle orientation in normal scar tissue is parallel to the epidermis. Keloid tissue has been shown to be more metabolically active and to use more oxygen than normal scar tissue. This leads to a relative state of hypoxia in keloid fibroblasts which is different in comparison to normal scar fibroblast. This high oxygen-consuming potential and low oxygen diffusion may contribute to the pathophysiology of keloid formation. The presence of mast cells and histamine in keloid tissue, especially early in the clinical course, explains the pruritus associated with these lesions. The etiology of keloid pain is unclear, but evidence suggests a small nerve fiber neuropathy affecting the perikeloidal tissue.

CONCLUSION

Majority of our study patients presented with a solitary keloid, and trauma was the major trigger factor. The commonest shape at presentation was oval with most patients having regular margins. Histologically mast cells and lymphocytes were the commonest inflammatory cells seen, and there was high keloid collagen. Finally, on correlation of patterns of clinical presentation with the histopathological findings of the keloids in our study; we came to the conclusion that there was strong association between pain,

pruritus and mast cells abundance which release histamine causing the symptoms.

Current approaches to keloid management are based on an algorithm including surgical excision, intralesional steroids, cryotherapy, laser removal, radiotherapy, compression garments and immunomodulators. From our study findings, there could be further role of mast cell stabilizers or leukotriene receptor antagonist such as montelukast. It is our recommendation that further studies be carried out on keloid immunocytochemistry and cytogenetics in correlation with clinical findings to improve our understanding and management of keloids.

REFERENCES

1. Brissett AE, Sherris DA. Scar contractures, hypertrophic scars, and keloids. *Facial Plast Surg.* 2001; 17: 263–272.
2. Ako'z T, Giderog'lu K, Akan M. Combination of different techniques for the treatment of earlobe keloids. *Aesthetic Plast Surg.* 2002; 26: 184–188.
3. Kelly AP. Medical and surgical therapies for keloids. *Dermatol. Ther.* 2004; 17:212–218.
4. Ramakrishnan KM, Thomas KP, Sundararajan CR. Study of 1,000 patients with keloids in South India. *Plast Reconstr Surg.* 1974; 53: 276–280.
5. Marneros AG, Norris JE, Olsen BR, Reichenberger E. Clinical genetics of familial keloids. *Arch Dermatol* 2001; 137: 1429–1434
6. Marneros AG, Norris JE, Watanabe S, Reichenberger E, Olsen BR. Genome scans provide evidence for keloid susceptibility loci on chromosomes 2q23 and 7p11. *J Invest Dermatol* 2004; 122: 1126–1132.
7. Mwika, J.B. Occurrence and management of Keloids in Surgical Patients Seen at KNH. M. Med dissertation; UoN; 2005.
8. Olabanji K.J. Clinical pattern and management of keloids in black Population. *East African Medical Journal* Vol. 88 No. 4 April 2011.
9. Bayat A, Arscott G, Ollier WE, McGrouther DA, Ferguson MW. Keloid disease: clinical relevance of single versus multiple site scare. *Br J Plast Surg.* 2005;58(1):28-37.
10. Lee SS, Yosipovitch G, Chan YH, Goh CL. Pruritus, pain, and small nerve fiber function in keloids: a controlled study. *J Am Acad Dermatol* 2004;51:1002–1006.