

Cutaneous Adverse Effects of Cancer Chemotherapy Drugs: A Cross-sectional Study from Tertiary Care Centre in Chennai, Tamil Nadu, India

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ABSTRACT

Introduction: The incidence of cancers is increasing over the past few decades. With the surge of cancer cases, the usage of cancer chemotherapy drugs has increased. These drugs cause a myriad of cutaneous adverse effects leading to decreased quality of life.

Aim: To study the frequency of cutaneous adverse effects of cancer chemotherapy drugs.

Materials and Methods: This cross-sectional study was conducted in the Department of Dermatology, Government Royapettah Hospital, Chennai, Tamil Nadu, India, from October 2024-November 2024. In present study, all the patients under cancer chemotherapy drugs for various malignancies with cutaneous adverse effects were included. All the cutaneous adverse effects were noted with proper documentation. The results were statistically analysed and tabulated in terms of frequency and percentage.

Results: A total of 70 patients were included in the study. Among the 70 patients, 32 (45.7%) were male and 38 (54.2%) were female. Among the patients, 6 (8.6%) were less than 40 years of age, 29 (41.4%) were between 40-49 years, 15 (21.4%) were between 50-59 years, 9 (12.9%) were between 60-69 years, 6 (8.6%) were between 70-79 years and 5 (7.1%) were between 80-89 years. Carcinoma (Ca) breast was the most common malignancy observed in 23 (32.8%) in our study followed by Ca lung in 11 (15.7%) and Chronic Myeloid Leukaemia (CML) in 6 (8.5%). Anagen effluvium was the most common adverse effect observed in 53 (75.7%) followed by xerosis in 48 (68.6%), acneiform eruptions in 17 (24.3%), hyperpigmentation involving the skin, mucosa and nail in 14 (20%) and sweet syndrome in 8 (11.4%).

Conclusion: The knowledge of adverse effects of chemotherapy drugs can help in early recognition and treatment. This helps in increasing the patient's compliance and thereby increasing the quality of life.

Keywords: Acneiform eruptions, Dyspigmentation, Hand foot syndrome, Sweet syndrome

INTRODUCTION

The incidence of cancers is increasing worldwide over the past few decades. In 2020, there were 19.3 million new cases and 10 million cancer deaths occurred globally [1]. Many new cancer chemotherapy drugs are used in the treatment of cancers [2] which leads to increase incidence of adverse effects. World Health Organisation (WHO) defines an adverse drug reaction as "any response to a drug which is noxious, unintended and occurs at doses used in man for prophylaxis, diagnosis, or therapy" [3]. The most common cutaneous adverse reactions are anagen effluvium, hyperpigmentation, dry skin, nail dystrophies, acneiform eruptions and hand foot syndrome. The cutaneous adverse effects though not fatal affect the quality of life and compliance of the patient. The present study was aimed to find the frequency of cancer chemotherapy related cutaneous adverse effects and their epidemiological distribution. The present study was conducted to understand the spectrum of cutaneous adverse effects which aids in their early diagnosis and increasing patient's compliance.

MATERIALS AND METHODS

This cross-sectional study was conducted in the Department of Dermatology, Government Royapettah Hospital, Chennai, Tamil Nadu, India, from October 2024-November 2024. The Institution Ethics Committee approval (IEC Protocol no.1328/2024) was obtained. All the patients were counselled about the study and written informed consent was obtained from all the patients.

Inclusion and Exclusion criteria: The patients who have completed atleast two months of cancer chemotherapy drugs for

various malignancies presenting with cutaneous adverse effects, patients of any age and patients who gave consent were included in the study. The patients with pre-existing skin diseases, patients on concomitant chemotherapy and radiotherapy, patients with cutaneous adversities due to internal malignancy and patients not willing to participate were excluded from the study.

Study Procedure

A detailed history including demographic datas, type of malignancy, treatment regimen and duration, and history regarding the cutaneous manifestations were noted. Thorough examination of skin, mucosa, hair and nail was done. All the cutaneous lesions were noted with proper documentation and photography. The results were statistically analysed and tabulated in terms of frequency and percentage.

RESULTS

A total of 70 patients were included in the study out of which 32 (45.7%) were male and 38 (54.2%) were female [Table/Fig-1]. Among the patients, 6 (8.6%) were less than 40 years of age, 29 (41.4%) were between 40-49 years, 15 (21.4%) were between 50-59 years, 9 (12.9%) were between 60-69 years, 6 (8.6%) were between 70-79 years and 5 (7.1%) were between 80-89 years [Table/Fig-1].

Ca breast was the most common malignancy observed in 23 (32.8%) in our study followed by Ca lung in 11 (15.7%) and CML in 6 (8.5%) [Table/Fig-2].

The frequency of various adverse effects in present study are listed in [Table/Fig-3,4]. Anagen effluvium was the most common adverse effect observed in 53 (75.7%) in our study followed by

Age group (in years)	Male (n=32)	Female (n=37)	Female child (n=1)	Total (N=70)
	n (%)	n (%)	n (%)	n (%)
<40	4 (12.5)	1 (2.7)	1* (100)	6 (8.6)
40-49	11 (34.4)	18 (48.6)	0	29 (41.4)
50-59	7 (21.9)	8 (21.6)	0	15 (21.4)
60-69	4 (12.5)	5 (13.5)	0	9 (12.9)
70-79	5 (15.6)	1 (2.7)	0	6 (8.6)
80-89	1 (3.1)	4 (10.8)	0	5 (7.1)

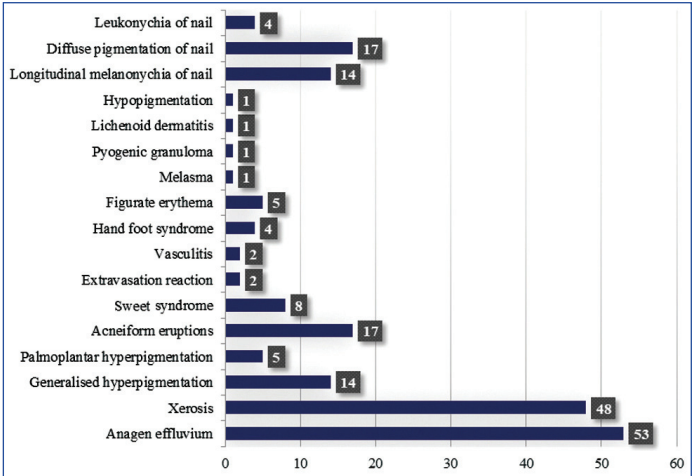
[Table/Fig-1]: Age and gender-wise distribution of the participants.
*Age six-year-old

Diagnosis	Age group (in years)					
	<40 n (%)	40-49 n (%)	50-59 n (%)	60-69 n (%)	70-79 n (%)	80-89 n (%)
Ca breast	1 (16.7)	11 (37.9)	3 (20)	5 (55.6)	1 (16.7)	2 (40)
Ca lung	3 (50)	5 (17.2)	1 (6.7)	1 (11.1)	1 (16.7)	0
CML	0	1 (3.4)	1 (6.7)	1 (11.1)	2 (33.3)	1 (20)
Ca oral cavity	0	3 (10.3)	0	0	1 (16.7)	1 (20)
Ca endometrium	0	1 (3.4)	2 (13.3)	0	0	0
Ca gall bladder	0	2 (6.9)	0	1 (11.1)	0	0
Sarcoma	1 (16.7)	1 (3.4)	1 (6.7)	0	0	0
Ca cervix	0	1 (3.4)	0	0	0	1 (20)
Ca colon	0	0	2 (13.3)	0	0	0
Ca ovary	0	1 (3.4)	1 (6.7)	0	0	0
NHL	0	1 (3.4)	1 (6.7)	0	0	0
AML	0	0	1 (6.7)	0	0	0
Ca duodenum	0	0	1 (6.7)	0	0	0
Ca hard palate	0	1 (3.4)	0	0	0	0
Ca larynx	0	0	1 (6.7)	0	0	0
Ca oesophagus	0	0	0	0	1 (16.7)	0
Ca tongue	0	1 (3.4)	0	0	0	0
GIST	0	0	0	1 (11.1)	0	0
Rhabdomyosarcoma	1 (16.7)	0	0	0	0	0

[Table/Fig-2]: Distribution of the malignancies with regard to age.
NHL: Non-Hodgkin's lymphoma; GIST: Gastrointestinal stromal tumour

Side-effects	n (%)
Anagen effluvium	53 (75.7)
Xerosis	48 (68.6)
Generalised hyperpigmentation	14 (20)
Palmoplantar hyperpigmentation	5 (7.1)
Acneiform eruptions	17 (24.3)
Sweet syndrome	8 (11.4)
Extravasation reaction	2 (2.9)
Vasculitis	2 2.9
Hand foot syndrome	4 (5.7)
Figurate erythema	5 (7.1)
Melasma	1 (1.4)
Pyogenic granuloma	1 (1.4)
Lichenoid dermatitis	1 (1.4)
Hypopigmentation	1 (1.4)
Longitudinal melanonychia of nail	14 (20)
Diffuse pigmentation of nail	17 (24.3)
Leukonychia of nail	4 (5.7)

[Table/Fig-3]: Distribution according to the adverse effects.



[Table/Fig-4]: Bar chart showing the frequency of each adverse effects.



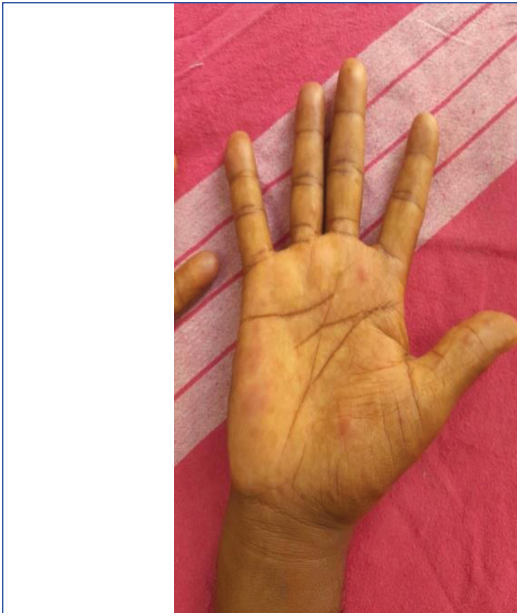
[Table/Fig-5]: Acneiform eruptions due to Gefitinib.

pigmentation [Table/Fig-6]. Sweet syndrome [Table/Fig-7] was observed in 8 (11.4%).



[Table/Fig-6]: Flagellate pigmentation due to Bleomycin.

Nail changes were noted in 35 (50%) of the patients. Among the nail changes, Diffuse pigmentation was the commonest seen in 17 (24.3%) followed by longitudinal melanonychia in 14 (20%), and leukonychia in 4 (5.7%). Other adverse effects noted were figurate erythemas [Table/Fig-8] in 5 (7.1%), hand foot syndrome [Table/Fig-9] in 4 (5.7%), vasculitis in 2 (2.9%), extravasation reaction [Table/Fig-10] in 2 (2.9%), melasma in 1 (1.4%), pyogenic granuloma in 1 (1.4%), lichenoid dermatitis in 1 (1.4%) and patchy depigmentation of the skin [Table/Fig-11] in 1 (1.4%). The frequency of adverse effects to various drug protocols is listed in [Table/Fig-12]. The adverse effects were most commonly observed in 40-49 years age group followed by 50-59 yrs. Among the patients with anagen



[Table/Fig-7]: Sweet syndrome due to Granulocyte-colony-Stimulating Factor (G-CSF).



[Table/Fig-10]: Extravasation reaction due to Vincristine.



[Table/Fig-8]: Erythema annulare centrifugum (figurate erythemas) caused by 5-Fluorouracil.



[Table/Fig-11]: Depigmentation of skin caused by Pazopanib.



[Table/Fig-9]: Hand foot syndrome due to Imatinib.

effluvium, 24 (45.2%) were in the 40-49 years age group and 13 (24.5%) in the 50-59 years age group [Table/Fig-13]. Among the patients with xerosis, 23 (47.9%) were in the 40-49 years age group and 10 (20.8%) were in the 50-59 years age group.

Among the male patients, 24 (75%) had anagen Effluvium, 24 (75%) had xerosis, 8 (25%) had acneiform eruptions and 17 (53.1%)

had nail changes. Generalised hyperpigmentation was observed in 6 (18%), sweet syndrome and hand foot syndrome each in 4 (12.5%) [Table/Fig-14]. Among the female patients, 29 (76.3%) had anagen effluvium, 24 (63.1%) had xerosis, 9 (23.6%) had acneiform eruptions and 18 (47.3%) had nail changes [Table/Fig-14]. Melasma and hand foot syndrome were observed only in male patients. Similarly patchy hypopigmentation, lichenoid dermatitis and pyogenic granuloma were observed only in female patients in present study [Table/Fig-14].

Anagen effluvium 19 (35.8%) and xerosis 16 (33.3%) were noted most commonly in patients with Ca breast. Acneiform eruptions was noted in 5 (29.4%) of patients with Ca breast and 5 (29.4%) with Ca lung. Sweet syndrome was observed in 2 (25%) of patients with Ca breast and 2 (25%) with Ca lung. Hand foot syndrome was noted in 2 (50%) patients with Ca lung and 2 (50%) with CML [Table/Fig-15].

DISCUSSION

Cancer chemotherapy agents are toxic to rapidly proliferating cells of the skin, hair and nails resulting in a wide array of cutaneous adverse effects [4]. A total of 70 patients undergoing treatment for various malignancies with chemotherapy drugs were included in the study. A wide range of chemotherapy drugs were used in these patients. This includes Adriamycin, Cyclophosphamide, Imatinib, Afatinib, Gefitinib, Vincristine, Paclitaxel, Docetaxel, Gemcitabine, Capecitabine, Cisplatin, 5-Fluorouracil. Newer agents like Pazapanib were also used.

In our study, 29 (41.4%) belonged to fifth decade (40-49 years) and 15 (21.4%) were between 50-59 years. This was comparable with studies conducted by Menon A et al., in which 56% of patients were between 41-60 years and Swagata D et al., which shows 31.14% of patients between 51-60 years [5,6].

Adverse effects	Drugs	Frequency of adverse effects due to various drug/protocol
Anagen effluvium	1. Adriamycin+Bleomycin+Vinblastine+Dacarbazine	18
	2. Cyclophosphamide+Doxorubicin+Vincristine+Prednisolone	20
	3. Cisplatin+Paclitaxel	6
	4. Ifosfamide+Etoposide	3
	5. Carboplatin+Docetaxel	3
	6. Cisplatin+5-Fluorouracil	2
	7. Capecitabine+Paclitaxel	1
Xerosis	1. Adriamycin+Bleomycin+Vinblastine+Dacarbazine	25
	2. Cyclophosphamide+Doxorubicin+Vincristine+Prednisolone	14
	3. Cisplatin+Paclitaxel	4
	4. Ifosfamide+Etoposide	3
	5. Carboplatin+Docetaxel	2
Generalised hyperpigmentation	1. Cyclophosphamide+Doxorubicin+Vincristine+Prednisolone	7
	2. Capecitabine+Paclitaxel	4
	3. Cisplatin+5-Fluorouracil	2
Flagellate pigmentation	Bleomycin	1
Melasma	Imatinib	1
Patchy depigmentation	Pazapanib	1
Sweet syndrome	1. Imatinib	2
	2. G-CSF	6
Extravasation reaction	Vincristine	2
Hand foot syndrome	1. Imatinib	2
	2. Sunitinib	2
Figurate erythemas	1. 5-Fluorouracil	3
	2. Cisplatin+Paclitaxel	2
Pyogenic granuloma	Capecitabine	1
Vasculitis	1. Ifosfamide+Etoposide	1
	2. Capecitabine+Paclitaxel	1
Lichenoid dermatitis	Cisplatin+5-Fluorouracil	1
Longitudinal melanonychia of nail	1. Cisplatin+Paclitaxel	4
	2. Adriamycin+Bleomycin+Vinblastine+Dacarbazine	3
	3. Cyclophosphamide+Doxorubicin+Vincristine+Prednisolone	4
	4. Cisplatin+5-Fluorouracil	2
	5. Ifosfamide+Etoposide	1
Diffuse pigmentation of nail	1. Cyclophosphamide+Doxorubicin+Vincristine+Prednisolone	11
	2. Cisplatin+Cyclophosphamide	2
	3. Cisplatin+Paclitaxel	2
	4. Adriamycin+Bleomycin+Vinblastine+Dacarbazine	2
Leukonychia of nail	1. Adriamycin+Bleomycin+Vinblastine+Dacarbazine	2
	2. Cyclophosphamide+Paclitaxel	2

[Table/Fig-12]: Frequency of cutaneous adverse effects to various drug protocols.

In present study, female outnumbered male which is consistent with the study conducted by Datta S et al., where female (62.57%) were more than male [6]. On the contrary, the study by Menon A et al., male patients (63%) was more compared to female [5]. This could be due to more number of patients with Ca breast seen in our study.

Carcinoma breast was the most common malignancy observed in 23 (32.8%) in this study which is consistent with the study conducted by Pavey RA et al., which also shows Ca breast (22.6%) to be the most common malignancy and study by Awal and Singh G which also shows Ca breast to be the most common malignancy observed in 21.33% [7,8].

Anagen effluvium (75.7%) was the most common adverse effect observed in our study. This finding is comparable with the study conducted by Menon A et al., which shows 68% of patients with

alopecia, Chiewchanvit S et al., which shows 76.68% of patients had alopecia and others [5,9-11]. The cessation of mitotic activity in hair matrix cells leads to Pohl-Pinkus constrictions which lead to fracture of the hair shaft [12]. The drugs associated are antimicrotubule agents; topoisomerase inhibitors; alkylators; and antimetabolites. Anagen effluvium was observed most commonly between 40-49 years and in female patients in our study. Anagen effluvium was most commonly noted in the patients with Ca breast in present study. Hair regrowth is observed after cessation of therapy [13]. Hence, reassurance ensures compliance and completion of treatment. Other hair changes like hypertrichosis, trichomegaly were not observed in our study. Scalp cooling methods which involve the introduction of cooling liquid to the scalp via a cap has 50% success rate in preventing alopecia [14].

Xerosis was observed in 68.6% of patients in present study which is comparable with the study conducted by Fabbrocini G et al., in

Side-effects	Age group (in years)					
	<40	40-49	50-59	60-69	70-79	80-89
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Anagen effluvium (n=53)	4 (7.5)	24 (45.2)	13 (24.5)	5 (9.4)	5 (9.4)	2 (3.7)
Xerosis (n=48)	4 (8.3)	23 (47.9)	10 (20.8)	5 (10.4)	4 (8.3)	2 (4.1)
Generalised hyperpigmentation (n=14)	1 (7.1)	6 (42.8)	4 (28.5)	2 (14.2)	1 (7.1)	0
Palmoplantar hyperpigmentation (n=5)	0	2 (40)	2 (40)	1 (20)	0	0
Acneiform eruptions (n=17)	2 (11.7)	7 (41.1)	4 (23.5)	1 (5.8)	2 (11.7)	1 (5.8)
Sweet syndrome (n=8)	1 (12.5)	5 (62.5)	0	0	0	2 (25)
Extravasation reaction (n=2)	1 (50)	0	0	0	1 (50)	0
Vasculitis (n=2)	0	1 (50)	0	1 (50)	0	0
Hand foot syndrome (n=4)	0	1 (25)	1 (25)	1 (25)	1 (25)	0
Figurate erythemas (n=5)	0	3 (60)	0	1 (20)	1 (20)	0
Melasma (n=1)	0	0	0	1 (100)	0	0
Pyogenic granuloma (n=1)	0	0	1 (100)	0	0	0
Lichenoid dermatitis (n=1)	0	1 (100)	0	0	0	0
Hypopigmentation (n=1)	0	0	1 (100)	0	0	0
Longitudinal melanonychia of nail (n=14)	2 (14.2)	5 (35.7)	4 (28.5)	1 (7.1)	1 (7.1)	1 (7.1)
Diffuse hyperpigmentation of nail (n=17)	1 (5.8)	8 (47)	4 (23.5)	3 (17.6)	1 (5.8)	0
Leukonychia of nail (n=4)	0	2 (50)	1 (25)	0	1 (25)	0

[Table/Fig-13]: Distribution of adverse effects according to age.

Side-effects	Sex		
	Male (n=32)	Female (n=37)	Female child (n=1)
	n (%)	n (%)	n (%)
Anagen effluvium	24 (75)	29 (78.4)	0
Xerosis	24 (75)	24 (64.9)	0
Generalised hyperpigmentation	6 (18)	8 (21.6)	0
Palmoplantar hyperpigmentation	2 (6.3)	3 (8.1)	0
Acneiform eruptions	8 (25)	9 (24.3)	0
Sweet	4 (12.5)	4 (10.8)	0
Extravasation reaction	1 (3.1)	0	1 (100)
Vasculitis	1 (3.1)	1 (2.7)	0
Hand foot syndrome	4 (12.5)	0	0
Figurate erythema	3 (9.4)	2 (5.4)	0
Melasma	1 (3.1)	0	0
Pyogenic granuloma	0	1 (2.7)	0
Lichenoid dermatitis	0	1 (2.7)	0
Hypopigmentation	0	1 (2.7)	0
Longitudinal melanonychia of nail	7 (21.9)	6 (16.2)	1 (100)
Diffuse pigmentation of nail	8 (25)	9 (24.3)	0
Leukonychia of nail	2 (6.3)	2 (5.4)	0

[Table/Fig-14]: Distribution of adverse effects according to gender.

Diagnosis	Anagen effluvium (n=53)	Xerosis (n=48)	Acneiform eruptions (n=17)	Sweet syndrome (n=8)
	n (%)	n (%)	n (%)	n (%)
Ca breast	19 (35.8)	16 (33.3)	5 (29.4)	2 (25)
Ca lung	5 (9.4)	7 (14.6)	5 (29.4)	2 (25)
CML	5 (9.4)	5 (10.4)	1 (5.9)	1 (12.5)
Ca oral cavity	3 (5.7)	5 (10.4)	1 (5.9)	0
Ca endometrium	3 (5.7)	2 (4.2)	1 (5.9)	0
Ca gall bladder	2 (3.8)	2 (4.2)	0	1 (12.5)
Sarcoma	1 (1.9)	2 (4.2)	1 (5.9)	0
Ca cervix	2 (3.8)	0	0	0
Ca colon	2 (3.8)	0	0	0
Ca ovary	2 (3.8)	2 (4.2)	0	1 (12.5)
NHL	2 (3.8)	2 (4.2)	1 (5.9)	1 (12.5)
AML	1 (1.9)	1 (2.1)	1 (5.9)	0
Ca duodenum	1 (1.9)	0	0	0
Ca hard palate	1 (1.9)	1 (2.1)	0	0
Ca larynx	1 (1.9)	1 (2.1)	0	0
Ca oesophagus	1 (1.9)	0	0	0
Ca tongue	1 (1.9)	1 (2.1)	1 (5.9)	0
GIST	1 (1.9)	1 (2.1)	0	0
Rhabdomyosarcoma	0	0	0	0

[Table/Fig-15]: Distribution of adverse effects among each malignancies.

It may be due to abnormal keratinocyte differentiation leading to sebaceous gland impairment and water retaining ability. Xerosis was mainly observed in males and between 40-49 years of age. It was also noted more with Ca breast patients in our study.

Acneiform eruption [Table/Fig-5] was observed in 24.3% of patients which is comparable with the studies conducted by Menon A et al., and Chiewchanvit S et al., the frequency observed was 26% and 20.3%, respectively [5,9]. Acneiform eruptions were commonly seen with Epidermal Growth Factor Receptor (EGFR) inhibitors, Tyrosine Kinase Inhibitors (TKI) and Mitogen-activated Protein Kinases (MAPKs) inhibitors. EGFR inhibitors interfere with EGFR-mediated signalling and cause growth arrest and premature differentiation of keratinocytes. The subsequent release of inflammatory cell chemoattractants recruits leukocytes and induces a folliculo-centric inflammatory response. In our study, acneiform eruptions were observed with Gefitinib, Afatinib and Imatinib. It was mostly seen in male patients between 40-49 years of age and in patients with Ca lung, Ca breast, Non-Hodgkin's lymphoma and acute myeloid leukaemia.

Hyperpigmentation involving the skin, mucosa and nail was noted in 20% of patients which is comparable with the study conducted by Menon A et al., where 22% had hyperpigmentation and Padhi T et al., where 22% had hyperpigmentation [5,17]. This may be due to: (i) a direct pigmentary effect of the deposited drug in the skin; (ii) a direct toxic effect on epidermal melanocytes stimulating increased melanin production; (iii) the suppression of adrenal function leading to increased adrenocorticotrophic hormone and melanocyte-stimulating hormone causing hyperpigmentation; and (iv) a depletion of tyrosinase inhibitors resulting in increased pigmentation. Hyperpigmentation was seen mainly with regimens containing cyclophosphamide and capecitabine in our study. Flagellate hyperpigmentation [Table/Fig-6] was seen in one patient undergoing treatment with Bleomycin.

Melasma was seen in one patient receiving Imatinib mesylate. Palmoplantar pigmentation was seen in 7.1% of patients. Patchy depigmentation involving the trunk was seen with one patient receiving Pazopanib. Inhibition of C-kit by TKI (Pazopanib) will result

which xerosis was seen in 41.17% of the patients and Lacouture ME et al., in which xerosis was seen in 40% of the patients [15,16].

in failure of melanocyte differentiation and its melanin production [18]. Sweet syndrome [Table/Fig-7] was observed in 11.4% of cases. In our study, it was seen in patients receiving Granulocyte Colony Stimulating Factor (G-CSF) as a treatment to neutropenia induced by chemotherapy similar to the case report by Paydas S et al., [19].

Extravasation reaction was seen in 2.9% of cases which is consistent with the finding of Awal G et al., where the frequency was 3.4% and Biswal SG and Mehta RD where such reaction was present in 1.8% [Table/Fig-10] [8,20]. In our study, extravasation reaction was seen with Vincristine which is a vesicant drug.

Nail changes were present in 50% of cases. Diffuse hyperpigmentation of nail was present in 24.3% of cases, longitudinal melanonychia in 20%, and leukonychia in 5.3% of cases. Other findings observed were hand foot syndrome, figurate erythema (Erythema annularae centrifugum), pyogenic granuloma, vasculitis and lichenoid dermatitis.

Limitation(s)

Since, combination of chemotherapy drugs were used in the treatment of cancers, the adverse effects could not be attributed to a single drug in present study.

CONCLUSION(S)

The morbidities caused by malignancies are distressing by themselves. The adverse effects caused by the cancer chemotherapy drugs add to the distress. Hence, the knowledge of such adverse effects of chemotherapy drugs can help in their early recognition and treatment. Prophylactic therapies with close monitoring of these untoward events are vital to ensure patient compliance and maximise clinical benefit from optimal dosing of such drugs. This aids in improving the quality of life of these patients.

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