

Original Research Article

Clinicopathological profile, diagnosis and treatment of skin cancers at a tertiary care center: a retrospective study

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ABSTRACT

Background: Majority of skin cancers are basal cell carcinoma, Squamous cell carcinoma and Malignant melanoma which account for more than 95% of total skin malignancies. There is an increase in incidence in India over some 10 years of period. This study was done for analysing clinicopathological profile of skin malignancies and association of human papilloma virus (HPV) in skin malignancies in Himalayan Institute of Medical Sciences (HIMS, Uttarakhand, India).

Methods: It was a retrospective study done on 101 patients having malignant skin lesions attending the Department of Surgery at HIMS from October 2005 to October 2008 and given their consent.

Results: Out of 101 patients, 68 had squamous cell carcinoma, 21 had basal cell carcinoma and 10 had malignant melanoma, prevalence is high in men of lower socioeconomic status (M:F) 1.9:1. The mean age was 54.50 years. Most of the patients were laborers, farmers and factory workers. Ulcers and ulceroproliferative growth were common mode of presentation. Most commonly associated risk factor was exposure to sunlight, the commonest location of skin cancer was face and scalp. Wide local excision was the commonest done procedure with closure of primary defect by SSG, fasciocutaneous or cutaneous flaps. No HPV association was seen.

Conclusions: Skin cancers are quite common and their incidence has increased in last few decades, in this study we found that skin cancer were more common in males of lower socioeconomic status, probable cause was increased sun exposure and chemical exposure, in respect to females. Cancer could manifest in many forms but ulcers quite common, Squamous cell carcinoma outnumbered basal cell carcinoma, Wide local excision with skin grafts was main stay of treatment.

Keywords: Skin cancers, Squamous cell carcinoma, Basal cell carcinoma, Malignant melanoma, HPV

INTRODUCTION

Malignant skin lesions have become increasingly prevalent over the past several years. In United States, approximately 5.4 million cases of non-melanoma skin cancers are treated in 2012.¹ Skin cancer account for

more than 40% of all malignancies. Majority of skin cancers are basal cell carcinoma (BCC), squamous cell carcinoma (SCC) and melanoma which account for more than 95% of total skin malignancies.¹

The incidence in males in Delhi for malignant melanoma is 0.29% and 0.90% for other skin cancers. The incidence

for females in Delhi is 0.18% for melanoma and 0.83% other skin cancers. There is an increase in incidence as available statistically of the incidence of skin cancers in India over a 10 year of period.²

Broadly malignant skin lesions fall in three groups

- Basal cell carcinoma
- Squamous cell carcinoma
- Malignant melanoma.

Basal cell and squamous cell are together called as NMSC.

There is increased buzz about human papillomavirus and its role in skin cancers. The role of human papillomavirus (HPV) in the development of SCC has been studied. Eliezri et al, found a direct correlation between the venereal spread of HPV-16 and the initiation of SCC, and others have demonstrated an association of HPV-16 with periungual SCC.³⁻⁴

Skin cancer is the 5th leading cost of deaths among all the cancers in the world. The aim of this thesis as to access the clinicopathological profile of malignant skin lesions and to evaluate their association with HPV (Human papilloma virus) in the patient's presenting in Himalayan Institute of Medical Sciences over a specified period of time.

METHODS

It was a retrospective study done on patients having malignant skin lesions attending the department of Surgery at Himalayan Institute of Medical Sciences from October 2005 to October 2008, by collecting all the details from the hospital records. A total number of 101 patients with skin cancer have been included in this study. The diagnosis of skin cancer was established on the basis of detailed history, examination and positive histopathological diagnosis. Staging investigations included histopathology, X-ray chest, USG abdomen/pelvis/neck and CECT and according to the TNM classification. Surgical procedures done for treatment and various procedures done to cover the surgical defect have been recorded. Association of malignant skin lesions with HPV has been done by Immunofluorescent study.

RESULTS

The clinicopathological profiles of all the patients were studied in detail. The total number of patients included in this study was 101.

Out of this 68 had squamous cell carcinoma, 21 had basal cell carcinoma, 10 had malignant melanoma, 1 had sebaceous carcinoma and 1 had juvenile xanthogranuloma.

Sex ratio

Among the patients of skin malignancy 66 were male and 35 were Female, thus the sex ratio being (M:F) 1.9:1. The mean age was 54.50 years the range being between 15 to 95 years the mean duration of patient coming with symptoms was 5.7 months.

Table 1: Sex wise distribution (n=101).

Sex	No. of patients	Percentage
Male	66	65.3
Female	35	34.7

Age distribution

54 (53.4%) patients were between the age of 51-70 years. 20 (19.8%) patients were between the age group of 21-40 years. 15 (14.9%) patients were between the age group of 41-50 years. 10 (10%) patients were between the age group of 71-100 years. 2 (2%) patients were below 20 years. Highest age of patient was 95 years and lowest age was 15 years.

Table 2: Age wise distribution (n=101).

Age	No. of patients	Percentage
0-9	0	0.0
10-20	2	2.0
21-30	10	9.9
31-40	10	9.9
41-50	15	14.9
51-60	27	26.7
61-70	27	26.7
71-80	5	5.0
81-90	4	4.0
91-100	1	1.0

Socioeconomic status

Out of the total 101 patients, 8(7.92%) were of upper class, 33 (32.67%) were of middle class and 60 (59.41%) were of low socioeconomic group.

Table 3: Socio economic status (n=101).

Socio economic status	No .of patients	Percentage
Upper class	8	7.92
Middle class	33	32.67
Lower class	60	59.41

Occupation

Out of the total 101 patients, 39(38.91%) were Laborers, 21 (20.79%) were Farmers, 14 (13.86%) were Factory workers, 10 (9.90%) were Retired Employees, 8 (7.92%) were Housewife, 7 (6.93%) were Drivers and 2 (1.98%) were students.

Table 4: Occupation wise distribution (n=101).

Occupation	No. of patients	Percentage
Laborer	39	38.61
Retired employee	10	9.90
Factory worker	14	13.86
House wife	8	7.92
Farmer	21	20.79
Driver	7	6.93
Student	2	1.98

Clinical features

Out of 101 patients, ulcers were present in 54 (53.47%) patients, ulceroproliferative growth was present in 35 (34.65%) patients, skin induration was present in 20 (19.80%), erythema was present in 12 (11.88%), plaque was present in 5 (4.95%) and papule were present in 7 (6.93%) cases, 4 (3.96%) patients presented with skin swellings and 2(1.98%) presented with naevus. Excoriation was present in 2 (1.98%) patients.

Table 5: Clinical features (n=101).

Clinical features	No. of patients	Percentage
Swelling	4	3.96
Ulcer	54	53.47
Ulceroproliferative growth	35	34.65
Naevi	2	1.98
Skin Induration	20	19.80
Erythema	12	11.88
Excoriation	2	1.98
Plaque	5	4.95
Papule	7	6.93

Clinical presentation

Out of 101 patients of skin cancer who presented with swelling or ulcer or UPF growth, 56 (55.45%) had discharge from pathological site, 15 (14.85%) had parasthesia, 82 (81.19%) had disfigurement, 40 (39.60%) had loss of function and 31 (30.69%) had pain.

Table 6: Other clinical presentations associated with Ulcer / swelling / UPF growth (n=101).

Presentation	No. of patients	Percentage
Discharge	56	55.45
Parasthesia	15	14.85
Disfigurement	82	81.19
Loss of function	40	39.60
Pain	31	30.69

Lymphadenopathy

Out of 82 Patients, lymphadenopathy was present in 13 (12.87%) patients and this was the commonest clinical finding after visible skin changes.

Table 7: Lymphadenopathy (n=101).

Findings	No. of patients	Percentage
Lymphadenopathy	13	12.87

Risk factors

Out of 101 patients of skin cancer, 62 (61.39%) had history of exposure to sunlight, 6 (5.94%) had H/O sexual exposure, 5 (4.95%) had Marjolin's ulcer due to previous burns, 4 (3.96%) had congenital Naevi, 10 (9.90%) had exposure to chemicals in factory like arsenic and 28 (27.72%) were fair skinned individuals.

Table 8: Risk factors (n=101).

Risk factors	No. of patients	Percentage
Exposure to sunlight	62	61.39
H/O sexual exposure	6	5.94
Marjolin's ulcer	5	4.95
H/O Naevi	4	3.96
Exposure to chemicals in factory	10	9.90
Fair skinned individual	28	27.72

Site of skin lesion**Table 9: Site of Skin lesion (n=101).**

Site of skin lesion	No. of patients	Percent age
Lip	9	9.8
Forehead	9	8.5
Medial canthus of eye	4	2.4
Eyelid	6	4.9
Cheek	8	8.5
Angle of mouth	5	4.9
Nose	3	3.7
Neck	8	8.5
Mastoid	1	1.2
Occipital region	1	1.2
Temporal region	1	1.2
Arm and hand	6	3.7
Back	3	2.4
Foot	14	13.4
Gluteal region	2	2.4
Perineal region	1	1.2
Heel of foot	2	1.2
Sole of foot	2	1.2
Penis	10	12.2
Vulva	4	4.9
Chest	2	2.4

- Out of 101 patients, site of lesion on lip was 9(8.91%), forehead 9 (8.91%), medial canthus of eye 4 (3.96%), eyelid 6 (5.94%), cheek 8 (7.92%), angle

of mouth 5 (4.95%), nose 3 (2.97%), neck 8 (7.92%), mastoid 1 (1.2%), occipital region 1 (1.22%), temporal region 1 (1.22%), arm and hand 6 (5.94%), beck 3 (2.97%), foot 14 (13.86%), gluteal region 2 (1.98%), perineal region 1 (1.99%), heel of foot 3 (1.98%), sole of foot 3 (1.98%), penis 10 (9.90%), vulva 4 (3.96%) and chest 2 (1.98%).

- The commonest location of skin cancer in the patients studied was found in face and scalp where 49 (48.51%) patients had these lesions. This was followed by lower limb in 18 (17.82%) patients, in penis affecting 10 (9.90%) patients followed by neck 8 (7.92%) patients followed by upper limb where 6 (5.99%) patients had these lesions. Other sites though less common were Vulva having 4 (3.96%), thorax 2 (1.98%), back 3 (2.97%) and perianal region 1 (0.99%) patients respectively.

Table 10: Site of lesion according to broad anatomical classification (n=101).

Risk factors	No. of patients	Percentage
Face	47	46.53
Scalp	2	1.98
Neck	8	7.92
Upper limb	6	5.94
Lower limb	18	17.82
Penis	10	9.90
UVLA	4	3.96
Thorax	2	1.98
Back	3	2.97
Perianal region	1	0.99

Investigations

USG findings

Out of 101 patients, USG findings were normal in 92 (91.09%) patients and showed Inguinal LPE in 9 (8.91%) cases.

Table 11: Investigations - imaging (n=101).

USG findings	No. of patients	Percentage
Normal Study	92	91.09
Inguinal LPE	9	8.91

Table 12: Imaging (n=101).

CECT findings	No. of patients
Right wrist soft tissue mass between thumb and index finger involving medial aspect of thumb	1
Erosion occipital bone to tumour with dural deposits	1
Left Inguinal LPE	4
Right Inguinal LPE	2

CECT findings

Out of 101 patients, 1 patient had right wrist soft tissue mass between thumb and index finger involving medial aspect of thumb, 1 patient had Erosion of occipital bone due to dural deposits of SCC, 4 patients had Left Inguinal LPE and 2 patients had right Inguinal LPE.

Histopathological examination

Out of 101 patients, SCC was diagnosed in 68 (67.33%) patients, BCC was in 21 (20.79%), malignant melanoma was diagnosed in 10 (9.90%) patients, and juvenile xanthogranuloma in 1 (0.99%) and sebaceous carcinoma was diagnosed in 1 (0.99%) patients.

Table 13: HPE of skin lesions (n=101).

Type of skin lesion	No. of patients	Percentage
SCC	68	67.33
BCC	21	20.79
Malignant melanoma	10	9.90
Juvenile xanthogranuloma	1	0.99
Sebaceous carcinoma	1	0.99

Surgical treatment

Among all the surgical procedures for skin cancer, wide local excision was the commonest. WLE was done in 81 (80.20%) patients, partial penectomy was done in 7 (6.93%) patients, total penectomy was done in 3 (2.97%) patients. Amputation of wrist was done on 1 (.99%) patient and great and adjacent toe amputation in 1 (.99%) patient. Nasal excision was done in 2 (1.98%) patients, inguinal lymph node dissection was done in 14 (13.86%) patients and cervical LND was done in 6 (5.94%) patients.

Table 14: Surgical treatment (n=101).

Type of skin lesion	No. of patients	Percentage
Wide local excision	81	80.20
Partial penectomy	7	6.93
Total penectomy	3	2.97
Lymph node dissection	20	19.80
Amputation	2	1.98
Nasal Excision	2	1.98

Table 15: Coverage over excised tissue.

Procedure	No. of patients	Percentage
SSG	51	50.50
Flap's	30	29.70
Primary closure	29	28.71

Various procedures used to cover or close the primary defect by surgery included SSG in 51 (50.50%), use of fasciocutaneous or cutaneous flap's in 30 (29.70%) patients. Primary closure of defect created by excision or amputation was done in 29 (28.71%) patients. In many cases SSG, primary closure and flaps were used together to cover the defect.

Grades of tumor

Out of 101 patients, moderately differentiated carcinoma was found in 44 (43.56%) cases followed by well differentiated carcinoma in 36 (35.64%) and poorly differentiated carcinoma was found in 21 (20.79%) cases.

Table 16: Grades of tumour (n=101).

Procedure	No. of patients	Percentage
Well differentiated	36	35.64
Moderately differentiated	44	43.56
Poorly differentiated	21	20.79

Stage of disease

Out of 101 patients suffering from skin cancer, 68 (67.33%) had stage I disease. 23 (22.77%) had stage II, 7 (6.93%) patients had stage III followed by 3 (2.97%) had stage IV disease.

Table 17: Tumour stage (n=101).

Stage	No. of patients	Percentage
Stage I	68	67.33
Stage II	23	22.77
Stage III	7	6.93
Stage IV	3	2.97

Association with HPV

Total of 67 patients slides and histopathology blocks were stained using immunofluorescent dye. HPV 16 kit was used but none of the subject's specimen showed any association with HPV.

Table 18: Association with HPV (n=67).

No. of patients	Association with HPV	Percentage
67	0	0

DISCUSSION

Skin cancer is one of the oldest cancers known to man. The earliest accredited report of skin cancer is found in the 5th Century BC in the writings of Hippocrates. The earliest incidence of skin cancer was discovered by paleopathologists in the skin of Peruvian mummies in 4th Century BC.

According to our study skin cancer constituted a 2.45% of all the cases of cancer coming to our hospital for treatment. There were 101 cases of skin cancer out of total 4123 patients suffering from cancer. This data was taken from October 2005 to October 2008. According to our study the highest incidence of skin cancer was in the 5th to 7th decade of life followed by the 4th decade. The least incidence of skin cancer according to our study was 2nd decade and below. In this study 53.4% of cases were between 50-70 years old followed by 10% in between the age group of 30-40 years. Only 2% (2 cases) were 20 years or less. Highest age of patient was 95 years and lowest age was 15 years in this study. According to a study by Berwick M and Weinstock MA, cutaneous melanoma skin cancer incidence varies dramatically, ranging for as low as 0.2/100000 for females in India to 42/100000 among females in N. Queensland, Australia. The ratio for male to female of BCC to SCC is 2:1. The incidence of MM in US and Australia is 1:1 for male to female.⁵

According to this study, out of 101 patients, 66 were male and 35 were female. Thus, the male to female ratio was 1.9:1 for all types of skin cancers. In this study BCC was found in 13 males and 8 females, thus the male to female ratio for BCC was 1.5:1. Malignant melanoma was found in 6 males and 4 females, thus the ratio for MM for male to female was 1.5:1. According to studies done by Marks R and Bernstein SC, Limkk and Heidelberg KA, SCC is the second most common skin cancer after BCC.

In this study SCC is commoner than BCC. Out of 101 patients, 68 (67.33%) had SCC and 21 (20.79%) had BCC followed by 10 (9.90%) cases of MM. A similar study done by Godbole VK and Toparani HT in 1968 and by NCRP data (1990-96) confirmed the same.^{6,7}

In this study 60 (59.41%) cases were from lower socioeconomic class followed by 33 (32.67%) in middle class and only 8 (7.92%) cases fell in upper class category. Our study indicated that 60 (59%) patients were farmers and daily labourers with history of increased exposure to sunlight. The next highest incidence of skin cancer was found in factory workers which formed 14 (13.86) of the total number of cases. This study pointed out a relation between occupation and skin cancer. This was confirmed by a HELIOS-1 multicentre case control study done by Berta Suarez, Gonzalo Lopez and Carmen Martinez, which analysed 1585 cases and found increased incidence of skin cancer in farmers, daily labourers and factory workers.⁸⁻¹⁰

In this study ulcer was the commonest mode of presentation and was found in 54 (53.47%) cases. This was followed by UPF growth in 35 (34.65%) cases. Skin induration was present in 20 (19.80%) followed by erythema in 12 (11.88%) and papule in 5 (4.95%) cases. Other clinical presentations associated with ulcer / swelling / UPF growth were discharge in 56 (55.45%) followed by loss of function in 40 (39.60%) and pain in

31 (30.69%) cases. All patients had or complained of disfigurement.

Armstrong and Krickler have estimated that approximately two-thirds of the world's cases of melanoma may be related to sun exposure. Increased exposure to sunlight is one of most important risk factors for development of skin cancer. The risk of developing MM after exposure to sunlight is increased and was assessed in a study by Osterlind A et al in a Danish case control study. Similar finding was confirmed in a study by Elwood JM et al.¹¹⁻¹³

Similarly, the pathogenesis of BCC most commonly involves exposure to ultraviolet light (UVL), particularly rays in the UVB spectrum (290 to 320 nm), as confirmed in a study by Leffell DJ.¹⁴

Factors involved in the pathogenesis of SCC are similar to those for BCC and include exposure to UVL, genetic mutations, immunosuppression, and viral infection. Eliezri et al found a direct correlation between the venereal spread of HPV-16 and the initiation of SCC, and others have demonstrated an association of HPV-16 with periungual SCC.¹⁵⁻¹⁹

In this study showed that 62 (61.39%) patients developing skin cancers had history of exposure to sunlight followed by 28 (27.72%) fair skinned patients. The next commonest risk factors were exposure to chemicals in the factory found in 10 (9.90%) patients. The next commonest risk factor in our study was Marjolin's ulcer found in 5 (4.95%) patients, 4 patients had congenital naevi and subsequently developed malignant melanoma.

According to this study, face, scalp and neck were the commonest site of malignant skin lesions accounting for 55.43 % of cases. This was followed by lower limb which was the second commonest site of pathology present in 17.82% cases. Next commonest site was penis in 9.90% and upper limb in 5.9% cases.

Study did USG in all and CECT in certain patients with skin cancer. LPE was found in 9 (8.91%) cases on USG and CECT was diagnostic for extent of lesion and demonstrating LPE. CECT was done in 8 patients only of which 3 had SCC, 3 had BCC and 1 had MM.

This study showed prevalence of SCC in the cases studied. SCC was present in 68 (67.33%) cases followed by BCC in 21 (20.79%) and MM in 10 (9.90%) cases. A similar study done in AIIMS by Deosv, Hazarika, Sidhartha and Shukla Nootan in department of Surgical Oncology also showed prevalence of SCC followed by MM in the skin cancer patients treated there.²⁰

In this study, surgical treatment of skin cancer consisted of various procedures like wide local excision, amputation, penectomy and nasal excision. WLE was the

commonest surgical modality employed on a total of 81 (80.20%) patients. Lymphnode dissection was done in 20 (19.80%) cases followed by penectomy in 10 (9.9%) cases. This was followed by amputation in 2 (1.98%) and nasal excision in 2 (1.98%) cases.

Coverage of surgical defect was achieved singly or by a combination of SSG, skin flaps and or primary closure. SSG was done in 51 (50.50%), flaps in 30 (29.70%) and primary closure in 29 (28.71%) patients either singly or combined together.

Epidemiologic studies have detected associations between markers of β -HPV infection and SCC, but not basal cell carcinoma (BCC) as shown in studies done by Harwood and Proby. Similar results were seen in studies done by Pfister, by Sterling and by Karagas et al, suggesting a potential etiological role in SCC Although a connection was discovered nearly a century ago, an etiological relationship between cutaneous HPV infection and skin cancers remains speculative and in our study no such relation was seen.^{21,23}

CONCLUSION

101 patients of skin cancer have been included in this study retrospectively from October 2005 to October 2008.

The incidence of skin cancer among all the malignancies treated in the department of General Surgery and Oncology in Himalayan Institute of Medical Sciences, according to this study is 2.45 % of all the malignancies. According to this study the incidence of skin cancer, in patients coming to HIMS, is more for males than females. The male to female ratio was 1.9:1. The highest incidence of skin cancer was in the 5th to 7th decade of life followed by 4th decade. Least incidence is below 20 years. This study showed higher incidence of skin cancer in patients of low socio- economic class. This is probably because of greater exposure to etiological factors like sunlight and chemicals like arsenic, associated with manual labour and working in factory, by people of this class.

The type of occupation turned out to be an important contributory factor in the patients of skin cancer. Almost 59% patients were farmers or daily labours. Next commonest occupation among patient's presenting with skin cancer was of factory workers (14%). This study showed that sunlight was the commonest contributory risk factor to the development of skin cancer as it was found in 61% patients. The next commonest risk factor was exposure to chemicals like arsenic and others which was present in 10% cases. Though easily diagnosable, a large chunk of the patients presented with locally advanced skin malignancy. This was probably because of the ignorance of patients towards their health and inability to discern skin changes as hazardous.

The mean duration of patients presenting with signs of skin cancer was 5.7 months. The commonest presenting symptoms of skin cancer are ulcer, ulceroproliferative growth, skin induration and erythema. The most commonly encountered clinical findings in skin cancer patients after skin changes was palpable lymphadenopathy.

In this study, we found that Squamous cell carcinoma was the commonest from of skin cancer followed by Basal cell carcinoma and then Malignant Melanoma. Histologically moderately differentiated carcinoma was the commonest grade followed by well and poorly differentiated carcinoma. The surgical modality primary used for treatment of malignant skin lesions was wide local excision. The commonest modality for coverage of surgical defect was use of SSG followed by flaps and primary closure in approximately equal measures. The commonest site of skin cancer was face followed by lower limb, penis and neck in our study.

Discharge was the commonest finding in patients having skin cancer lesions and was present in 55% cases. Pain was present in 31% patients. Though studies have shown that there is association between HPV and skin cancer especially SCC, in our study we studied and analyzed association between HPV16 and all forms of skin cancer and did not find any association between them.

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