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## Original Research Article

# Pattern and management outcomes of head and neck hemangiomas: a prospective study from Tanzania

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**Abstract – Introduction:** Hemangiomas arise from the proliferation of endothelial cells surrounding blood-filled cavities. They have a slightly higher female predilection and about 60–70% of them occur in the head and neck region. Various medical and surgical options are available for the treatment of hemangiomas. **Aim**: To determine the pattern and management outcomes of head and neck hemangiomas in Tanzania. **Material and methods**: This was a one-year prospective, cross-sectional study that involved all consecutive patients with head and neck hemangiomas treated in Muhimbili National Hospital. A structured questionnaire was used to collect information including age and sex of the patient, chief complaint and, duration, size and site of the lesion. The treatment modalities were surgery and/or intralesional bleomycin injection (IL-Bleo). A standard dose of bleomycin was 0.3 to 0.6 mg/kg per injection not exceeding 15 units per cycle with a maximum of 6 cycles. Frequency distribution and cross-tabulation were performed and association between variables was assessed by the Chi-square test, whereby the *p*-value was set at $p < 0.05$. **Results:** A total of 58 patients were included in the study. The male to female ratio was 1:1.4 and the median age was 6.15 years. Majority (74%) of the patients had infantile hemangioma. The most common presenting complaint of patients/guardians of the patients were facial disfigurement (94.8%), pain (32.8%) and ulceration (22.4%). The most frequently involved sites were the lips (55.2%) followed by the cheeks (37.9%). In patient who were managed surgically, there was a 100% reduction in size of the lesion. Of those who were treated with bleomycin, the percentage reduction in the area of the lesion ranged from 8.33% to 100% with mean of 72.6%. Only 6% of the patient had post IL-Bleo complications. **Conclusion:** Head and Neck hemangiomas are more common in females and majority are infantile hemangioma. Facial disfigurement is the commonest presenting complication of these lesions, and the lips and the cheeks are mostly affected areas. Intralesional bleomycin is an effective treatment modality which has low complication rates.

## Introduction

Hemangiomas arise from the proliferation of endothelial cells surrounding blood-filled cavities [1]. They constitute 7% of all benign tumors with about 60–70% of hemangiomas found in the head and neck region [2,3]. These lesions have slightly higher female predilection [4]. Hemangiomas are broadly classified as infantile or congenital hemangiomas. The infantile hemangiomas (IH) are either absent or present as a precursor lesion at birth [5] while the congenital hemangiomas (CH) occur fully grown at birth [2]. Congenital hemangiomas can either involute rapidly over a very brief period in infancy (rapidly involuting congenital hemangioma (RICH)) or never involute (non-involuting congenital hemangioma (NICH)) [6].

The CH is rare thus its pathogenesis is less understood [6], however, in case of IH, several theories/hypotheses have been proposed including the placenta, metastatic, progenitor cell, intrinsic defect and extrinsic factor theories [4,7]. Though no single theory can explain all clinical and molecular characteristics of IH, the placental theory is appealing as it explores the close similarities between placental and infantile hemangioma tissues and vasculatures, both at the molecular level, and the natural history [6,7].

Historically, hemangiomas were managed by a closed observation approach on the ground that involution would occur spontaneously and active management was reserved for "complicated" cases [8,9]. Currently, various medical and

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surgical options are available for the treatment of hemangiomas [6]. Some of the established treatments for hemangioma include intralesional bleomycin, corticosteroids, interferon-α, laser therapy, cryotherapy, and surgical excision [10].

Recently intralesional bleomycin injections (IL-Bleo) have been used to manage hemangiomas [11]. Bleomycin is primarily a cytotoxic anti-tumor antibiotic drug used in the management of various types of cancer, including lymphoma and cutaneous squamous cell carcinoma [11,12]. However, it also causes sclerosis by inducing endothelial mesenchymal transition, where endothelial cells change into fibroblast-like cells [12,13]. Due to this, it is the most commonly used sclerosing agent for the treatment of vascular anomalies in some countries [11] and studies have found that hemangioma responded with a greater than 75% reduction in size with the use of bleomycin [10].

In the recent years, the Tanzanian government made tremendous efforts in improving the provision of health services in the country. Such measures included capacitating the referral hospitals to manage patients with different conditions (including head and neck hemangiomas) who in the past were mostly referred overseas for management. This meant that there has been an increase in the number of patients with head and neck hemangiomas seeking for care in the department of oral and maxillofacial surgery in Muhimbili National Hospital. As such, IL-Bleo and Surgery have become the main treatment modality of these lesions in our institute. Considering this recently established management modality in our hospital, there was a need to conduct a study to assess the outcome of the management of hemangiomas in a tertiary health facility in Tanzania. The aim of this study therefore was to determine the pattern and management outcomes of head and neck hemangiomas in Tanzania.

## Material and methods

This was a one-year prospective, cross-sectional study that involved all consecutive patients with head and neck hemangiomas treated at the oral and maxillofacial department of the Muhimbili National Hospital (MNH) between March 2018 and February 2019. Muhimbili National Hospital is the only referral hospital in Tanzania where head and neck hemangiomas are managed and therefore receives patients from all over the country.

The inclusion criteria were all patients with head and neck hemangiomas who had never been treated for their condition before presenting to us. All patients who consented to be included in the study were interviewed using a structured questionnaire. The collected information included age and sex of the patient, chief complaint, duration of the lesion, size (in square centimeters) of the lesion and site of the lesion. The response to treatment was recorded by series of photographs and measurements.

The treatment modality was either surgery or intralesional bleomycin (IL-Bleo). The decision on treatment modality was made by a panel of oral and maxillofacial surgeons basing on the locally developed algorithm of treatment protocol for management of hemangiomas (Fig. 1). Other factors that were taken into consideration included but not limited to age of the patient, clinical course (*i.e.* bleeding, ulceration, *etc.*), and impairment of function. The size of lesion was ascertained using different imaging modalities including clinical examination, CT angiography, MRI and/or ultrasound.

A standard dose of bleomycin was 0.3–0.6 mg/kg per injection not exceeding 15 units per cycle. A mixture of bleomycin, sterile water for injection and 2% lignocaine was used at a ratio of 1:10:5 respectively. The injections were administered under local or general anesthesia by ultrasound guidance. Patients with multiple hemangiomas were only injected in the most prominent lesion in a single setting. During injecting, the needle was introduced through normal skin and, under ultrasound guidance, advanced into the lesion, and then the bleomycin injected radially. The needle was then withdrawn and the lesion compressed for about 2 min.

Regular follow-ups of the patients were done and injected at 4–6 weeks interval, and a maximum of 6 doses were given after which the therapy was discontinued. Post therapy, patients were followed up for a minimum duration of 6 months. The outcome was assessed by a panel of surgeons, and the response rate was graded depending on percentage of reduction in area of the lesion as follows: excellent (reduction by $\geq$75%), good (50–74% reduction), satisfactory (25–49%) and poor ($<$25%).

Data were analyzed using Statistical Package for Social Sciences software (SPSS) for Windows (version 23, IBM Corporation Chicago, IL, USA) whereby frequency distribution together with cross-tabulation were performed. The age was dichotomized as $<$20 years and $\geq$20 years, the site of lesion was grouped into intra-oral, extra-oral and both. The total area covered by lesion was dichotomized into $\leq$5 $cm^2$ and $>$5 $cm^2$. Frequency distribution of different variables was generated, the association between variables was assessed by the chi-square test, whereby the *p*-value was set at $p < 0.05$.

Ethical clearance for this study was provided by the Institutional Review Board of the Muhimbili University of Health and Allied Sciences (MUHAS) and permission to conduct the study was granted by the MNH. Participation was voluntary and for each participant, a signed informed consent form was obtained before data collection. The participants were assured of confidentiality and their right to participate or withdraw without any conditions.

## Results

In this study a total of 58 patients diagnosed with head and neck hemangioma were included, among these 34 were female and the male to female ratio was 1:1.4. The age range of patients was from 8 months to 101 years with a median age of

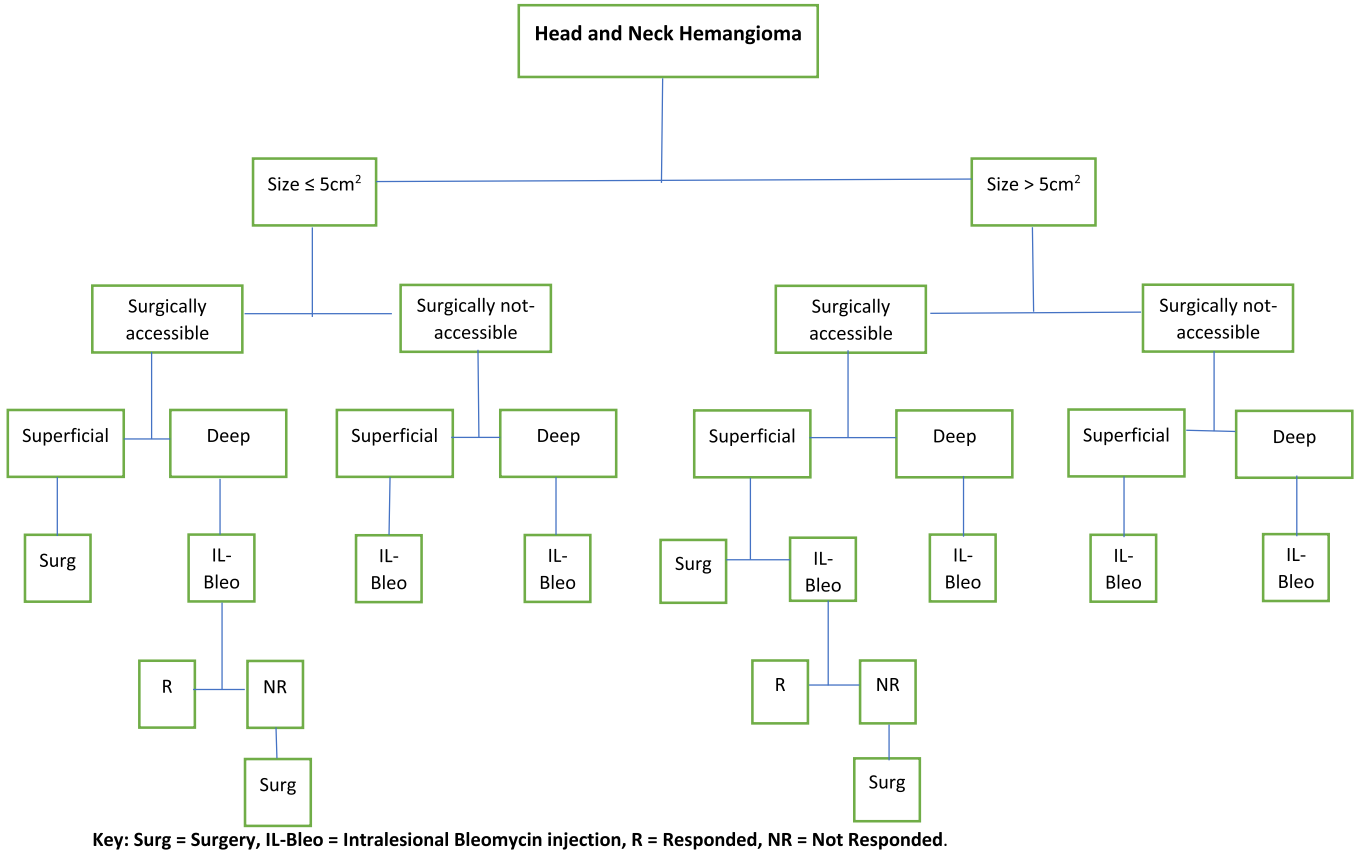


**Fig. 1.** The algorithm of treatment protocol used in management of head and neck hemangiomas.

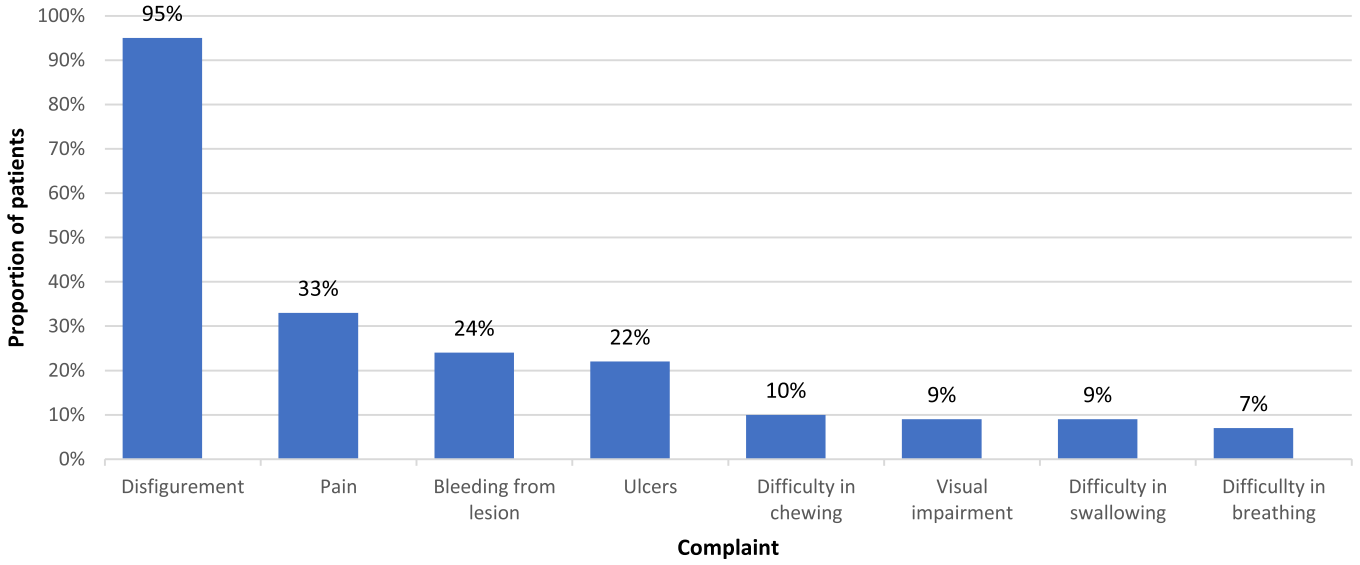


**Fig. 2.** Distribution of patients according to chief complaint.

6.15 years. In 15 (26%) patients, the lesions were present during birth (congenital hemangioma), while in the other 43 (74%) patients, the median duration of occurrence of lesion since birth was 2 years (ranging from 5 months to 75 years).

The most common presenting complaint of patients/guardian of the patients was facial disfigurement (55, 94.8%) others included pain (19, 32.8%) and ulcer (13, 22.4%) as seen in Figure 2.

**Table I.** Anatomical location of head and neck hemangiomas in relation to the total area of the lesion.

| Location of the lesion | Area involved | | Total |
|---|---|---|---|
| | $\leq 5$ cm$^2$ | $>5$ cm$^2$ | |
| Extraoral sites | | | |
| Cervical | 2 | – | 2 |
| Cheek | 4 | 18 | 22 |
| Lip | 16 | 16 | 32 |
| Submandibular | – | 2 | 2 |
| Forehead | 1 | – | 1 |
| Pre auricular | 2 | 1 | 3 |
| Periorbital/zygoma | – | 6 | 6 |
| Nose | 1 | 2 | 3 |
| Intraoral sites | | | |
| Tongue | 5 | 7 | 12 |
| Buccal mucosa | 6 | 16 | 22 |
| Labial mucosa | 6 | 9 | 15 |
| Oropharynx | – | 1 | 1 |
| Floor of the mouth | 1 | 1 | 2 |

Majority (30, 51.7%) of the patients had lesions that involved both intra- and extra-oral sites, 21 (36.2%) had only extra-oral involvement and 7 (12.1%) had lesions only in intra-oral sites. The most frequently involved extra oral site were the lips (32, 55.2%) followed by the cheeks (22, 37.9%). For the intraoral sites, the buccal mucosa (22, 37.9%) followed by labial mucosa (15, 25.9%) were commonly affected (Tab. I). The total area covered by the lesion in patients ranged from 0.1 cm$^2$ to 56 cm$^2$, with the median area of 4.96 cm$^2$.

Surgery was the treatment of choice in 8 (13.8%) patients, and intralesional bleomycin injection (IL-Bleo) was the modality of treatment in 50 (86.2%) patients. The number of cycles of IL-Bleo per patient ranged from 1 to 6, and most (15, 30%) had received 2 cycles (Fig. 3).

For the patients who were managed surgically, there was a 100% reduction in the size of the lesion. Of those who were treated with bleomycin, the percentage reduction in area of the lesion ranged from 8.33% to 100% with a mean of 72.6% (Fig. 4). Of the patients who had an excellent outcome after IL-Bleo, most (11, 40.7%) had received 4 cycles, while three out of the four (75%) patients with poor outcome had received only one cycle of IL-Bleo.

Nine (17.6%) patients who were given IL-BLeo had to undergo subsequent surgical excision of the lesion and the means percentage reduction of the lesion after IL-Bleo was 84%. Most of them (5, 55.6%) had received four cycles before surgery was done. There was no statistically significant association between treatment modality offered and age, sex and clinical characteristics of the lesions (Tab. II). The outcome of management was significantly associated with the number of cycles of IL-Bleo injection the patient received (Tab. III).

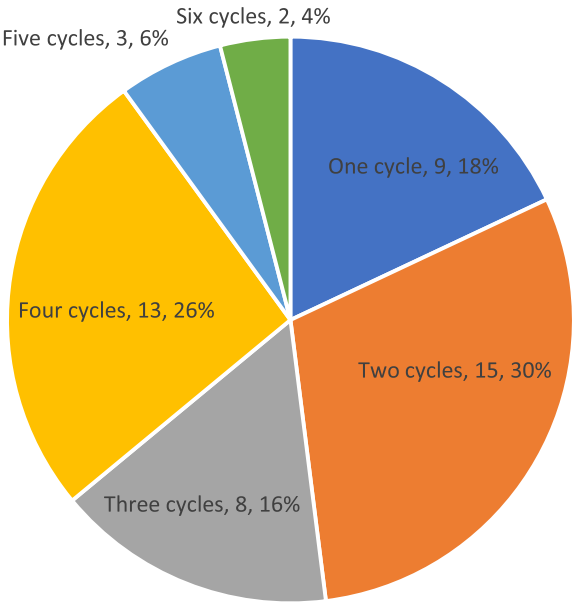


**Fig. 3.** Distribution of patients according to the number of cycles of intralesional bleomycin injection they received.

Of all the patients who had received IL-Bleo, only 3 (6%) patients had developed complications within 24 hours post-injection. These included pain in 2 patients and fever in one patient.

## Discussion

This was a hospital-based study carried out at the only oral and maxillofacial surgery unit in Tanzania with the capacity of

managing hemangiomas. Nearly all patients who suffer from head and neck hemangiomas in Dar es Salaam and elsewhere in the country are either referred to this center from other health facilities or report directly to MNH. Thus, this study provides almost a true picture of the situation regarding head and neck hemangiomas in the country.

A slightly higher predominance of females was noted in this study, which is in agreement with reports from elsewhere [14–16] but contrary to a finding from India [17] which reported a higher prevalence in males. Though the reason for female predominance is unclear [18], the role of hormonal regulation of hemangioma growth and differences in the factor expression between sexes may be the cause since higher levels of angiogenic factors have been demonstrated in females [4].

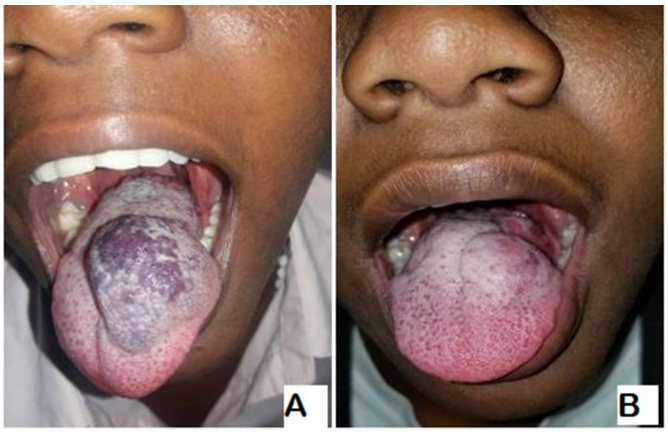


**Fig. 4.** (A) An infantile hemangioma of the tongue before treatment and (B) A significant reduction in size of the lesion after 5 cycles of intralesional bleomycin injections.

In the current study, majority of the patients had infantile hemangioma. The lesser number of cases of congenital hemangioma may be due to the fact that more than 50% of congenital hemangiomas do regress completely by 7 months of age *i.e.* rapidly involuting congenital hemangioma (RICH) and thus, these are rarely seen from management [19]. The CH which were seen during the study period were non-involuting congenital hemangioma (NICH).

Similar to findings in the literature [20–22], facial disfigurement, pain and ulceration were common complaints that forced the patients to seek treatment. The presenting complaint of patients with hemangioma is commonly due to the complications caused by the lesion. It has been documented that the risk of complications is dependent on the size, location, shape and growth phase of the hemangioma [5]. Large, superficial, and segmental hemangiomas are more likely to ulcerate [23] and lesions that are located on the central face, nose and lips are more readily visible and raise concern since these areas have particular curves and textures that may be permanently distorted [5].

In this study, it was found that the most frequently involved sites were the lips followed by the cheeks, this was in concurrence with the findings of studies from elsewhere [14,20,24]. Facial hemangiomas have been reported to have a predilection for regions of embryological fusion [25], and since the lip region contains the highest density of fusion lines found on the face [24], this may be the reason for seeing more than

**Table II.** Treatment modality according to age, sex and selected clinical features of the lesion.

| | Treatment modality | | | *P*-value |
|---|---|---|---|---|
| | Surgery | Intralesional bleomycin | IL Bleo. and surgery | |
| Age group | | | | |
| <20 years | 7 (87.5%) | 31 (75.6%) | 5 (55.6%) | 0.299 |
| ≥20 years | 1 (12.5%) | 10 (24.4%) | 4 (44.4%) | |
| Sex | | | | |
| Male | 3 (37.5%) | 18 (43.9%) | 3 (33.3%) | 0.820 |
| Female | 5 (62.5%) | 23 (56.1%) | 6 (66.7%) | |
| Congenital | | | | |
| Yes | – | 12 (29.3%) | 3 (33.3%) | 0.192 |
| No | 8 (100%) | 29 (70.7%) | 6 (66.7%) | |
| Site | | | | |
| Intra oral | – | 7 (17.1%) | – | |
| Extra oral | 5 (62.5%) | 15 (36.6%) | 1 (11.1%) | 0.063 |
| Both | 3 (37.5%) | 19 (46.3%) | 8 (88.9%) | |
| Total area of the lesion | | | | |
| $\leq 5cm^2$ | 4 (50%) | 20 (48.8%) | 2 (22.2%) | 0.332 |
| $>5cm^2$ | 4 (50%) | 21 (51.2%) | 7 (77.8%) | |
| Mean Percentage reduction in area of the lesion | 100% | 70% | 84% | |

NB: The last row of the third column presents % reduction in size of the lesions after bleomycin injection and before surgery was carried out.

**Table III.** Outcome of treatment of hemangioma against different associated factors.

| | Outcome of treatment | | | | *P*-value |
|---|---|---|---|---|---|
| | Excellent | Good | Satisfactory | Poor | |
| Age group | | | | | |
| <20 years | 27 (62.8%) | 7 (16.2%) | 6 (14%) | 3 (7%) | 0.168 |
| ≥20 years | 8 (53.3%) | 6 (40%) | – | 1 (6.7%) | |
| Sex | | | | | |
| Male | 11 (45.9%) | 8 (33.3%) | 3 (12.5%) | 2 (8.3%) | 0.271 |
| Female | 24 (70.6%) | 5 (14.7%) | 3 (8.8%) | 2 (5.9%) | |
| Congenital | | | | | |
| Yes | 8 (53.3%) | 4 (26.7%) | 2 (13.3%) | 1 (6.7%) | 0.981 |
| No | 27 (62.8%) | 9 (20.9%) | 4 (9.3%) | 3 (7%) | |
| Site | | | | | |
| Intra oral | 4 (57.1%) | 3 (42.9%) | – | – | |
| Extra oral | 13 (61.9%) | 5 (23.8%) | 3 (14.3%) | – | 0.363 |
| Both | 18 (60%) | 5 (16.7%) | 3 (10%) | 4 (13.3%) | |
| Total area of the lesion | | | | | |
| ≤5 $cm^2$ | 14 (53.8%) | 7 (26.9%) | 4 (15.4%) | 1 (3.8%) | 0.466 |
| >5 $cm^2$ | 21 (65.6%) | 6 (18.8%) | 2 (6.3%) | 3 (9.45) | |
| Total cycles of IL-Bleo | | | | | |
| One | 2 (22.3%) | 3 (33.3%) | 1 (11.1%) | 3 (33.3%) | |
| Two | 6 (40%) | 7 (46.7%) | 2 (13.3%) | – | |
| Three | 4 (50%) | 1 (12.5%) | 2 (25%) | 1 (12.5%) | 0.027 |
| Four | 11 (84.6%) | 1 (7.7%) | 1 (7.7%) | – | |
| Five | 2 (66.7%) | 1 (33.3%) | – | – | |
| Six | 2 (100%) | – | – | – | |
| Surgical management | 100% | – | – | – | – |

50% of patients presenting with hemangiomas in this site. It is worth noting that during the study period, we did not encounter any case of intraosseous hemangioma.

Since it is believed that hemangiomas tend to regress spontaneously, treatment is only required for complicated cases, and the indications for treatment include life-threatening (*e.g.* due to profuse bleeding), ulceration, functional impairment and disfigurement [8,19,23]. Different treatment options for managing hemangiomas have been proposed including laser photocoagulation, cryotherapy, excision, radiation, sclerotherapy, embolization, and chemotherapy methods [6,10,26]. In our institute, surgery and intralesional bleomycin injection are the preferred methods. We have developed a local treatment protocol for managing head and neck hemangiomas (Fig. 1) that takes into account the size, site/location and depth of the lesion. There are additional factors that are further considered when deciding treatment plan such as the clinical course of the lesion and age of the patient. For instance, if the lesion is located on the lip and measures more than 5 $cm^2$, then by the developed protocol, IL-Bleo will be the first choice, however, in case the same kind of lesion is ulcerated and bleeds, then surgery is the treatment to be considered. The protocol we have developed has been useful in our setting. And generally, most of the lesions were managed by IL-Bleo since it is s a simple, practical and non-invasive method of treatment [11]. Surgical management was an initial choice of management in patients who presented with relatively small and operable lesions.

In the current study 20% of the patients who received IL-Bleo, had a less than 50% reduction in the size of the lesion, this was similar to what was reported by Omidvari *et al.* [21], but contrary to the findings of Gatea *et al.* [14] who reported about 4% of patients had less than 50% reduction in the size of the lesion. Bleomycin is the drug of choice in our institute because it has shown to have a sclerosant effect on the endothelial cells of the cyst wall of hemangiomas, and also has an apoptotic effect on rapidly growing immature cells as in the proliferative phase of hemangiomas as an antineoplastic agent [14].

Bleomycin tends to damage the endothelial cells, consequently causing collapse, shrinkage, fibrosis and subsequent shrinkage in the size of the lesion [21]. In this study, it was observed that the outcome of management was significantly associated with the number of cycles of IL-Bleo injection the patient received and this may be attributed to the cumulative effect of the drug.

Only 3 patients developed complications post IL-Bleo and these included pain and fever. Short-term fever and pain after the procedure has been documented in the literature [12,14,27]. Pulmonary fibrosis is the most worrisome complication of the systemic use of bleomycin. In this study, however, none of the patient got this complication and this may be attributed to the fact that this complication is dose dependent, and it commonly occur when a doses of more than >5 mg/kg is given, which is much higher than the dose given during sclerotherapy [13,27].

The findings of this study give a highlight of the pattern of head and neck hemangioma and the outcome of its management in our locality. It provides evidence-based support to the current clinical practice in our institute. Use of IL-Bleo, has significantly decreased need for referring patients with hemangiomas abroad for management, as such, there is a significant relief to the patients and their families. Moreover, the cost of treatment which was incurred by the government on referring the patient abroad has been saved as well.

## Conclusion

Head and neck hemangiomas are more common in females. Most of the hemangiomas are of infantile type. Facial disfigurement is the commonest presenting complication of these lesions, and the lips and the cheeks are mostly affected areas. Intralesional bleomycin is an effective treatment modality with low complication rates.

## Authors contributions

A.M. Mungia: Conceptualization, Methodology, Data collection. S.S. Owibingire: Conceptualization, Methodology, Supervision; Reviewing and Editing. J.R. Moshy: Conceptualization, Supervision, Reviewing and Editing. K.S. Sohal: Conceptualization, Literature search, Analysis and interpretation, Writing an original draft, Editing. W. Sianga: Investigation, Supervision, Reviewing and Editing.

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## Conflict of interest

The authors declare that they have no conflicts of interest in relation to this article.

## Informed consent

The authors declare that informed consent was obtained from each patient aged 18 years and above the age of 18 and assent of the parents/ guardians was sought for those under the age of 17 years.

## Ethical commitee approval

Ethical clearance for this study was provided by the Institutional Review Board of the Muhimbili University of Health and Allied Sciences (MUHAS) and permission to conduct the study was granted by the MNH.

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