

PATHOMORPHOLOGY OF VERRUCAE: A CLINICOPATHOLOGIC STUDY

I. Emmanuel^{1,2}, P.O. Akpa^{1,2}, B.V. Kwaghe¹, C.N. Ibeanu¹, J.B. Atiku,³ I.A. Othman¹, N.Z. Bahausha¹, J.E. Ben,¹ J.A. Emmanuel¹, C. Amaike⁴, S.J. Winnie⁵, T. Leslie⁵, T.N. Fadok⁶.

1. Department of Anatomic Pathology and Forensic Medicine, Jos University Teaching Hospital, Nigeria, Jos, Plateau State, Nigeria.
2. Department of Pathology, University of Jos, Jos, Plateau State, Nigeria.
3. Department of Public Health Sciences, Adeleke University. Ede, Osun State, Nigeria.
4. Department of Community Medicine, Babcock University and Babcock University Teaching Hospital, Illishan Remo, Ogun State, Nigeria.
5. Department of Nursing Science, Babcock University and Babcock University Teaching Hospital, Illishan Remo, Ogun State, Nigeria.
6. Department of Histopathology, Federal Medical Center Jalingo, Taraba State, Nigeria.

Correspondence:

Dr. I. Emmanuel

Department of Pathology,
University of Jos,
Jos, Plateau State, Nigeria,
Email: bakare.ayobami.adebayo@ki.se

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ABSTRACT:

Introduction: Verrucae are benign squamous epithelial lesions affecting the skin and mucous membranes, as a result of infection with low-risk Human Papilloma virus, with an estimated 10% of the world's population affected. This work studies the clinicopathology of all histologically diagnosed warts at the Jos University Teaching Hospital between 1st January 2013 and 31st December 2022.

Methodology: The study was a descriptive study of all histologically diagnosed cases of verrucae during the study period. Patients with histological diagnosis of verrucae were included, while those with inadequate biodata (age and sex), inadequate clinical information, and missing archival slides and tissue blocks were excluded from the study. Patients' age, gender, clinical characteristics (site and symptoms) and histological diagnosis were obtained from the records.

Results: All 61 cases are of histologically diagnosed verrucae met the criteria for the study. These consisted of males 28 (45.9%), and 33 (54.1%) females. The age range, mean, median and modal age of the study were 1-70 years, 34.81±19.28years, 35.0 years, and 13.0 years, respectively. As much as 28 (45.9%) warts were seen between 30years and 49years of age. According to the anatomical site of occurrence, the lesions were broadly classified into cutaneous warts, 23 (37.7%) and anogenital warts, 38 (62.3%). Specifically, the vulva, penis, and other parts of the perineum were the sites with the highest frequency of wart accounting for 17 (27.9%), 6(9.8%), and 6 (9.8%) cases respectively. Bleeding, pain, itching, and cosmesis as a direct consequence of the lesion were reasons for clinical presentation, with cosmesis predominating (84.4%).

Conclusion: Warts in our environment is commoner in the anogenital region, the third and fourth decade of life, and in the female gender. Bleeding, pain, itching, and cosmesis were reasons for clinical presentation. Vaccination against the etiological agent of the disease is advised on a wide scale to reduce the incidence of this disturbing and distressing pathology.

Keywords: Verrucae, Warts, Cutaneous, Anus, Genital.

INTRODUCTION

Verrucae can be defined as benign squamous epithelial nodular eruptive lesions affecting the skin and mucous membranes as a result of infection with low-risk Human Papilloma virus. These lesions are seen in clinical practice on an expanse of anatomical locations from the skin of the head to the distal dorsal aspects of the extremities, and through the mucosa of the oral cavity, the nose and urethra.¹⁻⁴ Globally, an estimated 10% of the population are affected.¹ The Human Papilloma Virus, the etiological agent, is the world's commonest sexually transmitted disease,^{1,5} and sexually active

individuals in their lifetime will at least be infected once. The symptoms of the disease could be discomforting, with physical or emotional distress^{6,7} on the heels of a disease with no ideal treatment owing to the lack of standardization,⁸ from the myriad of treatment modalities.^{2,8} Fortunately, vaccination against the Human Papilloma Virus has shown efficacy of approximately 100% in prevention of the disease caused by this infection.⁹ It is worthwhile to document the clinicopathology of this discomforting and distressing disease in our environment to add to the literature,

setting the stage for a robust effort towards its prevention and treatment. Herein lies the purpose of this work encompassing all such histologically diagnosed lesions at the Jos University Teaching Hospital between 2013 and 2022 in relation to the clinical presentation.

METHODOLOGY

The study was a descriptive study of all histologically diagnosed cases of verrucae seen at the Jos University Teaching Hospital between 1st January 2003 and December 31st, 2022. The medical records of patients were obtained from the Medical Health Records Department and the Anatomical Pathology and Forensic Medicine Department of the Hospital. The record was the histopathological reports and folders. Patients with histological diagnosis of verrucae were included, while those with inadequate biodata (age and sex), inadequate clinical information, and missing archival slides and tissue blocks were excluded from the study. Patients' age, gender, clinical characteristics (site and symptoms) and histological diagnosis were obtained from the records. A data extraction form was developed which was used to manually extract the required information from the medical records of the patients.

Using the histologic diagnosis, archival slides were traced, retrieved and reviewed to confirm the histological diagnosis, with concurrence from two anatomic pathology consultant authors in the study. Any observed variation was discussed in a joint session where reviews were made and a decision taken. Cases of missing or broken slides were addressed by making new slides from archival tissue blocks. The protocol of making new slides was as follows: cutting of embedded tissue blocks to a thickness of 3 micrometres and picking on a glass slide after floating

in a warm water bath; immersion in xylene and incubation for 15minutes; immersion of slides in equal portions of xylene and ethanol (xylene: ethanol ratio of 1:1) for 5 minutes; immersion in 100% ethanol for 5 minutes, then 95%, 85%, 75%, 65% and 55% ethanol, each for 3 minutes; rinsing in distilled water for 5minutes; and staining with haematoxylin and eosin.

Data obtained was entered into Microsoft Excel, exported into IBM Statistical Package for Social Sciences (SPSS) version 2021, analysed and presented as frequency tables as proportions, simple frequencies, percentages, range, and measures of central tendencies. The limitation of the study was that not all patients in Plateau State with verrucae seek care from the Jos University Teaching Hospital. Many patients visit other tertiary health facilities, while others will opt for traditional medical care, and yet others manage the condition at home. However, this did not affect the findings of this study.

RESULTS

All 61 cases are of histologically diagnosed verrucae met the criteria for the study. These consisted of 28 (45.9%), and 33 (54.1%) females (Table 1). The age range of the distribution was 1-70 years. The mean, median and modal age of the study were 34.81 ± 19.28 years, 35.0 years, and 13.0 years respectively. Table 2. As much as 28 (45.9%) warts were seen between 30 years and 49 years of age. According to the anatomical site of occurrence, the lesions were broadly classified into cutaneous warts, 23 (37.7%) and anogenital warts, 38 (62.3%). Table 1. The age range, mean, median and modal age of cutaneous warts were, 1 - 70 years, 27.95 ± 21.36 years, 16.5 years, and 13.0 years, respectively. The age range, mean, median and modal age of anogenital warts were, and 10 - 70 years, 39.68 ± 16.30 years, 36.0 years,

Table 1: Anatomic site distribution of warts in relation to age and gender.

Anatomic Region	Number of cases	Age (Years)															
		<9		10-19		20-29		30-39		40-49		50-59		60-69		70-79	
		M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
Cutaneous Warts (CW)	23(37.7%)																
Head and Neck	5 (8.2%)		1							1			2				1
Upper limb	6(9.8%)			4								2					
Lower limb	11(18.0%)	1		2	5			1	1		1						
Trunk	1(1.6%)										1						
Anogenital Warts (AGW)	38(62.3%)																
Vulva	17(27.9%)				3				4		7		1		1	1	
Peri-Anal	6(9.8%)							2		1		1		2			
Perineum	5(8.2%)			1				1	1			1		1			
Cervix	4(6.6%)						1		2						1		
Penis	6(9.8%)					1		4		1							
Total		1	1	7	8	1	1	8	8	3	9	4	3	3	2	1	1
Grand Total	61(100%)	2(3.3%)		15 (24.6%)		2(3.3%)		16(26.2%)		12(19.7%)		7(11.5%)		5(8.2%)		2(3.3%)	

Table 2: Anatomic site distribution of warts in relation to measures of central tendency

Anatomic Region	Measures of central tendency			
	Age range	Mean	Median	Mode
Cutaneous Warts (CW)	1-70	27.95±21.36	16.5	13.0
Head and Neck	1-70	43.60±13.50	16.0	16.0
Upper limb	1-58	25.17±24.34	13.0	13.0
Lower limb	3-49	20.00±13.52	16.0	16.0
Trunk	46-46	46.00±0.00	46.0	46.0
Anogenital Warts (AGW)	10-70	39.68±16.30	36.0	35.0
Vulva	10-70	37.30±20.22	35.5	35.0
Peri-Anal	34-64	49.17±12.97	48.0	34.0
Perineum	15-60	39.20±18.35	34.0	15.0
Cervix	27-69	41.25±19.19	34.5	27
Penis	25-40	33.50±5.68	33.5	25.0
Total	1-70	34.81±19.28	35.0	13.0

and 35.0 years, respectively (Table 2). Specifically, the vulva, penis, and other parts of the perineum were the sites with the highest frequency of wart accounting for 17 (27.9%), 6 (9.8%), and 6 (9.8%) cases, respectively. Table 1. Bleeding, pain, itching, and cosmesis as a direct consequence of the lesion were reasons for clinical presentation, with cosmesis predominating, at 75.4% (Table 3).

for only 1% of the total body surface area in the estimation by Wallace and Edin.¹¹ The question now arises, why should such a small area of the body with largely the same cutaneous component accounted for an overwhelming majority of a particular pathology, the wart? The perinium with the penis and vulvovaginum, the anogenital region, defines a geographical anatomical locale which serves as the hub

Table 3: Anatomic site distribution of warts in relation to clinical presentation.

Anatomic Region		Clinical presentation			
		Bleeding	Pain	Itch	Cosmesis
Cutaneous Warts (CW)	23				
Head	5 (8.2%)	-	-	3	3
Upper limb	6(9.8%)	1	1	3	2
Lower limb	11(18.0%)	1	2	6	7
Trunk	1(1.6%)	-	-	1	1
Anogenital Warts (AGW)	38				
Vulva	17(%)	3	2	16	17
Peri-Anal	6(1.6%)	1	3	1	5
Perineum	5(8.2%)	-	-	3	5
Cervix	4(6.6%)	3	3	-	-
Penis	6(9.8%)	-	5	2	6
Total					
Grand Total	61(100%)	9(14.7%)	16(26.2%)	35(57.4 %)	46(75.4%)

DISCUSSION

The anogenital region harbored a staggering majority of warts in this study. This finding corroborated an earlier report, in which Ahmed *et al.* reported this anatomic region as a unit accounting for a higher frequency of verrucae than any other single anatomical locale.³ Also worthy of note is that for the myriads of dermatological pathologies, genital wart was reported to constitute 1.5% of all such cutaneous diseases.¹⁰ The anogenital region (the perineal area) however, accounts

of conventional sexual activities the world over.^{1,5} The etiological agent of warts, the human papilloma virus, is a sexually transmitted agent which is deposited primarily in this region during sexual activity thereby resulting in the higher frequency of verrucae in the perineum.^{1,5}

Historically, HPV related lesions (warts) were described in ancient times (Hippocrates, the 4th century B.C.);¹²⁻¹⁴ HPV cytopathic effects observed in collected smears

George N. Papanicolaou;¹⁵⁻¹⁷ HPV described with electron microscopy Strauss *et al.*;¹⁸ HPV DNA isolated and physical properties described, Crawford and Crawford.¹⁹ Low-risk HPVs cause warts while the high-risk counterparts cause squamous cell carcinoma by downregulating growth inhibitory signals, exploiting this pathway to stimulate proliferation of cells resulting in a clinically visible mass. The oncogenic capability of HPVs has been extensively studied and established,²⁰ however accumulating evidence has now revealed that low-risk HPVs exist in episomal and integrated forms and similarly inhibits the tumour suppressor genes RB and P53 using the viral proteins E7 and E6, respectively.^{21,22} Also, while high-risk HPVs bind avidly to these tumour suppressor genes, low-risk HPVs have been demonstrated to have low affinity of binding of the E7 and E6 to these genes, a factor responsible for the benignity of the low-risk HPVs.²³ Both low- and high-risk HPVs have been shown to activate the Wnt/ β -catenin signalling pathway by the E6 protein mediated degradation of the Na⁺/H⁺ Exchanger Regulatory Factor 1 (NHERF1).²⁴ Also, the degradation of the proapoptotic molecule, BAK, by the E6 protein provides a growth advantage for infected epithelial cells.²⁵ Furthermore, in immunocompromised individuals, low-risk HPVs have also been implicated in the causation of neoplasia amongst which are the Recurrent Respiratory Papillomatosis and the Epidermodysplasia Verruciformis.²⁶ These benign low-HPVs-related neoplasms were, however, not seen during the period of the study.

Studies have shown that warts are commoner in children and the young.^{27,28} A search through literature showed studies have concentrated on younger age groups perhaps due to this generalization. These studies however are largely true when the predominant finding is cutaneous warts.²⁷⁻³⁰ In this study, the third and fourth decade of life were affected in staggering proportion, accounting for about half (45.9%) of patients with verrucae. The higher frequency of the lesion in older age group in this study is not unconnected to the overwhelmingly higher occurrence of this pathology in the anogenital region. While contact transmission is responsible for the spread of HPV in children,²⁷ sexual intercourse is the culprit in adults.⁵ A study had similar findings as ours for anogenital warts, the vulva being the commonest site in females.³ The anogenital region has been reported as a common site of occurrence of viral warts,³¹ and the pathology is common in this anatomic region in Nigeria.³² The effectiveness of vaccination against the human papilloma virus, has been reported to be measured from prevalence of viral warts in a population.³² With effective and efficient vaccination programs in countries like Australia and England, a rapid and significant decline in the incidence

of genital warts amongst the young female folks was experienced.³³⁻³⁶

In this study verrucae were commoner in females than males. This was true for studies on anogenital warts,³ but reversed in those with predominance of cutaneous/common warts.^{8,27,29,30} A higher infectivity rate of HPV in men than in women has been demonstrated,³⁷⁻³⁹ however, the higher prevalence of clinically overt lesions in women is attributable to some factors amongst which is the rate of clearance of the virus.⁴⁰ Generally, more than 90% of HPV infections are cleared, but clearance rate is higher in males.⁴⁰ Furthermore, more women present themselves for screening and clinical visits for assessment by the physician.^{41,42} Clinical presentation could be owing to cosmesis or due to other symptoms. As in a report by Sudhakar *et al.*, this study found cosmesis to be the commonest reason for clinical visit.²⁷ It has been reported that women more likely than men present for cosmetic surgeries,⁴³ a fact that might be responsible for cosmesis as the major reason for presentation in our women dominated study.

CONCLUSION

Warts in our environment affects cutaneous and anogenital regions with predominance in the latter and are commoner in the third and fourth decades. The disease is commoner in females and bleeding, pain, itching, and cosmesis were reasons for clinical presentation. Vaccination against the etiological agent of the disease is advised on a wide scale to reduce the incidence of this disturbing and distressing pathology.

Conflict of Interest Statement

The authors affirm that they have no conflict of interests to declare.

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