

# THE HISTOPATHOLOGICAL PATTERN OF CUTANEOUS VASCULAR TUMOURS; AN INSTITUTION BASED STUDY

<sup>1</sup>Imasogie, Dele E. <sup>2</sup>Ugiagbe, Ezekiel E.

<sup>1</sup>Department of Morbid Anatomy, University of Benin Teaching Hospital, Benin City, Edo State

<sup>2</sup>Department of Morbid Anatomy, University of Benin Teaching Hospital, Benin City, Edo State

## ABSTRACT

**Background:** The skin is a typical site for vascular tumours. Researches on primary cutaneous vascular tumours as a sub group of cutaneous soft tissue tumours are virtually non-existence in our environment in particular and Nigeria in general. The aim of this study is to elucidate the histopathological types of primary cutaneous vascular tumours as well as their age and sex distribution at the University of Benin Teaching Hospital.

**Methods:** It was a 10 year retrospective study that covered the period from 1st of January 2004 to 31st of December 2013. The archived records of the Department of Morbid Anatomy were consulted for all cases of histologically diagnosed cutaneous vascular tumours. The data generated was analysed using Statistical Package for Social Sciences, version 16.

**Result:** One hundred four cases (104) of cutaneous vascular tumours were encountered during the period of study under review. The mean age of cases with cutaneous vascular tumours was in the 4th decade while a slight female predilection was observed. Kaposi's sarcoma accounted for 73.08% of cases while the haemangiomas and angiosarcomas accounted for 25% and 1.92% of cutaneous vascular tumours respectively. Sexual predilection was slightly in favour of the females with Kaposi's sarcomas and haemangiomas. The mean ages for haemangioma, Kaposi's sarcoma and angiosarcoma were in the 3rd, 4th and 7th decades respectively.

**Conclusion:** Kaposi sarcoma was the most common cutaneous vascular tumour followed by haemangioma, while the least is the rare angiosarcoma. Cases with haemangiomas have the least mean age.

**Key words:** Kaposi sarcoma, cutaneous vascular tumours

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## INTRODUCTION

Vascular neoplasms are a subset of soft tissue tumours.<sup>1,2</sup> Like the soft tissue tumours, they vary in the location from which they arise,<sup>2,4</sup> however the skin features prominently as a common site of origin for vascular tumours.<sup>3</sup> Giving credence to this, the World Health Organization (WHO) had documented that the skin is the most common location for the benign vascular tumours,<sup>1</sup> while it also typically serves as the site for Kaposi's sarcoma, a locally aggressive but rarely metastasizing malignant vascular tumour.<sup>5</sup>

Kaposi's sarcoma (KS) is a locally aggressive

endothelial tumour that typically presents with cutaneous lesions.<sup>5</sup> The population demographics and the risk associated with its development are the basis on which four clinical and epidemiological forms are recognized.<sup>4,5</sup> They are: Classic indolent form occurring predominantly in elderly men of Mediterranean/East European descent;<sup>4,6</sup> African KS occurs in middle-aged adults and children in Equatorial Africa who are not HIV infected;<sup>5</sup> Iatrogenic KS appearing in solid organ transplant recipients treated with immunosuppressive therapy and also in patients treated by immunosuppressive agents, particularly corticosteroids, for various diseases; Acquired immunodeficiency syndrome - associated KS (AAKS).<sup>4,6</sup>

**Correspondence to:** Imasogie, Dele E.  
Department of Morbid Anatomy,  
University of Benin Teaching Hospital,  
P.M.B 1111, Ugbowo, Benin City  
**E-mail:** eradebamwen4real@yahoo.com  
**Tel:** +234 803 447 2930, +234 705 526 3330

In sub-Saharan Africa in 2012, Kaposi's sarcoma ranked the 3<sup>rd</sup>, 5<sup>th</sup> and 5<sup>th</sup> in position amongst the most frequent cancers in males, females and both sexes respectively. The number of mortalities in this area in males and females were 16218 and 9134 respectively. The age adjusted mortality rate/100,000 is 6.5 and 3.7 in males and females respectively.<sup>7</sup> Previous studies in Nigeria have reported the incidence of Kaposi's sarcoma in relation to other malignant cutaneous tumour that ranges from keratinocytic (squamous and basal cell carcinomas) to melanocytic (malignant melanoma) through soft tissue neoplasm (dermatofibrosarcoma protuberance and angiosarcoma), and haematolymphoid tumours (cutaneous lymphomas),<sup>8-15</sup> however, our own study would look at KS through the window of cutaneous vascular tumours, a sub group of cutaneous soft tissue tumours. The prevalence of Kaposi's sarcoma in these previous studies that looked at it in relation to the other aforementioned malignant cutaneous tumours ranged from 7.5-38%.<sup>8-15</sup> Studies done in Burkina Faso, Togo, Ghana, Tanzania and Tunisia have shown that Kaposi's sarcoma accounted for 80.6, 13.9, 6.5, 10.4 and 4.5% respectively of all malignant skin tumours.<sup>16-20</sup> Barro Traore et al<sup>18</sup> reported that the predominance of KS in their study may be explained by the high prevalence of HIV infection (2.7-6.5%) in Burkina Faso. Several studies have shown that KS is more common in males than in females. The earliest of these studies in Nigeria was published in the early 60s by MaClean,<sup>21</sup> who collected data from every region of the country. He reported a male to female ratio of 7.5:1. Subsequently other studies in Nigeria were restricted to their respective environments i.e. Benin city,<sup>15</sup> Calabar,<sup>9</sup> Abuja,<sup>22</sup> Zaria<sup>23,24</sup> and Jos.<sup>25</sup> These studies also reported a male predilection. Mseddi et al<sup>16</sup> (Tunisia) and Chalya et al<sup>17</sup> (Tanzania) reported similar findings. In contrary, Akinde et al<sup>26</sup> (Lagos) reported a female predilection. Asuquo<sup>9</sup> and Onunu et al<sup>27</sup> observed that the number of females with the disease had increased due to HIV infection, while Chalya et al<sup>17</sup> reported that

HIV infection had increased the prevalence of KS, thus making it the second most common dermatological malignant tumour in their environment. Surprisingly, only a handful of studies reported on the peak age of KS. Mandong et al<sup>25</sup> (Jos) reported a peak age that spanned from the 3<sup>rd</sup> to the 5<sup>th</sup> decade while Forae and Olu-Eddo<sup>15</sup> reported a peak age in the 4<sup>th</sup> decade. The reported mean ages were in the 3<sup>rd</sup> and 4<sup>th</sup> decades. Forae and Olu-Eddo,<sup>15</sup> Akinde et al,<sup>26</sup> Onunu et al,<sup>27</sup> Ahmed et al,<sup>23</sup> and Ahmed et al<sup>24</sup> reported a mean age of 48, 45, 36.3, 32 and 39 years respectively.

The human herpes virus 8 (HHV-8) has been implicated as the oncogenic virus associated with this disease.<sup>4-6,28</sup> The role of growth factors and chromosomal aberrations in its pathogenesis have been reported.<sup>5</sup> They present to the clinicians as patches, plaques, nodules of the different sizes that are confined to the skin.<sup>5,29</sup> Microscopic features of patch stage shows slit-like spaces between the collagen bundles and extravasated red blood cells.<sup>29</sup> Microscopic features of plaque stage shows spindle cell proliferation and irregular vascular spaces while that of nodular stage shows solid proliferation of spindle-shaped cells, nuclear atypia, mitotic figures and extravasated red blood cells.<sup>29</sup>

Angiosarcoma is relatively rare when compared to the benign vascular tumours.<sup>29-32</sup>

Albores-Saavedra et al<sup>31</sup> reported very slight male predilection (222 males: 212 Females) with a male to female ratio of 1.1:1. Ohira et al<sup>33</sup> (M:F of 1.8:1) and Lydiatt et al<sup>34</sup> (M:F of 2.6:1) reported a male preponderance in their respective studies, while Requeena et al<sup>35</sup> (M:F of 1:2.2) reported a female predilection. Perhaps the sample size and the duration of study may have played a role in this disparity. The mean and median ages were reported from previous studies to occur in the elderly. Albores-Saavedra et al<sup>31</sup> reported a mean age of 73 years in their study. The mean and median ages have been previously documented by Requeena et al<sup>35</sup> as 67 and 71 years respectively, while Lydiatt et al<sup>34</sup>

reported a median age of 67 years. The majority of angiosarcoma arise spontaneously and are of unknown etiology.<sup>30</sup> Angiosarcoma can occur as complication of longstanding lymphedema and radiation therapy.<sup>29,30</sup> Cytogenetic changes found include gains of 5pter-p11, 8p12-qter, and 20pter-q12, losses of 7pter-p15 and 22q13-qter, and -Y.<sup>30</sup> Under the microscope, it is seen as an asymmetrical collection of angulated, irregular vascular channels that are infiltrating between collagen bundles and are lined by hyperchromatic irregular nuclei and prominent nucleoli with numerous mitotic figure.<sup>29</sup> Appear as dusky irregular erythematous plaques that are frequently ulcerated.<sup>29</sup>

Hemangiomas constitute 7% of all benign tumours of infancy and childhood.<sup>4</sup> Harris et al in their study reported that there was no sexual predilection with a peak incidence in the second decade. Studies done in Cameroon,<sup>36</sup> Benin city<sup>37</sup> and Sagamu<sup>38</sup> reported that haemangiomas were the most common benign vasoformative tumours accounting for 80.68%, 68% and 94.4% respectively of all cases of vasoformative tumours. It arises from developmental and acquired proliferation of blood vessel.<sup>39</sup> Under the microscope, they are seen as well-circumscribed proliferation of small vessels lined by flattened endothelial cells. While the congenital lesions are typically lobulated with several vessels, the acquired lesion characteristically develop luminal ectasia with age.<sup>29</sup> Appear clinically as small strawberry-red lesion of less than 1 cm.<sup>29</sup>

In Africa, there is paucity of data on vascular tumours with the exception of Kaposi's sarcoma.<sup>36</sup> Researches on primary cutaneous vascular tumours (CVTs) as a sub group of cutaneous soft tissue tumours are virtually non-existence in our environment in particular and Nigeria in general. The aim of this study is to elucidate the

histopathological types of primary cutaneous vascular tumours as well as their age and sex distribution at the University of Benin Teaching Hospital (UBTH), Benin City, Edo State. The histopathological pattern of primary CVTs in our environment if elucidated would offer the data baseline for the subject matter. The Pathologist and Dermatologist would then be acquainted with the most likely primary CVTs they would be encountering in their day to day respective jobs. This will also assist in prompt clinical and histopathological diagnosis as the ruling in or ruling out of tumours not within these base line data becomes relatively easy taking into cognizance their relative frequencies, age and sex distribution.

## METHODOLOGY

A ten year retrospective study was embarked upon between January 1<sup>st</sup>, 2004 and December 31<sup>st</sup>, 2013 at the Department of Morbid Anatomy, UBTH. The subjects of interest were all cases of histologically diagnosed primary cutaneous vascular tumours at the UBTH. The biodata and clinical information were collected from documented archived records of the department and hospital. The slides were retrieved and reviewed. The histopathological diagnosis, the biodata and available clinical information were documented on a data spread sheet created on excel. The data was subsequently transferred to Statistical Package for Social Sciences, version 16 (SPSS 16, SPSS Inc. Chicago, Illinois, United States of America). It was then analysed using the SPSS. The permission for the study was requested and duly obtained from the Ethics and Research Committee of the University of Benin Teaching Hospital.

## RESULTS

There were 104 cases of cutaneous vascular tumours (CVTs) observed during the period of study under review. Seventy eight (78)

were malignant while 26 were benign. Malignant CVTs were represented by Kaposi's sarcoma and angiosarcoma, while the haemangioma's represented the benign CVTs. The mean age of patients with CVTs was 35.97 years (SD=16.67), while their median and modal ages were 35 and 32 years respectively. Their ages ranged from 1 to 75 years with a range of 74 years. Cutaneous vascular tumours occurred slightly more commonly in females giving a female to male ratio of 1.12:1, (Table 1).

Kaposi's sarcoma was the most common tumour in this study and it represented 73.08% of CVTs. It also doubled as the most common primary malignant CVT accounting

for 76 cases which represented 97.44%.

The age and sex distribution is as shown in Table 1 and 2.

Angiosarcoma was the least common CVT observed. It accounted for 2 cases of the study population and this represented 1.92 % and 2.56% all CVTs and malignant cutaneous tumours respectively. The age and sex distribution is as shown in Table 1 and 2. Haemangioma accounted for 26 cases which represented 25 %, of cutaneous vasoformative tumour. The mean age for those cases with histological diagnosis of haemangioma was 24.04 years (SD = 19.28). The age and sex distribution is as shown in Table 1 and 2.

**Table 1: Age group and sex distribution of cutaneous vascular tumours**

Age	KS		HAEM		AGS		Total
	M	F	M	F	M	F	
0 – 9	-	-	1	4	-	-	5
10 – 19	-	-	5	6	-	-	11
20 – 29	1	16	2	1	-	-	20
30 – 39	16	14	-	-	-	-	30
40 – 49	8	6	1	1	-	-	16
50 – 59	3	2	3	-	-	-	8
60 – 69	6	2	-	2	1	1	12
70 – 79	2	-	-	-	-	-	2
<b>TOTAL</b>	<b>36</b>	<b>40</b>	<b>12</b>	<b>14</b>	<b>1</b>	<b>1</b>	<b>104</b>

**KEY:** KS=Kaposi's sarcoma. Haem=Haemangioma. AGS=Angiosarcoma)

**Table 2: Frequency, sex distribution, mean and peak ages of subtypes of cutaneous vascular tumour**

CVTs	NO OF CASES	FREQUENCY			MEAN ± SD (YEARS)	PEAK AGE
		MALE (NO.)	FEMALE (NO.)	MALE: FEMALE		
<b>Malignant</b>						
KS	76	36	40	1:1.1	39.30 ± 13.22	30 – 39
AGS	2	1	1	1:1	64.54 ± 4.95	
<b>Benign</b>						
HAEM	26	12	14	1:1.16	24.04 ± 19.28	10 – 19
<b>TOTAL</b>	<b>104</b>	<b>49</b>	<b>55</b>	<b>1:1.12</b>		

## DISCUSSION

In this study, the mean age of cutaneous vascular tumour (CVTs) was in the 4<sup>th</sup> decade, while a slight female predilection was observed. Cutaneous malignant vascular tumours were more prevalent when compared to their benign counterparts. Paucity of data on CVTs has limited the comparison of the above findings with other

studies, more so that with the exception of KS, data on vascular tumours are generally lacking in the Africa continent.<sup>36</sup> Kaposi's sarcoma (KS) and angiosarcoma were the 2 malignant cutaneous vascular tumours encountered in this study. The former was by far the more common to a tune that makes it double as the most common cutaneous vascular and malignant vascular tumour. As

earlier noted in the introductory section, previous studies in Nigeria have reported the incidence of Kaposi's sarcoma in relation to other malignant cutaneous tumour unlike this study that has looked at it in relation to other vascular tumours. Paucity of data on KS from this perspective has greatly limited the comparison of its prevalence with similar studies. Suffice to say that, the noted prevalence of Kaposi's sarcoma in this study (73.08%) is much higher than the value of the upper limit of the reference range (7.5-38 %) of this lesion in previous studies<sup>8-15</sup> that looked at it in relation to the other malignant cutaneous tumours. The prevalence of KS might be related to the human immunodeficiency virus (HIV) infection scourge with accompanying HIV associated KS.<sup>9,27</sup> Most previous studies done in Nigeria, Tunisia and Tanzania reported a male predilection.<sup>9,15,16,21,25,27</sup> This is contrary to our own finding that reported a slight female predilection (Male to Female ratio of 1.12:1). Similar to our own observation, Akinde et al<sup>26</sup> reported a female predilection. This disparity may be related to the increase in the number of females affected with AIDS associated KS.<sup>9,27</sup> The peak incidence was noted in the 4<sup>th</sup> decade and this is consistent with the previous study done in Benin city,<sup>15</sup> unlike the study done in Jos by Mandong et al,<sup>25</sup> that reported a peak incidence that spanned from the 3<sup>rd</sup> to the 5<sup>th</sup> decade. The mean age of KS was observed to be 39.3 years which is comparatively similar to that of previous studies from Benin City, Zaria and Jos.<sup>23-25,27</sup> It was however at slight variance with a previous study from Lagos and another previous study from Benin city that reported the mean age of 45 and 48 years respectively.<sup>15,26</sup>

Two cases of cutaneous angiosarcoma seen in this study occurred in the elderly (7<sup>th</sup> decade), accounting for 1.92 % and 2.56% all CVTs and malignant cutaneous vascular tumours (mCVTs) respectively. These figures give the impression of a rare tumour. This is in

keeping with previous documented reports.<sup>31,32,37,38,40</sup> This study noted no sex predilection. This is at variance with previous studies that reported a slight male preponderance,<sup>31</sup> a male preponderance<sup>33,34</sup> and a female predilection.<sup>35</sup> While no concrete reason may be given for these disparities, the sample size and study duration may play a role. These other studies<sup>31,33-35</sup> had sample sizes that ranged from 16 to 434 cases of angiosarcomas and a duration that spanned from 11 – 34 years. This is unlike our own study that observed 2 cases of angiosarcoma over a span of 10 years.

In this study, haemangiomas were the sole benign vasoformative tumour. It is also the second most common vasoformative tumour after Kaposi's sarcoma. This is consistent with reports from previous studies done in Cameroon, Benin city and Sagamu that reported this lesion as the most common benign vascular tumour.<sup>36-38</sup> Similar to the observation of Harris et al,<sup>41</sup> (Indiana, United States of America) this study reported a peak age in the second decade. While Harris et al<sup>41</sup> reported equal prevalence in male and female patients, this study noted only a slight female predilection (Male: Female ratio of 1:1.16). Harris et al<sup>41</sup> concluded their study by refuting the female hormonal influence on the induction of cutaneous capillary haemangioma. This slight female predilection in our study may seem to support this position of Harris et al,<sup>41</sup> but it is limited by the sample size (26 cases against 325 cases), more so that their study collated data from multi-centres.

From the foregoing, CVTs are very slightly more common in the female; their mean age was in the 4<sup>th</sup> decade. Kaposi sarcoma was the most common cutaneous vascular tumour followed by haemangioma, while the least is the rare angiosarcoma. Kaposi's sarcoma and haemangioma had slight female predilection while angiosarcoma had no sexual predilection. The peak ages was noted in the

4<sup>th</sup> and 2<sup>nd</sup> decades for KS and haemangioma's respectively. The mean ages for Haemangioma, KS and Angiosarcoma were in the 3<sup>rd</sup>, 4<sup>th</sup> and 7<sup>th</sup> decades respectively.

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