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Drug-Induced Hand-Foot Syndrome in Cancer Patients Receiving Capecitabine in A Tertiary Care Hospital

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ABSTRACT

Objective: To determine the frequency of hand-foot syndrome and associated factors among patients receiving Capecitabine for the management of cancer in a tertiary care setting.

Study Design: Cross-sectional study.

Place and Duration of Study: Oncology Department Combined Military Hospital, Rawalpindi Pakistan from Dec 2020 to May 2021.

Methodology: One hundred patients with malignant conditions taking Capecitabine for more than two weeks were included in the study. A detailed relevant dermatological examination was carried out on all the patients to diagnose hand-foot syndrome based on the National Cancer Institute Common Terminology Criteria for Adverse Events Version 4.0 Grading of Hand-Foot Syndrome.

Results: Out of 100 cancer patients using Capecitabine for more than two weeks included in the study. Sixty-eight showed the presence of hand-foot syndrome, while 32 did not show any features of hand-foot syndrome. Combination treatment was statistically significantly associated with hand-foot syndrome among the patients included in our study (p-value<0.001).

Conclusion: Hand-foot syndrome was a common side effect seen in patients managed with Capecitabine for their cancerous condition. Patients using other chemotherapeutic agents along with Capecitabine were more at risk of having hand-foot syndrome than those taking Capecitabine alone.

Keywords: Capecitabine, Cancer, Hand and foot syndrome.

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INTRODUCTION

Millions of hospital admissions and deaths have been attributed to neoplastic conditions in all parts of the word each year.[1,2] Recent advances in diagnostic and therapeutic interventions have equipped the oncologist to deal with these patients in a better way.[3] Adverse effects related to management options for cancer treatment have always been an area of concern for the patient and the treating team.[4] Management options for various neoplastic conditions vary according to the type and stage of the condition.[5] Capecitabine is a chemotherapeutic agent which is effective in the control of GI cancers but at the cost of certain short and long-term adverse effects which require regular monitoring from the treating team.[6]

Many dermatological adverse effects, including hand and foot syndrome, have been observed with routine chemotherapeutic agents used for managing various cancers.[7,8] Kwakman *et al*. highlighted that systemic and topical treatments, dose reductions, and switching to other drugs in the same class may be different options for managing the hand-foot syndrome. However, prevention or early detection is key to managing this condition.[9]

Cancer patients are prone to several health-related conditions due to underlying malignancy and various management options used to manage the condition. Despite its good effect on the control of underlying neoplastic conditions, Capecitabine has certain adverse effects. A local study done by Kamil *et al*. showed that using Capecitabine alone or in combination with other agents was associated with hand-foot syndrom.[10] Therefore, we planned this study to assess patients of various cancers taking Capecitabine for the presence of hand-foot syndrome and factors related to this complication.

METHODOLOGY

The cross-sectional study was conducted at the Oncology Unit of Combined Military Hospital Rawalpindi Pakistan for six months (December 2020 to May 2021) after ethical approval from the Ethical Review Board (B-157/5/21). The sample size was calculated using the WHO sample size calculator by

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using the population prevalence of hand-foot syndrome with Capecitabine as 41.2%.[11]The non-probability consecutive sampling technique was used to gather the sample.

Inclusion Criteria: Patients of either gender, aged 18 to 70 years who took any Capecitabine for any gastrointestinal or other malignant condition for more than two weeks were included in the study.

Exclusion Criteria: The study did not include patients with preexisting dermatological conditions like eczema, psoriasis, lichen planus, keratosis etc. Those taking combination medications and with a clear history of dermatological manifestations occurring after the introduction of agents other than Capecitabine were also not included in the study. Patients with skin lesions that did not meet the criteria for hand-foot syndrome were also excluded. In addition, the analysis did not include patients who gave a history of use of any alternate medicines that may be linked to dermatological adverse effects.

After taking written informed consent we included patients on any regimen taking this medication for more than two weeks. Detailed relevant dermatological examination was carried out on all the patients to diagnose hand-foot syndrome based on National Cancer Institute Common Terminology Criteria for Adverse Events Version 4.0 Grading of Hand-Foot Syndrome.[12,13] Examination was carried out by a consultant medical oncologist based on set criteria, and consultant dermatologist was involved in case of any ambiguity in diagnosis.

Data were analyzed using the Statistical Package for Social Sciences version 23.0. The qualitative data were presented as frequency distribution, and quantitative data were presented as Mean±SD. In addition, the relationship of various variables with Capecitabine-induced hand-foot syndrome was analyzed using Pearson Chi-square analysis, keeping *p*-value ≤0.05 as significant to establish the association.

RESULTS

Out of 100 cancer patients using Capecitabine for more than two weeks included in the study. The mean age of the cancer patients using Capecetabine included in the analysis was 42.34±4.55 years. Sixty-eight showed the presence of hand-foot syndrome, while 32 did not show any features of hand-foot syndrome (Table-I). The results of the chi-square test revealed that combination treatment was statistically significantly associated with the presence of hand-foot syndrome among the patients included in our study (*p*-value <0.001), while the duration of treatment had no such significant association with the presence of hand-foot syndrome (*p*-value-0.211) (Table-II).

Table-I: Characteristics of Study Participants (n=100)

Parameters	n(%)
Age of Mothers (years)	
Mean±SD	42.34±4.55
Range (min-max)	19 years-70 years
Gender	
Male	57
Female	43
Presence of Hand-foot syndrome	
No	32
Yes	68
Patients Receiving Combination Treatment	
No	77
Yes	23

Table-II: Relationship of Various Factors with Capecitabine induced hand-foot syndrome among the Study Participants (n=100)

Socio-Demographic Factors	No hand-foot Syndrome (n=68)	Hand-foot Syndrome (n=32)	*p*-value
Age			
<40 years	37(54.4%)	15(46.9%)	0.482
>40 years	31(45.6%)	17(53.1%)	
Gender			
Female	42(61.7%)	15(46.9%)	0.162
Male	26(38.3%)	17(53.1%)	
Duration of Capecitabine Used			
<3 months	43(63.2%)	16(50%)	0.211
>3 months	25(36.8%)	16(50%)	
Combination Treatment			
No	63(92.6%)	14(36.8%)	<0.001
Yes	05(7.4%)	18(63.2%)	

DISCUSSION

All pharmacological agents used for managing acute or chronic illness have been associated with different adverse effects related to their pharmacokinetic and pharmacodynamic properties. Chemotherapeutic agents used for cancer management are notorious for adverse effects as well. Epidemiological data from Pakistan suggest that many patients have been suffering from gastrointestinal and breast tumours requiring aggressive chemotherapy.[14] Capecitabine is commonly used to treat patients with advanced neoplastic lesions of the GI tract, breast and certain other tumours as well. We conducted this study to determine the presence of hand-foot syndrome and associated factors among patients receiving Capecitabine for managing cancer in a tertiary care setting.

Hoesly *et al*.[15] highlighted that sometimes a mild dermatological adverse effect of Capecitabine might lead to serious consequences. Unfortunately, we did not perform any long-term follow-up or study the comorbid medical problems. However, the high number of patients getting this adverse effect from Capecitabine should ring bells in the ears of clinicians. Yamagiwa *et al*.[16] revealed that the incidence of the hand-foot syndrome was high among these patients and significantly affected the quality of life of patients. Treatment of hand-foot syndrome significantly improved the quality of life of these patients. 32% of our study participants had developed hand-foot syndrome after using Capecitabine which was quite a high percentage. A large trial was conducted by Yap *et al*.[17] in 2017 regarding Predictors of Hand-Foot Syndrome and Pyridoxine for the Prevention of Capecitabine-Induced Hand-Foot Syndrome. They concluded that 31.4% of patients receiving pyridoxine had developed the hand-foot syndrome, while 37.1% developed this condition and were not taking pyridoxine. Suzuki *et al*.[18] in 2018 surveyed patients who have been prescribed Capecitabine for control of their cancer regarding various strategies patients employ to prevent or manage hand-foot syndrome secondary to using Capecitabine. Applying moisturizer and washing the body were common strategies used by the patients. Unfortunately, we did not check the management options in this regard. However, we generated baseline epidemiological data to help clinicians understand the burden of the problem among the vulnerable group of the population.

It was a small study with a limited sample size. The small sample size and data from only one oncology unit in the country are two main limitations of our study. However, more studies from patients from multiple centres with large cohorts of patients may generate generalizable results.

CONCLUSION

Hand-foot syndrome was a common side effect seen in patients with Capecitabine for their cancerous condition. Patients using other chemotherapeutic agents along with Capecitabine were more at risk of the hand-foot syndrome than those taking Capecetabine alone.

Conflict of Interest: None.

Author's Contribution

Following authors have made substantial contributions to the manuscript as under:

I & RA: Data acquisition, critical review, approval of the final version to be published.

MU & AZ: Study design, drafting the manuscript, data interpretation, approval of the final version to be published.

MJD & TML: Data analysis, concept, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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