Brief Report

# Nail Changes Caused by Chemotherapy among Cancer Patients: A Cross-Sectional Study of Northwest Rajasthan

**Madhvi Trivedi, R. D. Mehta, H. S. Kumar, B. C. Ghiya, Prasoon Soni, Manish Kumar Meena, Vineet Kumar, S Rekha**

*Department of Dermatology, Venereology and Leprosy, Sardar Patel Medical College, Bikaner, Rajasthan, India*

## Abstract

**Background:** The nail changes caused by chemotherapy in cancer patients are difficult to assess and often overlooked by clinician. The present study was undertaken to study nail changes caused by various chemotherapeutic agents and various drug protocols most commonly associated with them. **Materials and Method:** Five hundred patients with malignancies receiving chemotherapy in the oncology ward and skin outpatient department were screened in this cross-sectional observational study from November 2018 to October 2019. **Results:** Nail changes due to chemotherapy were observed in 37.6% patients. The most common condition observed was melanonychia (84.04%), followed by half and half nails (6.91%), erythronychia (5.31%), longitudinal grooves (2.12%), leukonychia (2.12%), Mees' lines (1.59%), Beau's lines (0.53%), pitting (0.53%), and subungual hyperkeratosis (0.53%). The usual protocol to cause melanonychia was platinum analogues + taxanes based combinations, half and half nails by platinum analogues + taxanes + 5 fluorouracil (5FU) based polypharmacy, and erythronychia by cisplatin-based adjuvants. **Conclusion:** The knowledge of the nail changes caused by chemotherapy will help in counseling of already worried patients with malignancy. It will also improve patient compliance and enrich the clinicians' knowledge pertaining to chemotherapy-induced nail changes.

**Keywords:** *Chemotherapy, melanonychia, nail changes*

## Introduction

New chemotherapeutic agents have improved the survival rate in patients with malignancy. The use of traditional as well as newer antimalignant agents is associated with cutaneous side effects affecting skin, hair, and nails.[1] These effects are rarely fatal but may result in significant morbidity, cosmetic disfigurement, and psychological distress.[2] The aim of our study is to identify various nail changes and the frequency of their association with the protocols of chemotherapeutic agent(s).

## Materials and Method

A cross-sectional (observational) study was conducted after seeking permission from Institutional Ethics and Research Board of our college. The study was conducted for a period of 12 months from November 2018 to October 2019 and included 500 patients of different malignancies receiving chemotherapy. All the patients with definite past history of nail diseases, who had cutaneous disease-causing nail changes and with occupations which could cause nail changes, were excluded in our study. After obtaining written informed consent, detailed history was taken regarding chemotherapeutic agents and patients were screened for nail changes. Photographs of nails were taken. The data was collected in proforma (attached) and master chart was prepared from the collected data using MS Excel.

## Results

Out of a total 500 patients, 251 (50.2%) were males and 249 (49.8%) were females. The mean age was 52.45 ± 16.06 years (range: 7–85 years). They had 45 different types of malignancies, out of which the most common was carcinoma of head and neck region in 135 (27%) patients, followed by genitourinary carcinoma in 83 (16.6%) patients. Nail changes *per se* due to chemotherapy were observed in 188 (37.6%) patients. The incubation period from the start of the chemotherapeutic agent and the onset of nail changes ranged



**How to cite this article:** Trivedi M, Mehta RD, Kumar HS, Ghiya BC, Soni P, Meena MK, *et al.* Nail changes caused by chemotherapy among cancer patients: A cross-sectional study of Northwest Rajasthan. Indian Dermatol Online J 2020;11:953-8.

**Received:** 19-Feb-2020. **Revised:** 27-Mar-2020. **Accepted:** 21-May-2020. **Published:** 19-Sep-2020

***Address for correspondence:***
*Dr. R. D. Mehta, 6-C-128 JNV Colony, Bikaner, Rajasthan, India.*
*E-mail: mehtarddr@yahoo.co.in*

**Access this article online**

**Website:** www.idoj.in

**DOI:** 10.4103/idoj.IDOJ_84_20

**Quick Response Code:**

from 3 to 6 weeks, with a median of 4 weeks. There were 9 different types of nail changes [Figures 1-6], out of which melanonychia was the most common nail change observed in 158 (84.04%) patients, followed by half and half nails in 13 (6.91%) patients. The various nail changes caused by chemotherapeutic agents and their frequency distribution to various drug protocols are tabulated in Tables 1-4.

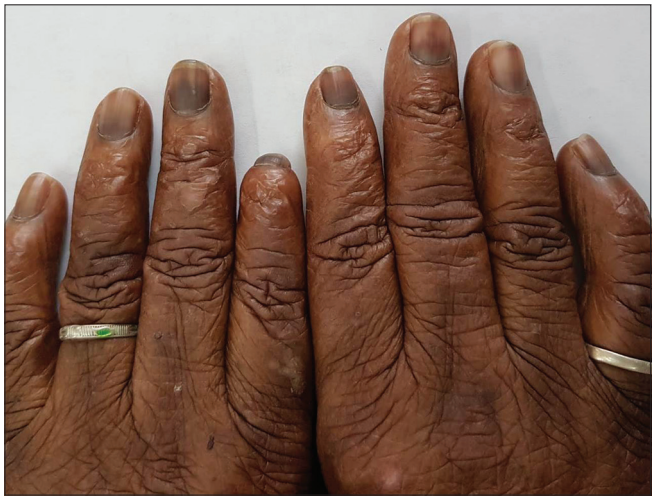

**Figure 1: Showing diffuse melanonychia of all finger nails due to cisplatin + paclitaxel combination chemotherapy**

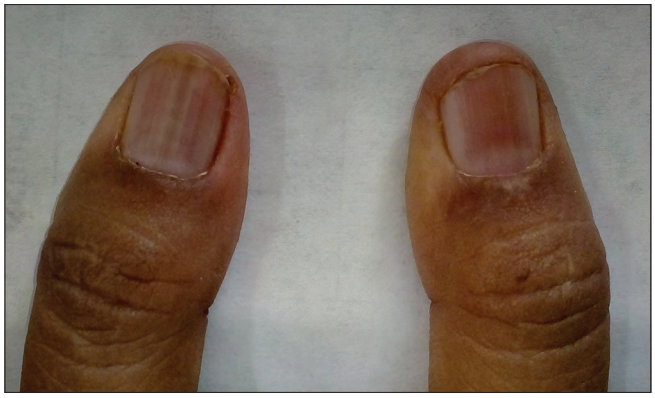

**Figure 3: Showing longitudinal erythronychia of both thumb nails due to cisplatin**

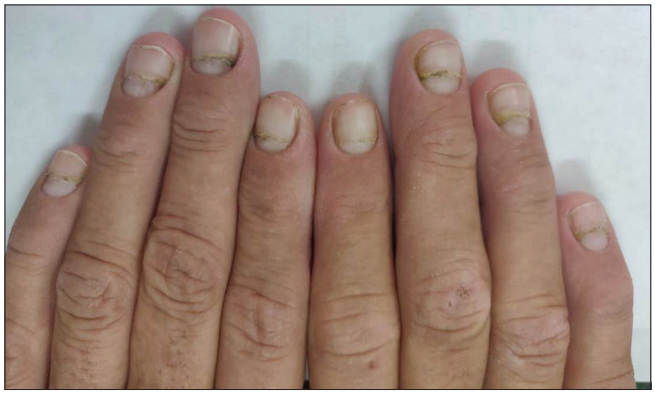

**Figure 5: Showing Beau's lines in all finger nails due to paclitaxel + carboplatin combination chemotherapy protocol**

## Discussion

Chemotherapeutic agents individually or in combination cause cutaneous adverse effects including nail changes, which cause cosmetic disfigurement and worsen the quality of life of the patient. Therefore, proper knowledge of these

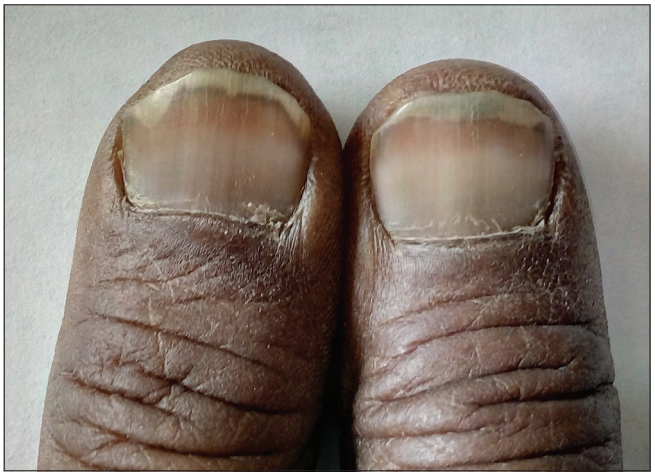

**Figure 2: Showing half and half nails of both thumb nails due to cisplatin + paclitaxel + 5FU based protocol**

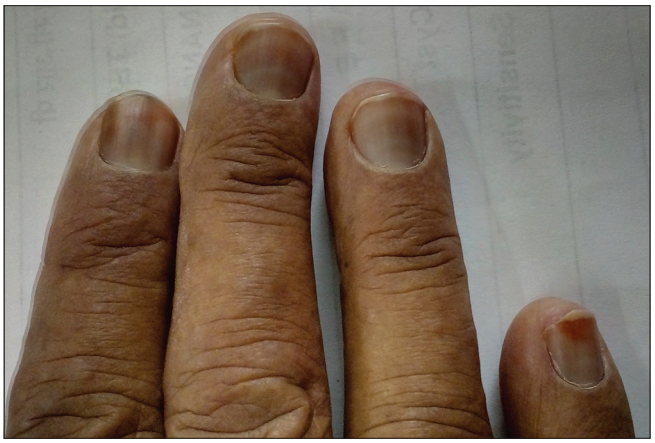

**Figure 4: Showing Mees' lines in second and third finger nails due to paclitaxel + 5 fluorouracil + doxorubicin + cyclophosphamide + trastuzumab combination chemotherapy**

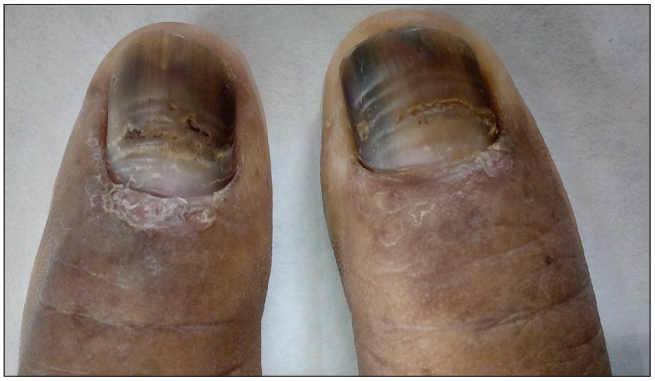

**Figure 6: Showing Beau's lines with melanonychia in both thumb nails due to paclitaxel + 5 fluorouracil + doxorubicin + cyclophosphamide + trastuzumab combination chemotherapy**

nail changes will help in counseling of patients by the clinician and thus will improve patient compliance.

Nail changes were observed in 188 (37.6%) patients in our study. Among these 188 patients, 101 (52.53%) were males and 87 (47.46%) were females. In the study conducted by Pavey *et al*. on 53 patients, nail changes were observed in 33 (62.2%) patients,[3] whereas Praveen Kumar *et al*. observed nail changes in 50/150 (33.33%) patients which is at par with our observation, i.e., 37.6%.[4]

Our study revealed melanonychia as the most common change observed in 158 (84.04%) patients, followed by half and half nails in 13 (6.91%) patients and erythronychia in 10 (5.31%) patients. Longitudinal grooves and leukonychia were seen in 4 (2.12%) patients each and Mees' lines were observed in 3 (1.59%) patients. Beau's lines, pitting, and subungual hyperkeratosis were specified in 1 (0.53%) patient each.

Pavey *et al*. also found melanonychia to be the most common nail change caused by chemotherapy in 26 (78.7%) patients followed by Muehrcke's lines, Mees' lines, and Beau's lines.[3] In the study conducted by Praveen Kumar *et al*., pigmentary nail changes were the most common nail changes similar to our observation.[4]

On analysis of the chemotherapy protocol of the patients with melanonychia in our study, we found that 63/158 (39.87%) patients received platinum analogues + taxanes based regimens followed by platinum analogues + 5FU based combinations in 19/158 (12.02%) and platinum analogues alone in 12/158 (7.59%) patients. Thus, we sum up that melanonychia was frequently seen in patients receiving combination chemotherapy protocol comprising of platinum analogues and taxanes.

Other patients with melanonychia in our study received platinum analogues (oxaliplatin) + folinic acid + 5 FU (FOLFOX) based combinations [9/158 (5.69%)], platinum analogues + antimetabolites (gemcitabine/capecitabine) based combinations [5/158 (3.16%)], platinum analogues + etoposide based combinations [3/158 (1.89)], and platinum analogues + doxorubicin based combinations [2/158 (1.26%)]. Hence, we are prompted to state that platinum analogues are the common agents in most of the combination chemotherapy protocols causing melanonychia.

Other combination chemotherapy protocols like taxanes + 5FU + daunorubicin/doxorubicin + nitrogen mustard (cyclophosphamide/ifosfamide) also led to melanonychia in 28/158 (17.72%) patients and vinca alkaloids + doxorubicin/daunorubicin + dactinomycin/ nitrogen mustard-based regimens in 10/158 (6.32%) patients.

Pavey *et al*. also commented that patients who developed melanonychia received platinum analogues (cisplatin), platinum analogues (carboplatin) + taxanes (paclitaxel) combination, vincristine + daunorubicin and cyclophosphamide + doxorubicin based combinations, which is at par with our observation.[3]

Praveen Kumar *et al*. observed longitudinal pigmentary bands in 67.7% patients following chemotherapy with platinum analogues and in 16.1% patients following CHOP [cyclophosphamide, hydroxydaunorubicin (doxorubicin), oncovin (vincristine), prednisone] regimen. Diffuse pigmentation of nails was the most common nail plate change seen in their study in

**Table 1: Frequency of nail changes caused by chemotherapy**

| Nail changes | Number of patients *n*=188 | Percentage |
|---|---|---|
| Melanonychia | 158 | 84.04 |
| Half and half nails | 13 | 6.91 |
| Erythronychia | 10 | 5.31 |
| Longitudinal grooves | 4 | 2.12 |
| Leukonychia | 4 | 2.12 |
| Mees' lines | 3 | 1.59 |
| Beau's lines | 1 | 0.53 |
| Pitting | 1 | 0.53 |
| Subungual hyperkeratosis | 1 | 0.53 |

**Table 2: Number of patients developing melanonychia with different chemotherapy combinations**

| Chemotherapy protocol | Number of patients with melanonychia *n*=158 | Percentage |
|---|---|---|
| Platinum analogues + taxanes based combinations | 63 | 39.87 |
| Platinum analogues + 5 Fluorouracil based combinations | 19 | 12.02 |
| Platinum analogues | 12 | 7.59 |
| Folinic acid + 5 Fluorouracil + oxaliplatin (FOLFOX) based combinations | 9 | 5.69 |
| Platinum analogues + antimetabolites (gemcitabine/capecitabine) | 5 | 3.16 |
| Platinum analogues + etoposide | 3 | 1.89 |
| Platinum analogues + doxorubicin | 2 | 1.26 |
| Taxanes + 5 Fluorouracil + daunorubicin/doxorubicin + nitrogen mustard (cyclophosphamide/ifosfamide) based combinations | 28 | 17.72 |
| Vinca alkaloids (vincristine/vinblastine) + doxorubicin/daunorubicin/ dactinomycin/nitrogen mustard-based combinations | 10 | 6.32 |
| Others | 7 | 4.43 |

**Table 3: Number of patients developing half and half nails with different chemotherapy regimens**

| Chemotherapy protocol | Number of patients with half and half nails *n*=13 | Percentage |
|---|---|---|
| Platinum analogues + taxanes + 5 FU | 5 | 38.46 |
| Platinum analogues | 4 | 30.76 |
| Platinum analogues + taxanes | 1 | 7.69 |
| Platinum analogues + 5 FU | 1 | 7.69 |
| Others | 2 | 15.38 |

**Table 4: Number of patients developing erythronychia with different chemotherapy groups**

| Chemotherapy protocol | Number of patients with erythronychia *n*=10 | Percentage |
|---|---|---|
| Cisplatin (platinum analogue) | 2 | 20 |
| Cisplatin + 5 FU | 2 | 20 |
| Cisplatin + 5 FU + paclitaxel (taxanes) | 2 | 20 |
| Cisplatin + paclitaxel±methotrexate | 2 | 20 |
| Others | 2 | 20 |

16.1% patients following chemotherapy with taxanes.[4] Falkson and Schulz in their study on patients treated with 5 FU observed melanonychia in 14/64 (21.85%) patients.[5] In the study conducted by Pratt and Shanks on patients receiving doxorubicin alone or in combination with other agents, 5 out of 13 patients developed hyperpigmentation of nails.[6] These findings are in concurrence to the findings of our study. However, exact cause of melanonychia is not known. Postulated mechanisms include accumulation of drug in skin and nail which causes toxic effect on melanocytes in nail matrix leading to increase melanin production. An increase in ACTH (adrenocorticotropic hormone) and MSH (melanocyte-stimulating hormone) also stimulates pigment production.[7-11]

On enquiring the patients with half and half nails, we found that 5/13 (38.46%) patients had received platinum analogues + taxanes + 5FU based combinations followed by platinum analogues alone in 4/13 (30.76%) patients and regimen of platinum analogues with taxanes and 5FU, respectively, in 1/13 (7.69%) patient each. The platinum analogues are the common agents in the combination chemotherapy protocol causing half and half nails, as per our result analysis, whereas Afsar *et al*. reported the development of half and half nails with modified Berlin-Frankfurt-Munster protocol (vincristine, daunorubicin, prednisone, L-asparaginase, cyclophosphamide, cytosine arabinoside, and 6-thioguanine) followed by maintenance therapy with methotrexate and 6 mercaptopurine.[12] In half and half nails, the proximal part is white and distal part (20%–60%) is brownish with sharp demarcation. Histopathological examination reveals increased vessel wall thickness and melanin deposition in the distal portion of nail.[13] The brownish discoloration of distal portion of nail is due to melanin deposition which is seen as a result of insult to the nailbed melanocytes.[14]

The study at our center showed that out of 10 patients with erythronychia, 2 (20%) had received cisplatin, 2 got cisplatin + 5 FU, 2 were on cisplatin + 5FU + paclitaxel regimen, and 2 had received cisplatin + paclitaxel ± methotrexate. In all these chemotherapy groups, cisplatin was the common agent causing erythronychia. Chang *et al*. also reported erythronychia in a patient who had received cisplatin for testicular tumor.[15]

All the 4 (2.12%) patients who developed longitudinal grooves in our study had received carboplatin + paclitaxel based combinations. This observation is similar to the findings of the study conducted by Praveen Kumar *et al*. in which longitudinal grooves were seen in 58% patients treated with platinum analogues and taxanes.[4] Longitudinal grooves are produced due to damage to proximal germinative matrix.[16]

We observed leukonychia in 4 (2.12%) patients who received different chemotherapeutic protocols like FOLFOX (folinic acid, 5FU, oxaliplatin) regimen, cisplatin + 5FU, carboplatin + paclitaxel, and CHOP regimen-based combinations. Out of these 4 patients, 1 patient had transverse leukonychia. Similarly, Praveen Kumar *et al*. in their study found leukonychia in 3.2% cases and was seen in patients treated with oxaliplatin.[4] Chapman and Cohen commented that there is no specific chemotherapeutic drug or drug class that causes transverse leukonychia; however, cyclophosphamide, doxorubicin, and vincristine may be most commonly involved drugs.[17] True leukonychia is produced by defect in nail matrix. The opaque white appearance of nail plate is due to disorganization of keratin fibrils and diffraction of light.[18]

Three patients (1.59%) in our study developed Mees' lines, out of which 2 patients had received platinum analogues + taxanes based combinations and 1 patient had received cyclophosphamide + doxorubicin based combinations. Gupta *et al*. observed Mees' lines in a patient who received daunorubicin + cytarabine + methot rexate + thioguanine + etoposide.[9] Sunil Kumar *et al*. noticed Mees' lines in a patient who received cytarabine + daunorubicin combination.[19] Beau's lines were observed in 1 patient in our study who received carboplatin + gemcitabine. Slee reported the development of Beau's lines in patient treated with docetaxel.[20] Our result analysis revealed pitting of nails in a single patient who had received 5FU + cisplatin + doxorubicin.

We found more than one nail changes in 3/188 (1.59%) patients. Two patients developed Beau's lines with melanonychia [Figure 6] who

had received paclitaxel + carboplatin + etoposide and paclitaxel + carboplatin + 5FU. One patient developed melanonychia with longitudinal grooves and subungual hyperkeratosis who had received cyclophosphamide + carboplatin + capecitabine + doc etaxel + 5 FU + gemcitabine + paclitaxel + trastuzumab. This observation is comparable to the findings of the study of Kim *et al*. who also noticed Beau's lines and Mees' lines simultaneously in a patient receiving paclitaxel + cisplatin.[21] Beau's lines are transverse depressions in the nail plate with variable depth and width. It moves distally as the nail grows.[22] It is produced due to acute toxicity to nail matrix with transient arrest in nail plate production.[21] The distance of the line from proximal nail fold indicates the time of nail matrix insult. The width of the line indicates the duration of insult and the depth shows the degree of damage.[23]

The limitation of our study was to imply a specific drug as a causative agent for nail changes since protocols of chemotherapy were prescribed to the patients.

## Conclusion

We conclude that 37.6% patients developed chemotherapy-induced nail changes. Nine different types of nail changes were observed out of which melanonychia was the most common nail change observed in 84.04% patients followed by half and half nails in 6.91% patients and erythronychia in 5.31% patients.

Melanonychia was seen most commonly in patients receiving platinum analogues and taxanes based combinations. Platinum analogues were among the common agents in the combination chemotherapy protocol causing half and half nails. Erythronychia was found to be associated with either cisplatin alone or cisplatin-based polypharmacy. More than single nail changes were observed only in 3/188 (1.59%) patients.

Thus, we sum up that chemotherapeutic drugs can cause different types of nail changes in varying frequency. Nail is an apparent cutaneous appendage on human body; though nail changes are not fatal, the changes can cause significant morbidity, cosmetic disfigurement, and psychological distress. The chemotherapy-induced onychopathologies are not only of cosmetic concern to the patients but also affect routine daily activities, disrupt the dermatological quality of life, and also cause undue fear regarding the progression of underlying malignancy. The study will enrich the clinicians' knowledge pertaining to chemotherapy-induced nail changes and simultaneously it will also help them to counsel the patient and their caregivers beforehand regarding the possibility of associated nail changes during and thereafter the chemotherapy regimens. The counseling will improve the compliance of patient and may allow achievement of ideal duration of chemotherapy administration, as well as optimization of response rates. At the same time, clinicians can widen their vision pertaining to onychal changes which would assist them to distinguish the nail changes *per se* lest the changes might be attributed to the underlying malignancy.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

## Financial support and sponsorship

Nil.

## Conflicts of interest

There are no conflicts of interest.

## References

1. Susser WS, Whitaker-Worth DL, Grant-Kels JM. Mucocutaneous reactions to chemotherapy. J Am Acad Dermatol 1999;40:367-98.
2. Berthelot C, Kunishige JH, Apisarnthanarax N, Duvic MM. Dermatologic complications of cancer chemotherapy. In: Cancer Medicine. 8th ed. Hamilton, ON: B.C. Decker; 2010. p. 1779-87.
3. Pavey RA, Kambil SM, Bhat RM. Dermatological adverse reactions to cancer chemotherapy. Indian J Dermatol Venereol Leprol 2015;81:434.
4. Praveen Kumar S, Shyam Prasad AL, Sumanthy TK, Reddy RV. Nail changes in patients undergoing cancer chemotherapy. Int J Res Dermatol 2017;3:49-54.
5. Falkson G, Schulz EJ. Skin changes in patients treated with 5-fluorouracil. Br J Dermatol 1962;74:229-36.
6. Pratt CB, Shanks EC. Hyperpigmentation of nails from doxorubicin. JAMA 1974;228:460.
7. Dasanu CA, Alexandrescu DT, Wiernik PH. Recognizing nail and skin changes associated with chemotherapy. Resident and Staff Physician 2006. p. 52.
8. Dasanu CA, Vaillant JG, Alexandrescu DT. Distinct patterns of chromonychia, Beau's lines and melanoderma seen with vincristine, adriamycin, dexamethasone for multiple myeloma. Dermatol Online J 2006;12:10.
9. Gupta A, Parakh A, Dubey AP. Chemotherapy induced nail changes. Indian J Dermatol 2008;53:204-5.
10. Issaivanan M, Khairkar PH. Doxorubicin induced melanonychia. Indian Pediatr 2003;40:1094-5.
11. Gilbar P, Hain A, Peereboom VM. Nail toxicity induced by cancer chemotherapy. J Oncol Pharm Pract 2009;15:143-55.
12. Afsar FS, Ozek G, Vergin C. Half and half nails in a pediatric patient after chemotherapy. Cutan Ocul Toxicol 2015;34:1-2.
13. Lindsay PG. The half – and – half nail. Arch Intern Med 1967;119:583-7.
14. De Berker DAR, Baran R. Disorders of nails. In: Burns T, Breathnach S, Cox N, Griffiths C, editors. Rooks Textbook of Dermatology. 9th ed. Wiley-Blackwell; 2010. p. 65.9-30.
15. Chang C, Beutler BD, Cohen PR. Polydactylous transverse

erythronychia: Report of a patient with multiple horizontal red bands affecting the fingernails. Dermatol Ther (Heidelb) 2017;7:255-62.
16. Piraccini BM. Nail Disorders: A Practical Guide to Diagnosis and Management. E book: 2014. Springer. Chapter 2 Nail signs; Section 2.1.2 Pitting. p8.
17. Chapman S, Cohen PR. Transverse leukonychia in patients receiving cancer chemotherapy. South Med J 1997;90:395-8.
18. Baran R, Dawber RP. Physical science. In: Baran R, Dawber RP, Hanche E, editors. Diseases of the Nail and its Management. London: Blackwell Science; 2001. p. 85-103.
19. Kumar S, Diwan S, Dekate M, Goyal S. Mee's lines following chemotherapy. Our Dermatol Online 2013;4:382.
20. Slee PH. Nail changes after chemotherapy. N Engl J Med 1997;337:168.
21. Kim IS, Lee JW, Park KY, Seo SJ, Hong CK. Nail change after chemotherapy: Simultaneous development of Beau's lines and Mee's lines. Ann Dermatol 2012;24:238-49.
22. Capriotti K, Capriotti JA, Lessin S, Wu S, Goldfarb S, Belum VR, *et al*. The risk of nail changes with taxane chemotherapy: A systematic review of the literature and meta-analysis. Br J Dermatol 2015;173:842-5.
23. Piraccini BM, Iorizzo M, Starace M, Tosti A. Drug-induced nail diseases. Dermatol Clin 2006;24:387-91.