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RESEARCH ARTICLE

A Clinical Prospective Study of Chemotherapy-Induced Mucocutaneous Adverse Effects in Cancer Patients

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Abstract

Chemotherapy remains the mainstay of cancer management but is frequently accompanied by diverse mucocutaneous adverse effects due to its action on rapidly proliferating cells. These toxicities can range from mild cosmetic issues to severe reactions necessitating dose modification or discontinuation. This prospective observational study conducted at the Department of Dermatology, Government Coimbatore Medical College, systematically evaluated the prevalence, pattern, timing, and drug associations of mucocutaneous adverse reactions among 30 adult patients undergoing single or combination chemotherapy regimens over one year. Nail changes (73.3%), hair changes (50%), mucosal changes (10%) and cutaneous changes (63.3%) were the most common adverse effects, with higher rates than comparable studies like Pavey *et al.*[2]. Specific skin changes noted were xerosis, hand and foot syndrome, cutaneous extravasation, facial hyperpigmentation and supravenous hyperpigmentation. Specific nail changes were onycholysis and melanonychia. Hair changes included anagen effluvium, and mucosal changes included mucosal pigmentation. Early-onset reactions within the first 2-4 cycles were frequent. Proactive counselling, dermatological management, and patient education were effective in minimising morbidity and ensuring uninterrupted therapy. The study highlights the critical role of dermatology-oncology collaboration in holistic cancer care.

Keywords: Anagen Effluvium, Chemotherapy, Cutaneous Extravasation, Facial Hyperpigmentation, Hyperpigmentation, Melanonychia, Onycholysis, Supravenous

1. Introduction

Chemotherapy targets rapidly dividing malignant cells but lacks selectivity, affecting normal cells with high turnover, such as those in the skin, hair follicles, nails, and mucous membranes.

Consequently, mucocutaneous adverse reactions are among the most common non-haematological toxicities seen in oncology practice. These reactions may cause considerable physical discomfort, psychological stress, and cosmetic concerns, severely impacting a patient's quality of life and self-image. Globally, the prevalence of these reactions ranges from 60% to 85% depending on cancer type, drug class, and population studied[1,2]. Studies in India, such as those by Naveed *et al.*[1] and Pavey *et al.*[2], confirm that nail changes and alopecia are predominant, with combination regimens increasing both frequency and severity. In many cases, patients may refuse or delay treatment due to fear of disfigurement or stigma[3]. Therefore, early detection, multidisciplinary management, and preventive counselling are integral to comprehensive oncology care and better patient compliance.

2. Aim and Objectives

2.1 Aim

To study the various patterns, onset and timing of mucocutaneous adverse effects associated with specific chemotherapy regimens in cancer patients.

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2.2 Objectives

- To identify the frequencies and types of mucocutaneous adverse effects in cancer patients undergoing chemotherapy.
- To evaluate the onset and association between specific chemotherapy regimens and mucocutaneous adverse effects.

3. Review of Literature

Over the past two decades, there has been a significant evolution in chemotherapeutic options for cancer management. These drugs include traditional alkylating agents, antimetabolites, antitumor antibiotics, mitotic inhibitors, topoisomerase inhibitors, as well as targeted therapies such as EGFR inhibitors, tyrosine kinase inhibitors, multikinase inhibitors, mTOR inhibitors, proteasome inhibitors, and antiangiogenic agents. Because these agents target rapidly proliferating cells, they often cause adverse effects on the skin, hair, nails, and mucous membranes, making mucocutaneous toxicities some of the most common non-haematological side effects of cancer chemotherapy[1-3].

3.1 Cutaneous Adverse Effects

Toxic Erythema of Chemotherapy (TEC) is among the most significant skin reactions and includes conditions like palmar-plantar erythrodysesthesia (hand-foot syndrome), intertriginous eruptions, and neutrophilic eccrine hidradenitis[4].

Hand-foot syndrome is a well-documented adverse effect characterised by painful, well-demarcated erythematous rashes with oedema on the palms and soles, sometimes progressing to blistering and ulceration. Drugs most commonly implicated include doxorubicin, cytarabine, docetaxel, and fluorouracil. Sekine *et al.*[4] and Hofheinz *et al.*[5] highlighted that hand-foot syndrome is particularly common with capecitabine and liposomal doxorubicin and may be dose-limiting if not recognised early.

Papulopustular eruptions are more frequently observed with EGFR inhibitors, such as cetuximab, erlotinib, and gefitinib. Lacouture *et al.*[6] clearly described the high frequency of papulopustular rash, xerosis, and paronychia linked with this class of targeted therapy. Sibaud[7] also emphasised that newer targeted therapies require updated dermatological guidelines due to these specific skin toxicities.

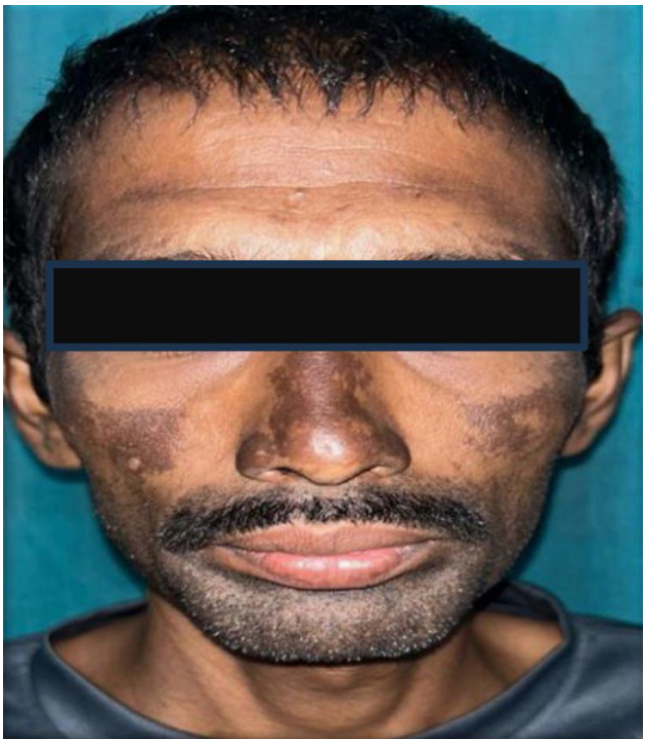

Figure 1. Melasma-like pigmentation.

Extravasation reactions, resulting in chemical cellulitis and ulceration, are common with agents such as anthracyclines, bendamustine, carmustine, vinblastine, vincristine, vinorelbine, and mitomycin C[8]. Hyperpigmentation that follows the path of veins, known as serpentine supravenous hyperpigmentation, has been described with fluorouracil, vinorelbine, and daunorubicin[7]. Similarly, flagellate hyperpigmentation, often due to bleomycin, presents as linear macular streaks that form a whip-like criss-cross pattern[8].

Other cutaneous reactions include chemotherapy-induced hypopigmentation, photosensitivity, and ulcerations from agents like hydroxyurea[8].

Supporting this, Naveed *et al.*[1] reported that skin changes occurred in 84.5% of patients, while Pavey *et al.*[2] found skin toxicities in 33.9% of their cohort, highlighting variations due to different regimens and populations.

3.2 Nail Changes

Onycholysis, caused by matrix damage, is the most frequent nail toxicity, seen with MEK, EGFR, and mTOR inhibitors[2,6]. These drugs can also lead to

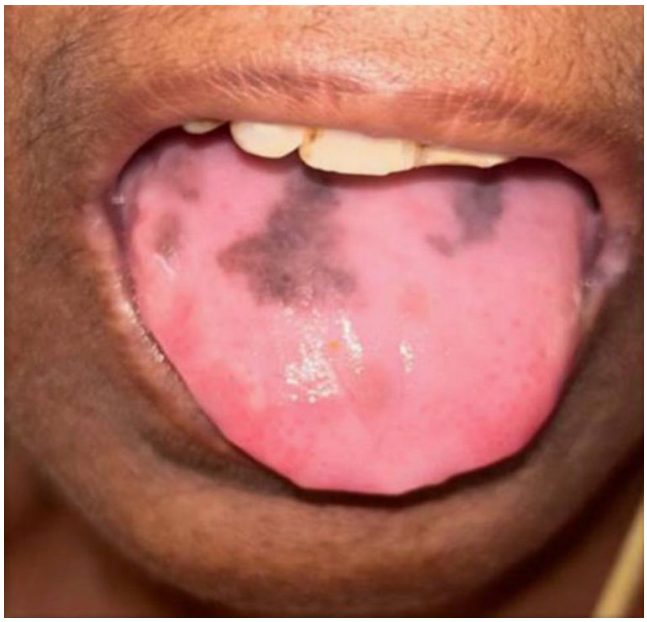

Figure 2. Mucosal pigmentation.

paronychia and periungual pyogenic granulomas due to periungual tissue inflammation.

Chromonychia (nail plate colour changes) is commonly reported with 5-fluorouracil, cyclophosphamide, daunorubicin, doxorubicin, hydroxyurea, methotrexate, and bleomycin[2].

In their large cohort, Naveed *et al.*[1] found nail changes in 85.8% of patients, while Pavey *et al.*[2] documented them in 62.2%, with melanonychia seen in 78.7% of these cases.

3.3 Hair Changes

Chemotherapy-Induced Alopecia (CIA) is one of the most common and psychologically distressing adverse effects of cancer treatment. It results from damage to the anagen phase hair follicles, also known as anagen effluvium. This is typically caused by antimicrotubule agents (paclitaxel, docetaxel), topoisomerase inhibitors (etoposide, doxorubicin), alkylating agents (cyclophosphamide, ifosfamide), and antimetabolites (5-fluorouracil)[1,2,6]. Susser *et al.*[3] emphasised that alopecia is one of the key reasons patients fear or even refuse chemotherapy.

Rarely, chemotherapy-induced hypertrichosis (excessive growth of scalp or body hair) and trichomegaly (excessive eyelash growth) are seen, commonly associated with EGFR inhibitors, interferon-α, cetuximab, erlotinib, and gefitinib[6].

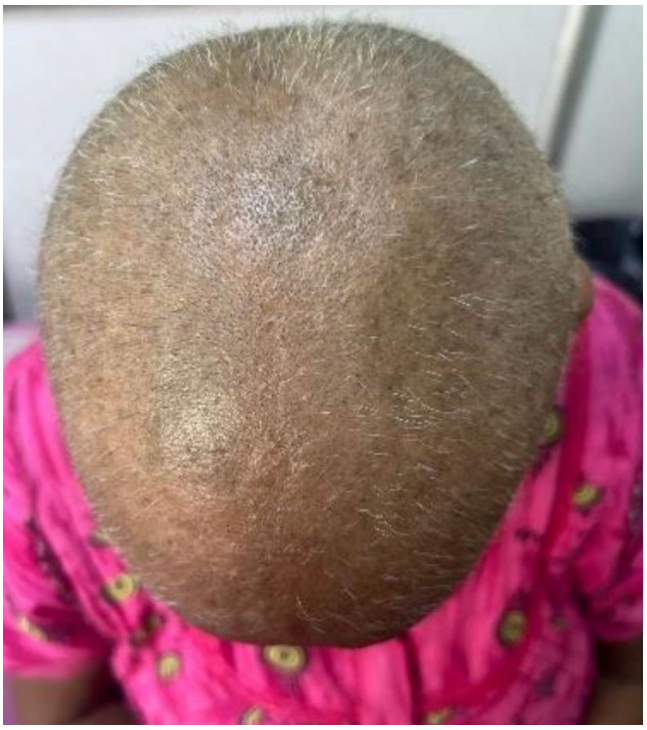

Figure 3. Anagen effluvium.

Naveed *et al.*[1] reported hair changes in 70.3% of patients, while Pavey *et al.*[2] found them in 37.7%, with anagen effluvium as the dominant pattern.

3.4 Mucosal Changes

Oral and gastric mucositis is another significant, dose-limiting side effect. It is especially associated with daunorubicin, doxorubicin, high-dose methotrexate, melphalan, topotecan, cyclophosphamide, taxanes, hydroxyurea, and continuous infusions of 5-fluorouracil[9]. Mucosal hyperpigmentation, often seen with busulfan, 5-fluorouracil, hydroxyurea, and cyclophosphamide, is also reported[9].

While mucosal changes are less common compared to skin, nail, or hair toxicities, Naveed *et al.*[1] found them in 15% of patients, while Pavey *et al.*[2] documented only 3.7%.

Together, these studies consistently demonstrate that although mucocutaneous adverse effects are rarely life-threatening, they contribute substantially to treatment-related morbidity, psychological stress, and can limit the patient's ability to tolerate optimal chemotherapy dosing if not recognised and managed appropriately[1-10]. Understanding the adverse effects of anti-cancer drugs is crucial for accurate diagnosis and management, ultimately enhancing the quality of life.

4. Materials and Methods

4.1 Study Design and Duration

This was a prospective, observational study conducted over 12 months from August 2024 to July 2025.

4.2 Study Setting

The study was carried out in the Department of Dermatology in collaboration with the Oncology Department at Government Coimbatore Medical College, a tertiary care centre in South India.

4.3 Study Population

A total of 30 adult patients diagnosed with various malignancies and undergoing chemotherapy were studied. Both inpatients and outpatients were included.

4.4 Inclusion Criteria

Patients aged ≥18 years of any gender.

Patients receiving at least one cycle of chemotherapy (single-agent or combination regimen). Patients who are willing to provide written informed consent.

4.5 Exclusion Criteria

Patients with pre-existing dermatological disorders affecting skin, hair, nails, or mucosa.

Patients with mucocutaneous conditions unrelated to chemotherapy, patients on radiotherapy and patients who did not complete at least one follow-up visit after chemotherapy initiation.

4.6 Data Collection

A detailed baseline dermatological and mucosal examination was performed prior to starting chemotherapy to document pre-existing conditions.

Patients were examined at each chemotherapy visit for any new or worsening mucocutaneous reactions.

Adverse effects were recorded systematically: type, site, severity, cycle number, and suspected drug.

4.6.1 Parameters Assessed

Demographic details (age, gender, diagnosis). Type and regimen of chemotherapy.

Onset and timing of mucocutaneous adverse effects (early: ≤2 cycles; mid: 3-4 cycles; late: >4 cycles).

4.7 Statistical Analysis

Data was entered into Microsoft Excel and analysed using SPSS version 20.0. Descriptive statistics were used for frequency and percentage calculations.

Associations between demographic factors, drug regimens, and adverse effects were assessed using the Chi-square test or Fisher's exact test, with $p<0.05$ considered statistically significant.

5. Results (Including Observations)

5.1 Demographic Distribution

Out of the total 30 patients, 19 (63.3%) were males and 11 (36.7%) were females. The mean age of male patients was 44.3 years, while the mean age of female patients was slightly higher at 48.2 years.

5.2 Distribution of Primary Malignancies

Breast cancer was the most common, affecting 8 patients (26.7%). Non-Hodgkin lymphoma was the second most frequent malignancy with 5 patients (16.7%), followed by carcinoma buccal mucosa, carcinoma ovary, and carcinoma lung, each observed in 4 patients (13.3%).

5.3 Adverse Effects Observed

Nail changes were the most prevalent, seen in 22 patients (73.3%), followed by skin changes in 18 patients (63.3%). Hair changes were reported in half of the patients (50%), while mucosal changes were the least common, seen in

Table 1. Demographic distribution

Gender	Number of patients (percentage)	Mean age (Years)
Male	19(63.3%)	44.3
Female	11(36.7%)	48.2

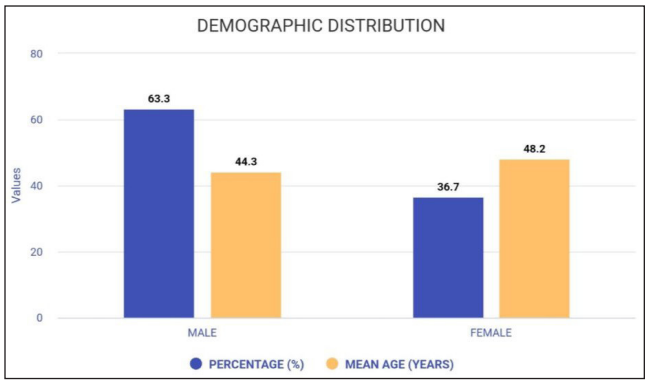

Chart 1. Demographic distribution.

Table 2. Distribution of primary malignancies

Type of malignancy	Number of patients (percentage)
CA breast	8(26.7)
CA buccal mucosa	4(13.3)
CA tongue	2(6.7)
CA colon	3(10)
CA ovary	4(13.3)
CA lung	4(13.3)
Non-hodgkins lymphoma	5(16.7)

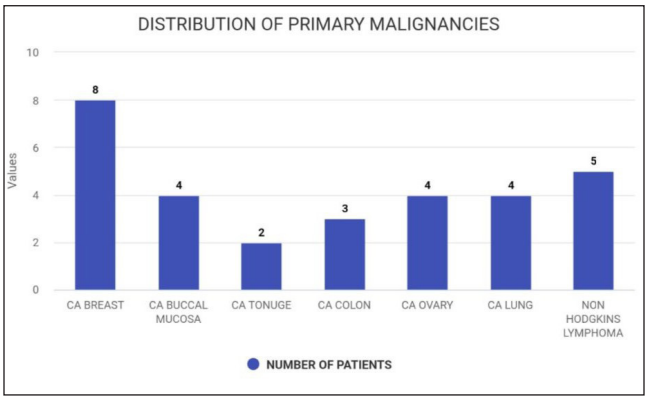

Chart 2. Distribution of primary malignancies.

Table 3. Adverse effects observed

Adverse effect	Number of patients (percentage)
Nail changes	22(73.3)
Skin changes	18(63.3)
Hairchanges	15(50)
Mucosal changes	3(10)

only 3 patients (10%). This indicates that nail and skin toxicities were the dominant chemotherapy-induced adverse effects in this group. Specific Skin Changes Xerosis (dry skin) was the most frequently reported skin manifestation, found in 10 patients (33.3%). Hand-foot syndrome was seen in 3 patients (10%), supravenous hyperpigmentation was seen in 3 patients (10%). While cutaneous extravasation of chemotherapy and facial hyperpigmentation were each noted in one patient (3.3%).

5.4 Specific Nail Changes

Onycholysis (nail separation) was the most common nail change, observed in 12 patients (54%). Melanonychia (nail pigmentation) was seen in 10 patients (45.4%).

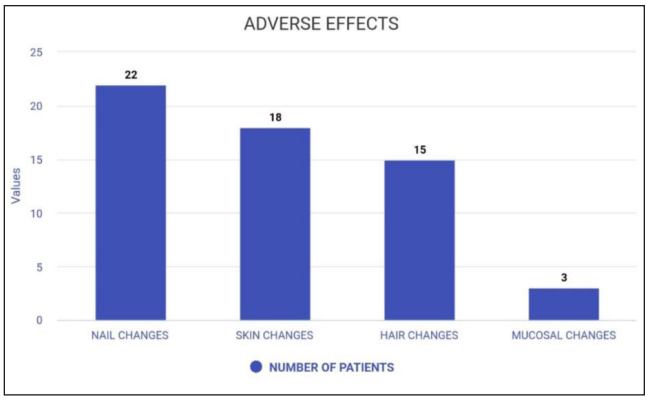

Chart 3. Adverse effects.

Table 4. Specific skin changes

Skin findings	Number of patients (percentage)
Xerosis	10(33.3)
Hand foot syndrome	3(10)
Cutaneous extravasation	1(3.3)
Facial hyperpigmentation	1(3.3)
Superavenous hyperpigmentation	3(10)

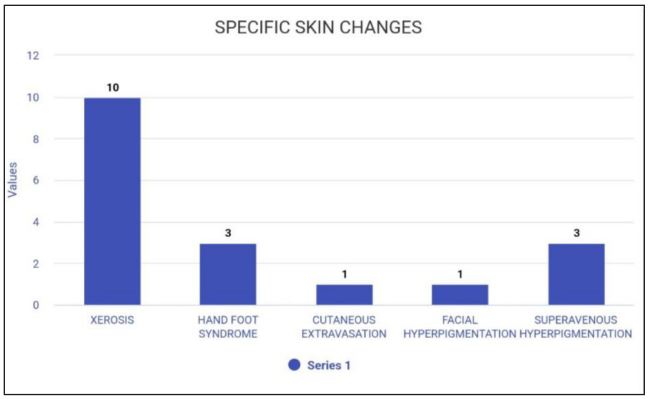

Chart 4. Specific skin changes.

Table 5. Specific nail changes

Nail findings	Number of patients (percentage)
Onycholysis	12(54)
Melanonychia	10(45.4)

5.5 Specific Hair and Mucosal Changes

All hair changes were in the form of anagen effluvium (chemotherapy-induced hair loss), affecting 15 patients (50%). Mucosal changes were limited to tongue pigmentation, which was seen in 3 patients (10%).

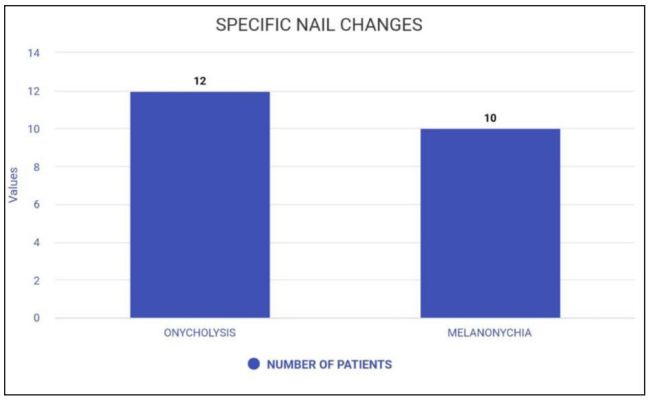

Chart 5. Specific nail changes.

Table 6. Specific hair and mucosal changes

Finding	Number of patients (percentage)
Anagen effluvium (hair)	15(50)
Tongue pigmentation	3(10)

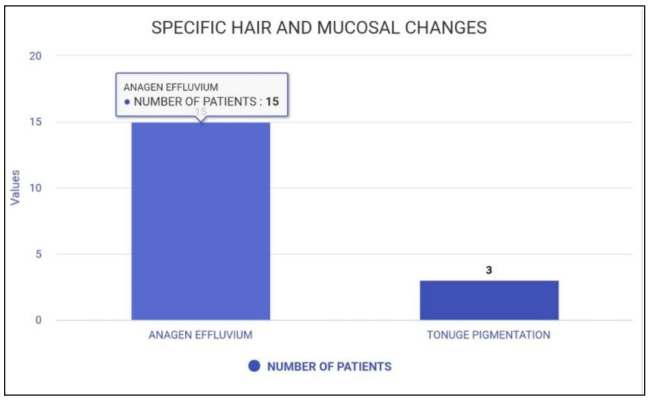

Chart 6. Specific hair and mucosal changes.

5.6 Onset and Timing of Mucocutaneous Adverse Effects

The mucocutaneous reactions associated with various drugs included xerosis occurring in the 3rd-4th cycle with Cetuximab and EGFR inhibitors, hand and foot syndrome in the 1st cycle from Dasatinib and Cytarabine, Capacetabine, Gemcitabine + carboplatin, cutaneous extravasation in the 1st cycle due to ABVD regimen, supravenous hyperpigmentation in the 2nd cycle from the Paclitaxel + carboplatin and facial pigmentation in the 2nd cycle with Imatinib. Additionally, onycholysis is noted in the 4th cycle from Capecitabine, EGFR inhibitors and taxanes, melanonychia occurs in the 3rd cycle with Paclitaxel and Carboplatin, CHOP regimen, anagen effluvium is seen 1 month after using Paclitaxel, doxorubicin, CHOP regimen and mucosal pigmentation develops within 20 days from Hydroxyurea.

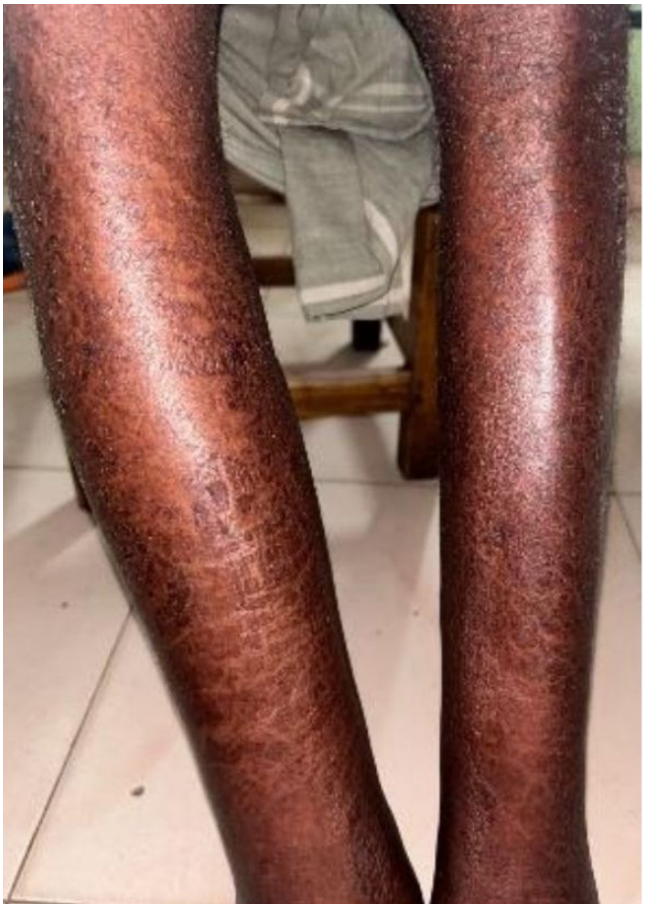

Figure 4. Xerosis.

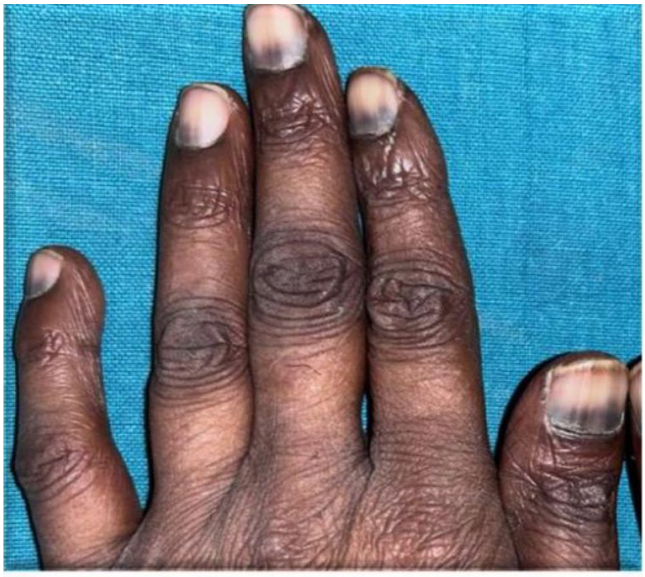

Figure 5. Nail dyspigmentation.

Table 7. Onset and timing of mucocutaneous adverse effects

Mucocutaneous reaction	Time of onset	Causative drug
Xerosis	3-4thcycle	Cetuximab, EGFR inhibitors
Hand and foot syndrome	1st cycle	Dasatinib + cytarabine, Capecitabine, Gemcitabine + carboplatin
Cutaneous extravasation	1st cycle	ABVD regimen,
Supravenous hyperpigmentation	2nd cycle	Paclitaxel + carboplatin
Facial pigmentation	2nd cycle	Imatinib
onycholysis	4th cycle	Capecitabine, taxanes, EGFR inhibitors
Melanonychia	3rd cycle	Paclitaxel+ carboplatin, CHOP regimen
Anagen effluvium	1 month	Paclitaxel , doxorubicin , CHOP regimen
Mucosal pigmentation	20 days	Hydroxyurea

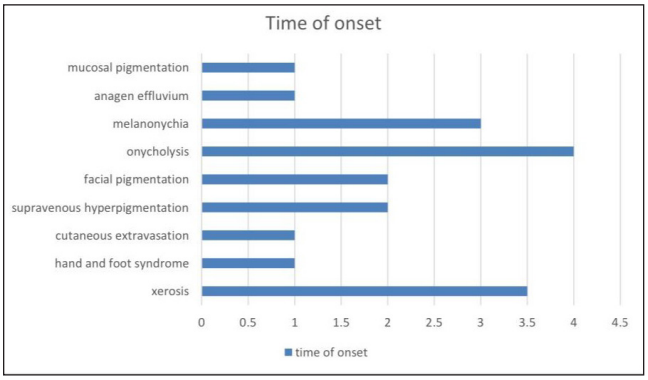

Chart 7. Time of onset.

6. Discussion

6.1 Demographics

In our study, males constituted 63.3% with a mean age of 44.3 years, while females accounted for 36.7% with a slightly higher mean age of 48.2 years. This male predominance is comparable to the observations by Naveed *et al.*[1], who also noted a higher proportion of male patients in their study from an Indian tertiary care setting. This reflects the regional cancer profile, especially the high burden of tobacco-related head and neck cancers in men.

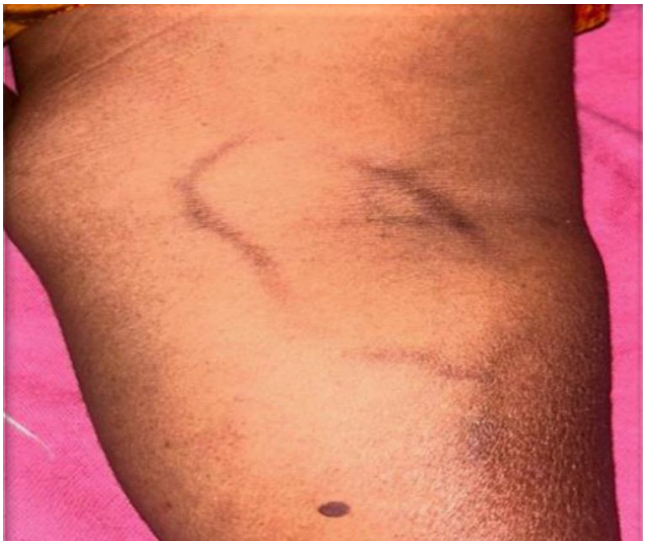

Figure 6. Serpentine supravenous hyperpigmentation.

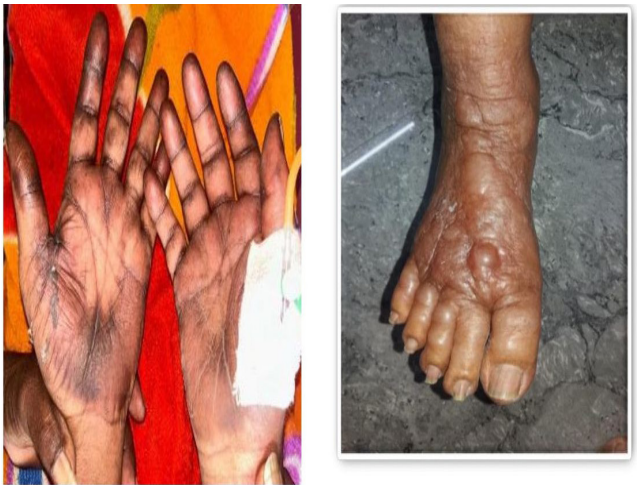

Figure 7. Hand and foot reaction.

6.2 Primary Malignancies

Breast cancer was the most common primary malignancy in this study (26.7%), followed by non-Hodgkin lymphoma (16.7%), carcinoma buccal mucosa, ovary, lung, colon, and tongue. This distribution aligns with Pavey *et al.*[2], who also reported breast and gastrointestinal malignancies as frequent indications for chemotherapy, reflecting the common cancer trends in India and globally.

6.3 Overall Mucocutaneous Adverse Effects

Nail changes were the most frequent adverse effect, observed in 73.3% of patients, followed by skin changes (63.3%), hair changes (50%), and mucosal changes (10%).

These findings are comparable to those of Naveed *et al.*[1], who reported nail changes in 85.8% and skin changes in 84.5% of patients. Pavey *et al.*[2] documented slightly lower rates of nail (62.2%) and skin changes (33.9%), which may be due to differences in patient ethnicity, chemotherapy protocols, or drug combinations used.

6.4 Specific Skin Changes

Xerosis was the most common skin manifestation (33.3%), followed by hand-foot syndrome (10%). Other presentations, like cutaneous extravasation, facial hyperpigmentation, and supravenous hyperpigmentation, were also noted. Similar patterns have been described by Lacouture *et al.*[6], who highlighted xerosis and papulopustular rash as common reactions, particularly with Epidermal Growth Factor Receptor (EGFR) inhibitors. Hand-foot syndrome, predominantly linked with capecitabine and liposomal doxorubicin, was reported in 10% of our patients, aligning with findings by Sekine *et al.*[4] and Hofheinz *et al.*[5], who emphasised its dose-limiting potential if not recognised early.

Cutaneous extravasation and supravenous hyperpigmentation are well described with vesicant drugs like anthracyclines, vinblastine, and 5-fluorouracil[7]. Flagellate hyperpigmentation due to bleomycin and pigmentary changes related to imatinib are also documented[7,8].

6.5 Specific Nail Changes

Onycholysis (54%) and melanonychia (45.4%) were the most prevalent nail toxicities in our study. Pavey *et al.*[2] similarly reported melanonychia in 78.7% of patients with nail involvement, reinforcing the known association between drugs like taxanes (paclitaxel, docetaxel) and nail dystrophies. Onycholysis is common with MEK, EGFR, and mTOR inhibitors due to matrix damage[6,7].

6.6 Hair Changes

Anagen effluvium was seen in 50% of patients in our study, which is in line with the 70.3% reported by Naveed *et al.*[1] and the 37.7% reported by Pavey *et al.*[2]. Hair loss remains one of the most distressing chemotherapy-induced side effects, often leading to significant psychological impact, as emphasised by Susser *et al.*[3]. Rarely, chemotherapy-induced hypertrichosis and trichomegaly can occur, especially with EGFR inhibitors and TKIs[6].

6.7 Mucosal Changes

Mucosal involvement was infrequent, limited to tongue pigmentation in 10% of patients. This is comparable to the 3.7% mucosal changes documented by Pavey *et al.*[2]. Sonis[9] highlights that mucositis remains an important dose-limiting factor in patients receiving drugs like methotrexate, fluorouracil, and anthracyclines.

7. Onset and Timing of Mucocutaneous Adverse Effects

Table 7 presents the relationship between the timing of onset of mucocutaneous adverse effects and the specific chemotherapy regimens used.

In this study, xerosis was most commonly noted in patients on cetuximab and EGFR inhibitors, typically appearing around the 3rd-4th cycle. This pattern is well documented by Lacouture *et al.*[6] Sibaud[8] emphasised that xerosis and papulopustular rash are hallmark reactions of EGFR inhibitors, occurring within the first few weeks of therapy. A recent study by Langer *et al.*[10] similarly found that xerosis peaks during the second month of EGFR blockade and can become chronic if not managed with prophylactic emollients.

Hand-foot syndrome was seen with dasatinib and cytarabine, Capacetabine, Gemcitabine + carboplatin, manifesting by the 1st cycle. Hand-foot syndrome is widely recognised with capecitabine, cytarabine, liposomal doxorubicin, and multikinase inhibitors like sorafenib. Recent data by Saif *et al.*[11] states that the timing of such reactions aligns with cumulative drug exposure, often worsening with each cycle and requiring dose adjustments or treatment breaks.

Cutaneous extravasation, which can appear as early as the first cycle in an ABVD regimen, underscores the well-known vesicant nature of anthracyclines. Recent consensus from the European Oncology Nursing Society[12] stresses that prompt detection and immediate local measures can prevent deep tissue necrosis and chronic ulceration.

Supravenous hyperpigmentation appeared in a patient on paclitaxel + carboplatin, during the 2nd cycle, consistent with older reports and reinforced by Ho *et al.*[13], who described similar patterns with

fluorouracil, taxanes, and anthracyclines, particularly when administered via peripheral veins.

Facial hyperpigmentation was seen with imatinib by the 2nd cycle. Recent evidence by Ockenfels *et al.*[14] confirms that imatinib-induced pigmentary changes can appear within weeks due to its direct effect on melanocyte signalling pathways.

Onycholysis, recorded during the 4th cycle with capecitabine, taxanes, and EGFR inhibitors, reflects the classic nail matrix toxicity described for taxanes and EGFR inhibitors. Sekulic *et al.*[15] detailed that taxane-related nail changes are dose-dependent, cumulative, and can require treatment modification in severe cases.

Melanonychia, emerging by the 3rd cycle in patients on paclitaxel, carboplatin, CHOP regimen, aligns with studies showing that these agents can stimulate melanocyte activity within the nail matrix[2,16]. This highlights the need for patient counselling, as patients may mistake pigmentation for a fungal infection.

Anagen effluvium, seen within 1 month of paclitaxel initiation, is a well-known abrupt hair loss pattern seen with antimicrotubule agents. Trüeb[17] confirms that nearly 65-80% of patients on taxanes experience significant hair loss within the first cycle due to mitotic arrest of hair matrix keratinocytes.

Mucosal pigmentation, detected within 20 days of starting hydroxyurea, aligns with reports by Gambichler *et al.*[18], who described hydroxyurea-induced oral pigmentation and tongue discolouration as dose-related and reversible with discontinuation.

Overall, this study's timing data emphasises that:

Early toxicities like extravasation and alopecia need pre-treatment education.

Mid-cycle events like xerosis, pigmentary changes, and nail changes require ongoing dermatological monitoring.

Dose adjustments and supportive care must be initiated proactively to avoid treatment interruptions.

The importance of early recognition, patient counselling, and multidisciplinary dermatology-oncology care is well supported by these global findings[1-18].

8. Summary

- Out of the 30 patients, 19 patients were males with a mean age of 44.3 years, and 11 patients were females with a mean age of 48.2 years.
- Breast cancer was seen in 8 patients, ca buccal mucosa in 4 patients, ca tongue in 2 patients, non-Hodgkin lymphoma in 5 patients, ca colon in 3 patients, ca ovary in 4 patients, ca lung in 4 patients.
- The most common adverse effects observed in the study were nail changes in 22 (73.3%) patients, followed by skin changes in 18 (63.3%) patients, hair changes in 15 (50%) patients, and mucosal changes in 3 (10%) patients.
- Most common skin changes included xerosis (33.3%), followed by hand-foot syndrome (10%), supravenous hyperpigmentation (10%), cutaneous extravasation of chemotherapy and facial hyperpigmentation in one patient each.
- The most common nail findings were onycholysis in 12 (54%) patients and melanonychia in 10 (45.4%) patients.
- Hair changes were in the form of anagen effluvium, seen in 15 (50%) patients.
- Mucosal changes included pigmentation of the tongue in 3 patients.
- Early cycle reactions were Hand and Foot syndrome, cutanrous extravasation and facial pigmentation.
- Mid-cycle reactions were xerosis, mucosal pigmentation, and anagen effluvium.
- Late cycle reactions were onycholysis and melanonychia.

9. Conclusion

Our study highlights the high prevalence and varied spectrum of mucocutaneous adverse effects among patients receiving chemotherapy at a tertiary care centre in South India. Notably, most reactions manifested within the first four cycles, emphasising the need for early intervention and patient counselling from the first visit. Our findings demonstrate that while these reactions are not life-threatening, they can cause significant psychosocial distress, treatment interruptions, or refusal if not addressed promptly. Dermatologist involvement, anticipatory guidance, and supportive care measures—such as scalp cooling, emollients, and nail care—can greatly mitigate morbidity and enable patients to complete planned chemotherapy regimens without unnecessary modifications. Thus, early diagnosis, patient counselling, and close dermatology-oncology collaboration remain vital for comprehensive cancer care.

10. References

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