Original Research Paper

Volume-8 | Issue-4 | April-2018 | PRINT ISSN No 2249-555X

Dermatology

STUDIES ON CUTANEOUS MALIGNANCY IN TERMS OF CLINICAL FEATURES AND DIFFERENT ANATOMICAL LOCATIONS – A TIRTIARY HOSPITAL BASED STUDY

Dr. Chayanika Kalita — Assistant Professor, Department of Dermatology & STD, Gauhati Medical College & Hospital, Guwahati, Assam, P/O: Indrapur, P/S: Bhangagarh, Guwahati- 781032, City – Guwahati, District – Kamrup (Metro), State – Assam, India,

Dr. Lohit Kumar Kalita — Assistant Professor, Department of Oncology, Gauhati Medical College & Hospital, Guwahati, Assam, P/O: Indrapur, P/S: Bhangagarh, Guwahati- 781032, City – Guwahati, District – Kamrup (Metro), State – Assam, India,*Corresponding Author

Dr. Umesh Ch. Sarma — MD (community medicine), M.Sc. in Epidemiology (London University), P.G. Training in Epidemiology (London University), Vice-Chanchellor, Srimanta Sankadeva University of Health sciences, Narakasur Hill Top, Guwahati Assam, P/O: Indrapur, P/S: Bhangagarh, Guwahati- 781032, City – Guwahati, District – Kamrup (Metro), State – Assam, India,

ABSTRACT **Background:** The incidence of skin cancer has been increasing. Hence it is now more important than ever to have an accurate and early clinical diagnosis of skin cancer to pave the way for appropriate preventive measures to be taken.

Methods: This study was conducted at Gauhati Medical College & Hospital, Guwahati, Assam understand the clinical feature and different anatomical sites of cutaneous malignancy. A total 150 numbers of newly diagnosed cases of cutaneous malignancy were procured from the Out Patient Department of Dermatology & STD of the institute over a period of November, 2010 to October, 2013.

Results : (1) In the study, the presenting symptoms in order of frequency were swelling 65 (43.33%) , ulcer 34 (22.67, bleeding 22 (14.67%) , pigmentation 12 (8%) , skin changes in 8 (5.33 %), pain 6(4%), itching in 1 (0.67 and others in 2(1.33 %) patients. (2) Distribution of different types of cutaneous malignancies: In the present study 111(74%) patients were SCC { 70 (64.22%) male and 41 (27.335) female} ; Twelve (8%) patients had cutaneous malignant melanoma (MM) { 3(2%) male and 9(6%) female}. Eleven (7.33%) patients had BCC { 5(3.33%) male and 6(4%) female}; other category group consist of 16 (10.67%) { 4 (2.67%) male and 12 (8%) female}.

Conclusion : (1) The presenting symptoms were swelling and ulcer followed by bleeding , pigmentation, skin changes pain, itching. (2) SCC, malignant melanoma, BCC are highly significant in number compare to other cutaneous malignancies. (3) Anatomical location in order of frequency may be oral cavity followed by lower limbs, penis, face, upper limbs, vulva (in female), trunk, scalp, neck, abdominal wall, perineal region, anal canal, inguinal region. A high number of skin cancer may appear over sun exposed areas. SCC has tendency to develop over burn scar. (4) In BCC favoured anatomical sites in order of frequency may be face, oral cavity, trunk, upper limb. That is most commonly over sun-exposed areas. (5) For malignant melanoma favoured anatomical sites in order of frequency may be lower limbs, oral cavity, upper limbs, trunk and abdominal wall.

KEYWORDS : : Cutaneous, Malignancy, Causation

INTRODUCTION

Tumours of the skin are by far one of the most common of all tumours affecting humans in all age groups from neonate to elderly of both sexes. Of the skin tumours, non melanoma skin cancers {principally, squamous cell carcinoma (SCC) and basal cell carcinoma (BCC)}, are the most common malignant neoplasms in the world. Numerous variations in clinical presentation has been described by various studies. Similarly various significant and non-significant anatomical relationship of cutaneous malignancies has been described by various studies.

RESULTS AND OBSERVATIONS

1. Distribution of presenting symptoms of the patients N = 150

Table 1: Distribution of presenting symptoms of the patients

Presenting symptoms	Total	
	No.s	%
Swelling	65	43.33
Ulcer	34	22.67
Bleeding	22	14.67
Pigmentation	12	8
Other skin changes	8	5.33
Pain	6	4
Itching	1	0.67
Other symptoms	2	1.33
Total	150	100

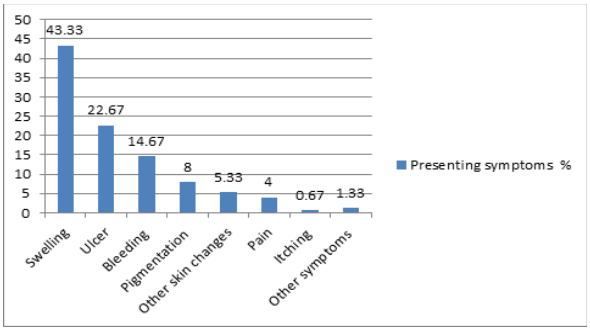

Figure-1: Bar diagram showing distribution of presenting symptoms of the patients

The above table-1 shows that swelling is the most common presenting symptom observed in 65 (43.33%) patients followed by ulcer which was observed in 34 (22.67%) patients. Other symptoms were bleeding in 22 (14.67%) patients, pigmentation in 12 (8%) patients, other skin changes in 8 (5.33 %), pain in 6(4%) patients, itching in 1 (0.67%) patients and others in 2(1.33 %) patients.

From statistical analysis it can also be inferred that a highly significant number of patients have the symptoms of swelling and ulcer.{chi square (X2)= 3.96, degree of freedom = 4, p = 0.0348}.

2. Distribution of different types of cutaneous malignancies N=150

Table 2: Distribution of different types of cutaneous malignancies N=150

Cutaneous malignancies		Total	%
Squamous Cell Carcinoma (SCC)		111	74
Malignant melanoma (MM)		12	8
Basal Cell carcinoma (BCC)		11	7.33
OTHERS	Cutaneous T Cell Lymphoma (CTCL)	5	3.33
	Pleomorphic sarcomas of skin	3	2
	Spindle cell carcinoma of skin	2	1.33
	Paget's disease of nipple with ductal carcinoma	1	0.67
	Adenocarcinoma of anal canal	1	0.67
	Dermatofibrosarcoma protruberans	1	0.67
	Malignant fibrous histiocytoma of skin	1	0.67
	Lymphomatoid papulosis	1	0.67
	Acute lymphoblastic leukemia with skin infiltration	1	0.67
Total	150	100	

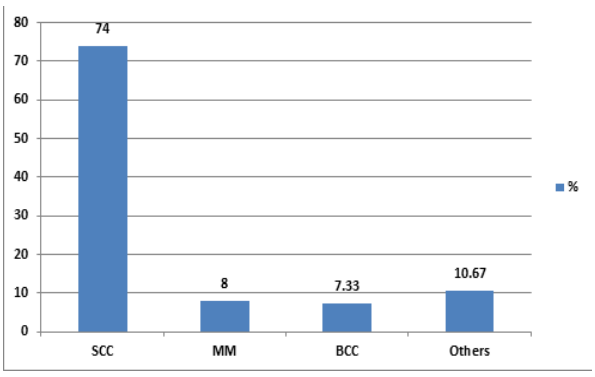

Figure-2: Bar diagram showing distribution of different types of cutaneous malignancies of the patients

The table-2 shows that there were 111(74%) patients of SCC out of which 70 (64.22%) were male and 41 (27.335) were female. Twelve (8%) patients had cutaneous malignant melanoma (MM) among which 3(2%) patients were male and 9(6%) were female. Eleven (7.33%) patients had BCC of which 5(3.33%) were male and 6(4%) were female. The other category group consist of 16 (10.67%) patients out of which 4 (2.67%) patients were male and 12 (8%) patients were female.

From the observed data, it is seen that the effect of CM due to SCC, MM, BCC were found to be highly significant and others were less significant.

3. Distribution of cutaneous malignancies with different anatomical sites N= 150

Table-3: Distribution of cutaneous malignancies with different anatomical sites

Skin cancers	No.s	%	Statistical inference
Scalp	3	2	Not significant
Face	14	9.33	Significant
Oral cavity	50	33.33	Highly significant
Neck	3	2	Not significant
Upper limbs	8	5.33	Not significant
Trunk	4	2.67	Not significant
Abdominal wall	2	1.33	Not significant
Inguinal region	1	0.67	Not significant
Perineal region	2	1.33	Not significant
Anal canal	2	1.33	Not significant
Penis	23	15.33	Significant
Vulva	5	3.33	Not significant
Lower limbs	25	16.67	Significant
Secondary skin infiltration	2	1.33	Not significant
Others	6	4	Not significant
Total	150	100	

The table-3 shows that 50 (33.33%) patients had cutaneous malignancy of oral cavity. Other anatomical locations in order of sequence were 25 (16.67%) patients over lower limbs, 23 (15.33%) patients over the penis, 14 (9.33%) patients over face, in 8 (5.33%) patients affecting the upper limbs, 5 (3.33%) patients had lesions over vulva, 4 (2.67%) patients over trunk, 3 (2%) patients over scalp, 3 (2%) patients over neck, 2 (1.33%) patients over abdominal wall, 2 (1.33%) patients in the perineal region, 2 (1.33%) patients in anal canal and 1 (0.67%) in the inguinal region. Only 2 (1.335) patient had secondary skin infiltration. Moreover, 6 (4%) patients fall in other category. So it appears that 37.33 % lesions occurred in sun exposed areas which is the highest number of cases among the study population

Statistically, all are not significant except those located over oral cavity, face, lower limbs.

4. Distribution of SCC in different anatomical sites N=150

Table-4: Distribution of SCC in different anatomical sites

Cutaneous malignancies (SCC)	No.s	%	Statistical inferences
Scalp	2	1.33	Not significant
Face	7	4.67	Significant
Oral cavity	48	32	Highly significant
Neck	3	2	Not significant
Upper limbs	6	4	Not significant
Trunk	2	1.33	Not significant
Inguinal region	1	0.67	Not significant
Perineal region	2	1.33	Not significant
Anal canal	1	0.67	Not significant
Penis	23	15.33	Significant
Vulva	5	3.33	Not significant
Lower limbs	11	7.33	Significant
Total No.s of SCC cases	111	74	
Total No.s of CM cases	150	100	

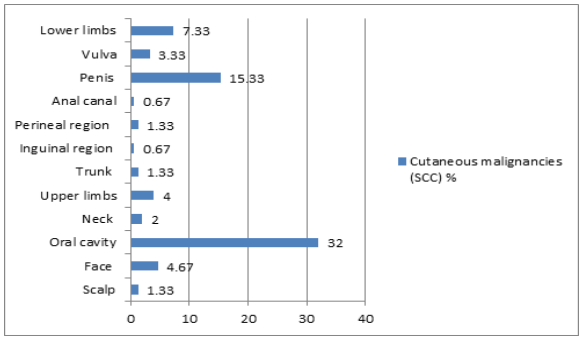

Figure-4: Bar diagram showing distribution of SCC in different anatomical sites

The table-4 it shows that 2 (1.33%) SCC patients had lesions over scalp, 7 (4.67%) patients over face, 48 (32%) patients in the oral cavity, 3 (2%) patients over neck, 6 (4%) patients over upper limbs, 2 (1.33%) patients over trunk, 1 (0.67%) patient over inguinal region, 2 (1.33%) patients over perineal region, 1 (0.67%) patient in the anal canal, 23

(15.33%) patients at penis, 5 (3.33%) patients over vulva and 11 (7.33%) patients over lower limbs.

Statistically, all are not significant except those located over oral cavity, penis and lower limbs.

5. Distribution of BCC over different anatomical sites N=150

Table-5: Distribution of BCC over different anatomical sites

Skin cancers (BCC)	No.s	%	Statistical inferences
Face	7	4.67	Significant
Oral cavity	1	0.67	Not significant
Trunk	1	0.67	Not significant
Upper limb	1	0.67	Not significant
Lower limb	1	0.67	Not significant
Total No.s of BCC cases	11	7.3	
Total No.s of CM cases	150	100	

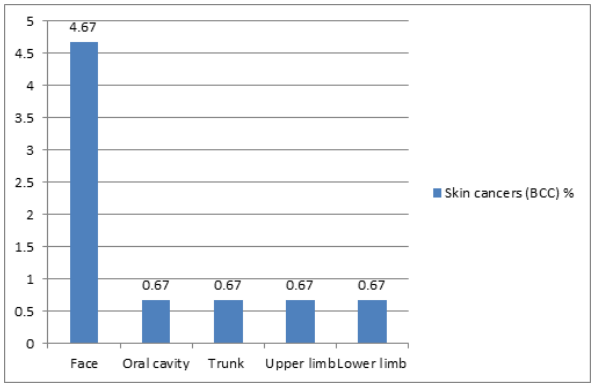

Figure- 5: Bar diagram showing distribution of BCC over different anatomical sites

The table-5 shows that 7 (4.67%) patients with BCC had lesions over face and 1 (0.67%) patient each over the oral cavity, trunk, upper limb and lower limbs. Thus suggests that lesions have occurred most commonly over sun-exposed areas.

Statistically, all are not significant except those located over the face. Thus, in the present study, we observed maximum number of BCC lesions over the sun exposed areas, commonly in the head, face and neck region.

6. Distribution of MM in different anatomical sites N = 150

Table-6: Distribution of MM at different anatomical sites

Malignant melanoma(MM)	No.s	%	Statistical inferences
Oral cavity	1	0.67	Not significant
Upper limbs	1	0.67	Not significant
Trunk	1	0.67	Not significant
Abdominal wall	1	0.67	Not significant
Lower limbs	8	5.33	Significant
Total No.s of MM cases	12	8	
Total No.s of CM cases	150	100	

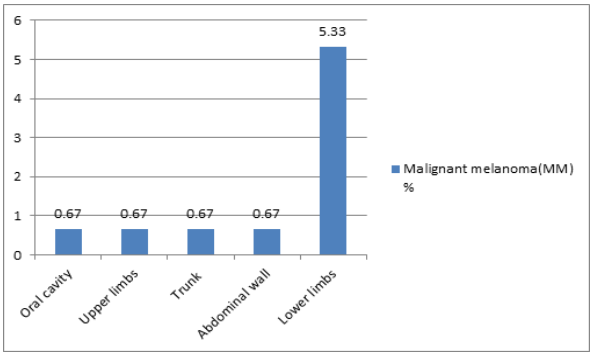

Figure- 6: Bar diagram showing distribution of MM at different anatomical sites

The table-6 shows that 8 (5.33%) patients with MM had lesions over lower limbs and 1 (0.67%) patient each over oral cavity, upper limbs, trunk and abdominal wall. Statistically, all are not significant except those located over lower limbs.

DISCUSSION

1. Distribution of presenting symptoms of the patients

The present study shows that swelling was the most common presenting symptom observed in 65 (43.33%) patients followed by ulcer which was observed in 34 (22.67%) patients. Other symptoms were bleeding in 22 (14.67%) patients, pigmentation in 12 (8%) patients, skin changes in 8 (5.33 %), pain in 6(4%) patients, itching in 1 (0.67%) patients and others in 2(1.33 %) patients.

From statistical analysis it can also be inferred that a highly significant number of patients have the symptoms of swelling and ulcer.{chi square (X2)= 3.96, degree of freedom = 4, p = 0.0348}. In 2009, Jainkittivong A, Swasdison S et al.1 reported that pain and burning is the common complaint of SCC. Moreover, ulceroproliferative growth is also common clinical presentation. Buijan M, Bulat V, Situm M, et al.(2008)2 reported that are numerous variations in clinical presentation of BCC, such as nodular BCC (most common), ulcerating BCC, pigmented BCC, sclerosing BCC, superficial BCC, and fibroepithelioma of Pinkus. Each varies in terms of clinical presentation, histopathology and aggressive behavior.

In the present study, swelling was the commonest presentation. These swellings were commonly due to growth of the lesion. In the present study, there were 111(74%) patients SCC. So the present study can be comparable with the study by Jainkittivong A, Swasdison S et al.(2009)1 Nodular BCC was most common observation of Buijan M, Bulat V, Situm M, et al.(2008).2 As swelling is the presentation of nodular lesion our study is comparable with the study by Jainkittivong A, Swasdison S et al.1

2. Distribution of different types of cutaneous malignancies

It is observed that there were 111(74%) patients of SCC out of which 70 (64.22%) were male and 41 (27.335) were female. Twelve (8%) patients had cutaneous malignant melanoma (MM) among which 3(2%) patients were male and 9(6%) were female. Eleven (7.33%) patients had BCC of which 5(3.33%) were male and 6(4%) were female. The other category group consist of 16 (10.67%) patients out of which 4 (2.67%) patients were male and 12 (8%) patients were female.

From the observed data, it is seen that the effect of CM due to SCC, MM, BCC were found to be highly significant and others were less significant. In 1992, Preston DS, Stern RS, et al. 3 reported that Basal cell carcinoma is the most common malignant skin tumor. In 2012, Sekulic A, Migden MR et al.4 reported that BCC accounts for as many as 80 percent of all non-melanoma skin cancers. In 2015, Vaidhehi Narayan Nayak et al.5 in their study reported that there were 84 (57.9%) cases of well differentiated SCC , 50 (34.4%) cases of moderately differentiated SCC and 11 (7.5%) cases of poorly differentiated SCC. Thus our study finding in this regard is comparable with Vaidhehi Narayan Nayak et al.,s study.5

3. Distribution of different anatomical sites of cutaneous malignancy

In the present study, 50 (33.33%) patients had cutaneous malignancy of oral cavity. Other anatomical locations in order of sequence were 25 (16.67%) patients over lower limbs, 23 (15.33%) patients over the penis, 14 (9.33%) patients over face, in 8 (5.33%) patients affecting the upper limbs, 5 (3.33%) patients had lesions over vulva, 4 (2.67%) patients over trunk, 3 (2%) patients over scalp, 3 (2%) patients over neck, 2 (1.33%) patients over abdominal wall, 2 (1.33%) patients in the perineal region, 2 (1.33%) patients in anal canal and 1 (0.67%) in the inguinal region. Only 2 (1.335) patient had secondary skin infiltration. Moreover, 6 (4%) patients fall in other category. Also, 18 patients (12%) among the SCC had lesions over old scar. So it appears that 37.33 % lesions occurred in sun exposed areas which is the highest number of cases among the study population

Statistically, all are not significant except those located over oral cavity, face, lower limbs. In 1997, Nordin P, Larko O, Stenquist B. et al.6 reported that skin tumour especially can occur at the sites of long standing scar. In 1997, Lear JT, Smith AG, Kuflik AS, Nanniger CK, Miller DL, Weinstock MA et al.7 reported that more than 80 percent

BCCs and more than 70 percent of SCCs are in head & neck region. Non-melanoma skin cancer (NMSC) occur in the most conspicuous location of the body, with approximately 80% occurring in the cervicofacial region; the nose alone accounts for roughly 25% of all cutaneous malignancies and is followed closely by the external ear and surrounding skin. Collectively, the H-shaped region of the face containing the nose, midface, and auricular-preauricular skin has been designated the H-zone. Not only is NMSC most common within this anatomic region, the H-zone is also associated with the highest rate of tumour recurrence. (Velazquez EF, Werchniack AE et al. 2010) 8 In 1998, Miller DL, WEinstock MA et al.9 reported that all skin tumours are seen more frequently at sites of frequent sun exposure.

In 1998, Mooney MM, Kulas M, Mckinley B, Michalek AM, et al.10 reported that most of the skin cancers occur at sites of frequent sun exposure. In 1999, Munyao TM, Othieno-Abinya NA. et al. S11 reported that BCCs & SCCs occur in head & neck region in 90 percent of cases. Buijan M, Bulat V, Situm M, Mihic LL et al.(2008)2 reported that in most cases, BCC develops on chronically sun-exposed skin in elderly people, most commonly in the head and neck region. In our series it is seen that most of the malignant skin tumors occurred at the face, neck, dorsum of hands, forearm and upper back. This distribution can possibly be explained by the fact that these are the sites of the body most frequently exposed to direct sunlight. These are also the sites where there is constant or frequent contact with varieties of environmental agents including carcinogens (hands & feet in case of outdoor manual workers). Eighteen SCC patients (12%) had developed lesions over old scars which is a known risk factor to the development of cutaneous SCC. Thus, our study findings are comparable with these studies.

4. Distribution of SCC at different anatomical sites

In the present study, it was observed that 2 (1.33%) SCC patients had lesions over scalp, 7 (4.67%) patients over face, 48 (32%) patients in the oral cavity, 3 (2%) patients over neck, 6 (4%) patients over upper limbs, 2 (1.33%) patients over trunk, 1 (0.67%) patients over inguinal region, 2 (1.33%) patients over perineal region, 1 (0.67%) patient in the anal canal, 23 (15.33%) patients at penis, 5 (3.33%) patients over vulva and 11 (7.33%) patients over lower limbs.

Statistically, all are not significant except those locations were over oral cavity, penis and lower limbs. About 90 percent of the patients having SCC of oral cavity had history of taking betel nut, 70 percent betel nut with tobacco chewing, 65 percent smoking, 23 percent taking Gutka and 2 percent had history of chronic friction of tongue against sharp teeth. In the study, two patients had carcinoma of vulva. In the study, we observed that 18 (12%) SCC patients developed at old scar sites commonly burn scar. In present study we observed that of the oral SCC cases most common site was buccal mucosa and least common site was gingiva. In 1992, Brodland DG, Zitelli JA, et al.12 reported that in SCC the most common sites of occurrence are the ears, the cheeks, the lower lip, and the backs of the hands. 154 In 2005, Chan K, Craig JC, Shumack S et al,13 reported that people who smoke are more likely to develop SCC. Smoking is not a risk factor for BCC.
In 2000, Gamer KI, Rodney WM et al. 14 reported cases of SCC developed at burns, scars, and chronic ulcerations. In 2015, Vaidhehi Narayan Nayak et al.15 in their study of SCC reported that there were a total of 136 (93.7%) cases of oral SCC occurring in non-keratinized mucosa (buccal mucosa, labial mucosa, floor of the mouth, lateral and ventral tongue) and 9 (6.2%) cases occurring in keratinized mucosa (gingiva, hard palate). No cases were reported over the specialized mucosa (dorsal tongue).

Buccal mucosa belongs to the gingivobuccal complex of which lower gingivobuccal complex is more common site for SCC. This is the typical site associated with tobacco chewing. In Assam, people use Gutka which is placed in the buccal vestibule region. The toxins from the tobacco are absorbed after dilution with saliva whenever the tobacco is swallowed or spat. The areas coming in close proximity with the tobacco products probably become the site of maximum insult and thus are maximally affected. Thus, our study findings are comparable with these international studies although there are some variations with regard to some parameters.

5. Distribution of BCC at different anatomical sites

The present study observed that 7 (4.67%) patients with BCC had lesions over face and 1 (0.67%) patient each over the oral cavity, trunk, upper limb and lower limbs. Thus suggests that lesions have occurred most commonly over sun-exposed areas.

Statistically, all are not significant except those located over the face. Thus, in the present study, we observed maximum number of BCC lesions over the sun exposed areas, commonly in the head, face and neck region. In 1992, Preston DS, Stern RS; et al.3 reported that Basal cell carcinoma usually appear on the face and are more common in men than women. In 1993, Marghoob A. et al 16 reported that 80 percent of BCCs are located on head & Neck region. In 1994, Miller DL, WEinstock MA et al.17 reported that all skin tumours are seen more frequently at sites of frequent sun exposure. In 1997, Nordin P, Larko O, Stenquist B; et al.6 reported that BCC was often seen on the face.In 2003, Gaspari A.A. Sauder D.N. et al.18 reported that BCCs occur commonly on sun exposed areas.

In 2010, Jung GW, Metelitsa AI, Dover DC et al.19 reported that BCCs tend to occur in areas of chronic sun exposure and therefore a large proportion, around 74%, occurs on the head and neck.Thus, our study findings are comparable with these international studies.

6. Distribution of MM at different anatomical sites

In the present study, 8 (5.33%) MM patients had lesions over lower limbs and 1 (0.67%) patient each over oral cavity, upper limbs, trunk and abdominal wall. Statistically, all are not significant except those locations were over lower limbs. In 2002, Karagas MR, Stannard VA, Mott LA, et al. 20 reported that in women, melanomas arise more commonly over the lower extremities, whereas men have a disproportionate number arising on the trunk and head and neck. Thus findings of our study is consistent with these international studies though there is disparity with some other studies

COCLUSIONS

1) Swelling may be the most common presenting symptom of cutaneous malignancy followed by bleeding , pigmentation , skin changes pain , itching. A highly significant number of patients may present with the symptoms of swelling and ulcer
(2) Squamous cell carcinoma, malignant melanoma, basal cell carcinoma are highly significant in compare to other cutaneous malignancies.
(3) Anatomical location in order of frequency may be oral cavity followed by lower limbs, penis, face, upper limbs, vulva (in female), trunk, scalp, neck, abdominal wall, perineal region, anal canal, inguinal region. A high number of skin cancer may appear over sun exposed areas. Squamous cell carcinoma has tendency to develop over burn scar.
(4) In Basal cell carcinoma favoured anatomical sites in order of frequency may be Face, oral cavity, trunk, upper limb. That is most commonly over sun-exposed areas.
(5) For malignant melanoma favoured anatomical sites in order of frequency may be lower limbs, oral cavity, upper limbs, trunk and abdominal wall.

RECOMMEDATIONS

1) The clinical manifestations of cutaneous malignancy range from total absence of any symptoms in subjects with premalignant conditions to formation of swelling, ulcer, bleeding, pigmentation, certain skin changes, pain and itching etc. Differentiating cutaneous malignancy from other causes with similar features and from other cutaneous conditions is important for prognosis and treatment. Evaluation of patients suspected of cutaneous malignancy in a timely fashion is also critical, as a delay in diagnosis can have a negative impact on the disease course.

Health education of the society should form an important aspect of the health care so that they could learn certain do's and don'ts related to different diseases like cutaneous malignancy specially in persons having past and family history of cutaneous malignancy and other diseases and inculcate these in their behavioral patterns through constant practice so as to prevent the occurrence of diseases or reduce the effects of illness. The common symptoms of cutaneous malignancy which are similar to common diseases should be included in the health education programme so that it can be detected early in those high risk areas with history of chronic exposure of UV radiations. Environmental, occupational and life style factors which are risk for development of cutaneous malignancy should be included into the health education programmes so that the disease can be prevented.

2) Moreover, some screening tests should be held periodically by the

health agencies to detect the disease early, especially in persons taking intoxicants for long duration who are high risk for development of cutaneous malignancy. Health agencies should be encouraged to organize periodic camps, health mela for screening of the disease.

3) Preventive maintenance is wiser and less expensive than crisis management. So, promoting awareness about the concept of environmental, occupational and life style risk factors for development of cutaneous malignancy and its common symptoms and to involve community in the process of their mitigation, there is need to conduct awareness campaign programmes in the community level.
4) The study was a descriptive study. So, any conclusions drawn will have to be guarded and will have to confirm with further trials in India.

REFERENCES

(1) Jainkittivong A, Swasdison S, Thangpisityotin M, Langlais RP.Oral squamous cell carcinoma: A clinicopathological study of 342 Thai cases. J Contemp Dent Pract 2009; 10:E033-40.
(2) Buijan M, Bulat V, Situm M, Mihic LL, Stanik-Duktaj-S, Variations in clinical presentation of basal cell carcinoma. Acta Clin Croat 2008 March; 47(1): 25-30.
(3) Preston DS, Stern RS. Non-melanoma cancers of the skin. N Engl J Med 1992; 327:1649-62.
(4) Sekulic A, Migden MR, Oro AE, et al. Efficacy and safety of vismodegib in advanced basal-cell carcinoma. N Engl J Med 2012;366:2171-9
(5) Miller K, Goodlad JR, Brenn Tam J Sug Pathol 2012 Sep 36 (9): 1317-36
(6) Nordin P, Larko O, Stenquist B. Br J Dermatol. 1997 Feb;136(2):180-3
(7) Lear JT, Smith AG, Kuflik AS, J armiger CK, Miller DL, Weinstock MA et al. Epidemiology of skin cancer; Cancer 1997: 943-948
(8) Sakorafas GH, Blanchard K, Sarr MG, Farley DR. Paget's disease of the breast. Cancer Treat Rev. 2001; 27:9–18. [PubMed]
(9) Diepgen TL, Mahler V. The epidemiology of skin cancer. Br J Dermatol. 2002;146(suppl 61):1-6., 1998
(10) Mooney MM, Kulas M, Mckinley B, Michalek AM, Kraybil WG. Impact on survival by method of recurrence deyection in stage I and II Cutaneous melanoma. Ann Surg Oncol 1998;5:54-63
(11) Johnson TM, Tschen J, Ho C, Lowe L, Nelson BR. Xeroderma Pigmentosa, Unusual basal cell carcinomas. Cutis 1994;54:85-92
(12) Brodland DG, Zitelli JA: Surgical margins for excision of primary cutaneous squamous cell carcinoma. J Am Acad Dermatol 1992 Aug; 27(2 Pt 1): 241-8
(13) Chen K, Craig J C, Shumack S: Oral retinoids for the prevention of skin cancers in solid organ transplant recipients: a systematic review of randomized controlled trials. Br J Dermatol 2005 Mar; 152(3): 518-23
(14) Gamer KI, Rodney WM. Basal and squamous cell carcinoma. Prim care.2000;27(2):447-458
(15) Vaidhehi Narayan Nayak, Mandana Donoghue, Selvamani M3; Oral squamous cell carcinoma: A 5 years institutional study; Selvamani M3, Journal of Medicine, Radiology, Pathology & Surgery (2015), 1, 3-6.
(16) Marghoob A, Kopf AW, Bart RS, Sanfilippo L, Silverman MK, Lee P, et al. Risk of another basal cell carcinoma developing after treatment of a basal cell carcinoma. J Am Acad Dermatol 1993; 28:22-8.
(17) Miller DL, Weinstock MA. Non-melanoma skin cancer in the United States: Incidence. J Am Acad Dermatol. 1994; 30:774-7 78.
(18) Gaspari A.A. Sauder D.N: Immunotherapy for basal cell carcinoma evolving approaches Dermatol Surg 2003; 29:1027-34
(19) Jung GW, Metelitsa AI, Dover DC, Salopek TG. Trends in incidence of non-melanoma skin cancers in Alberta, Canada, 1988–2007. British Journal of Dermatology. 2010;163(1):146–154
(20) Karagas MR, Stannard VA, Mott LA, et al: Use of tanning devices and risk of basal cell and squamous cell skin cancers. J Natl Cancer Inst 2002 Feb 6; 94(3): 224-6