International Journal of Health Sciences and Research
Volume 14; Issue: 10; October 2024
Website: www.ijhsr.org
Original Research Article *ISSN: 2249-9571*

Effect of Chemotherapy on Diaphragm Mobility and Diaphragm Thickness in Breast Cancer Patients: An Observational Study

Dr. Apurva Bipin Joshi[1], Dr. Abhijit Diliprao Diwate[2], Dr. Arijit Kumar Das[3]

[1]Department of Cardiovascular and Respiratory Physiotherapy, [2]Department of Cardiovascular and Respiratory Physiotherapy, [3]Department of Cardiovascular and Respiratory Physiotherapy
DVVPF's College of Physiotherapy, MUHS University, Ahmednagar, India.

Corresponding Author: Dr. Apurva Bipin Joshi

DOI: https://doi.org/10.52403/ijhsr.20241034

ABSTRACT

Background: Breast cancer being the common malignancy that affect many women nowadays and those patients with breast cancer often experience dyspnea after chemotherapy associated with the chemotherapy-induced injury of respiratory muscles and peripheral nerves. Also, Chemotherapy is known to induce diverse side effects including damage to the mitochondrial DNA.
Objective: To find out the effect of chemotherapy on diaphragm mobility and diaphragm thickness in breast cancer patients.
Materials & Method: The study was conducted with 30 diagnosed breast cancer patients who met the inclusion criteria using a cross-sectional research design. After approval of ethical clearance, informed consent was obtained from the participants. Data was collected by Ultrasonography before starting of chemotherapy and after 5 weeks of chemotherapy. Demographic data and baseline measures were recorded before starting the examination. The collected data were measured using the open Epi Instat version for Windows statistical software.
Result: In the present study of 30 patients, the mean age group was 50.23±12.31, height 157.03±5.18, weight 56±6.0. In our study, we found a result showing statistically significant changes in diaphragm mobility and diaphragm thickness in breast patients.
Conclusion: The study concludes that patients with breast cancer showed significant decline in diaphragm mobility and diaphragm thickness after administration of 5 weeks of chemotherapy.

Keywords: Diaphragm mobility, Diaphragm thickness, Breast cancer, respiratory muscles, Ultrasonography.

INTRODUCTION

Breast cancer is seen to be the most common malignancy affecting women and its incidence is increasing by 1% per year. Nowadays it is often detected at an early stage and it is often managed with surgery, radiotherapy and systemic chemotherapy.[1] In 2020, approximately 2.3 million cases of breast cancer were diagnosed globally, and about 685,000 women died from the disease.[2] As per the prediction by GLOBOCAN cancer cases in India would rise up to 2.08 million, accounting for a

increase of 57.5 per cent in 2040 from 2020.[3]

Patients with breast cancer often experience dyspnea after chemotherapy, which might be associated with the chemotherapy-induced injury of respiratory muscles and peripheral nerves.[4]

Age, reproductive factors, personal or family history of breast disease, genetic pre-disposition and environmental factors have been associated with an increased risk for the development of female breast cancer.[5]

Breast cancer typically causes no pain and manifests as a lump in the breast. Nonetheless, 90% of breast masses including fibroadenomata, cysts, and fibrocystic change - are benign in nature. Breast cancer symptoms can include a bulge in the breast or axilla that may have hard, stationary, swelling of breast tissue or alterations in size and shape, skin abnormalities include ulceration, pitting, erythema, and dimpling, changes in the breasts, including inversion, skin changes, or discharge.[6]

The diaphragm being the major muscle of respiration, its dysfunction is an underestimated cause of respiratory impairment in postsurgical patients.[7]

Chemotherapy is known to induce diverse side effects including damage to the mitochondrial DNA. Doxorubicin (DOX) is a well-known anticancer drug for treating solid tumors and hematologic malignancies. DOX is a drug of choice for patients with breast cancer or prostate cancer and it is known to cause muscle atrophy and fatigue during therapy.[8]

A common chemotherapy drug, doxorubicin (adriamycin), is administered to cancer patients. Doxorubicin depressed diaphragm force, a response that was exaggerated by IP administration, which stimulated muscle inflammation and injury further leading to weakened respiratory muscles. Doxorubicin IP also decreased the weight and cross-section of diaphragm fiber bundles. Loss of muscle mass confirms prior reports in the literature. Paclitaxel, which is a frequently used chemotherapeutic agent in breast cancer was reported to be responsible for respiratory symptoms such as non-productive cough, wheezing, dyspnea, shortness of breath, etc.[9]

Literature suggests that the incidence of drug-induced hiccups, including those associated with corticosteroids like Dexamethasone which is used in the treatment of chemotherapy. Hiccups are explained as reflex-like spasmodic contraction of the diaphragm with a sudden inspiration which is terminated by the abrupt closure of the glottis to produce the characteristic sound.[10]

Therefore, this study aims to study the effects of chemotherapy on diaphragm mobility, and diaphragm thickness in breast cancer patients undergone breast cancer surgeries

MATERIALS & METHODS

We conducted an observational study in the department of oncology in a tertiary care hospital. The duration of the study was from 2023-24. Ethical clearance was obtained from institutional ethics committee, and written informed consent was taken from the patients. Our study included a convenient sample size of 30 post operative breast cancer patients scheduled for adjuvant chemotherapy. We included patients from age group 40-64 and above, diagnosed with T1-T4, N1-N2 staging of breast cancer and those who underwent Modified radical mastectomy, radical mastectomy, partial radical mastectomy, lumpectomy. Patients with other cancer, pulmonary function dysfunction, metastatic breast cancer, neuromuscular diseases, lung pathology, chronic musculoskeletal conditions, and metabolic or any other diagnosed condition impacting diaphragm mobility and thickness were excluded from the study. The outcome measures included assessing the diaphragm mobility and diaphragm thickness by Ultrasonography before starting the chemotherapy and after 5 weeks of chemotherapy.

STATISTICAL ANALYSIS

Data was entered in an MS Excel sheet and analysed using OpenEpi software version 3.06. Quantitative data was expressed in terms of mean and standard deviation. For within-group analysis, a paired t-test was used for normally distributed data and the Wilcoxon rank sum test was used for data that were not normally distributed. A p-value of ≤ 0.05 was considered statistically significant.

RESULT

A total of 30 patients were included in this study aged (40-64 and above). The demographic data of these patients are illustrated in Table 1. Baseline analysis, including the Mean and SD of outcome measures, are shown in Table 2.

PARAMETER	Mean and SD
Age (years)	50.23±12.31
Weight (kg)	56±6.0
Height (cm)	157.03±5.18
BMI (kg/m^2)	22.52±2.26

Table 1 shows the demographic data of the subjects

Interpretation:

This Table shows baseline characteristics of patient's data represented in Mean, SD and percentage of gender, age, weight, height and BMI

OUTCOME	Mean± SD		P value	Significance
	Pre	Post		
Right hemidiaphragm excursion during quiet breathing	1.39±0.50	1.07±0.47	<0.0001	Extremely Significant
Left hemidiaphragm excursion during quiet breathing	1.62±0.48	1.19±0.38	<0.0001	Extremely Significant
Right hemidiaphragm excursion during deep inspiration	1.39±0.52	1.01±0.45	<0.0001	Extremely Significant
Left hemidiaphragm excursion during deep inspiration	1.53±0.42	1.13±0.41	<0.0001	Extremely Significant
Right hemidiaphragm thickness during quiet breathing	1.35±0.08	1.29±0.06	<0.0001	Extremely Significant
Left hemidiaphragm thickness during quiet breathing	1.38±0.08	1.28±0.06	<0.0001	Extremely Significant
Right hemidiaphragm thickness during deep inspiration	1.37±0.07	1.29±0.06	<0.0001	Extremely Significant
Left hemidiaphragm thickness during deep inspiration	1.36±0.08	1.29±0.07	<0.0001	Extremely Significant

Table 2 shows the mean and SD of pre and post values of the outcome measures including their p value and significance

Interpretation

This table represents the pre and post values of diaphragm excursion and diaphragm thickness along with their p value and statistical significance.

Variables	Normality passed	Test used
Pre Right hemidiaphragm excursion during quiet breathing	No	Wilcoxon matched pair test
Post Right hemidiaphragm excursion during quiet breathing	No	
Pre Left hemidiaphragm excursion during quiet breathing	No	Wilcoxon matched pair test
Post Left hemidiaphragm excursion during quiet breathing	No	
Pre Right hemidiaphragm excursion during deep inspiration	No	Wilcoxon matched pair test
Post Right hemidiaphragm excursion during deep inspiration	No	

Pre Left hemidiaphragm excursion during deep inspiration	No	Wilcoxon matched pair test
Post Left hemidiaphragm excursion during deep inspiration	No	
Pre Right hemidiaphragm thickness during quiet breathing	No	Wilcoxon matched pair test
Post Right hemidiaphragm thickness during quiet breathing	No	
Pre Left hemidiaphragm thickness during quiet breathing	Yes	Paired t test
Post Left hemidiaphragm thickness during quiet breathing	Yes	
Pre Right hemidiaphragm thickness during deep inspiration	Yes	Paired t test
Post Right hemidiaphragm thickness during deep inspiration	Yes	
Pre Left hemidiaphragm thickness during deep inspiration	Yes	Paired t test
Post Left hemidiaphragm thickness during deep inspiration	Yes	

Table 3 represents the normality test for each outcome measure. For analysis of outcomes, if data pass the normality, parametric tests are used, and if not, then nonparametric tests are used.

Interpretation:

This Table shows the normality test used for all the outcome measures. For within-group analysis, a paired t-test was used for normally distributed data and the Wilcoxon rank sum test was used for data that were not normally distributed.

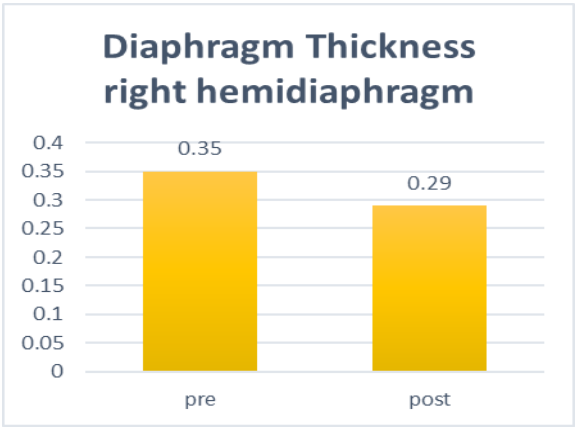

Figure 1 shows the mean of pre and post values of right hemidiaphragm thickness during quiet breathing

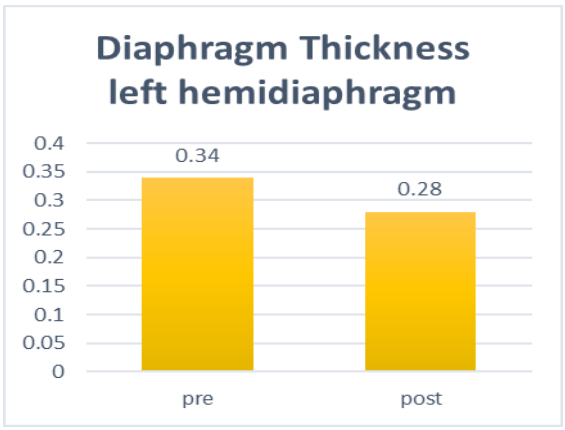

Figure 2 shows the mean of pre and post values of left hemidiaphragm thickness during quiet breathing

Interpretation:

Figure 1 and figure 2 compares the values of right and left hemidiaphragm thickness during quiet breathing before and after 5 weeks of chemotherapy respectively.

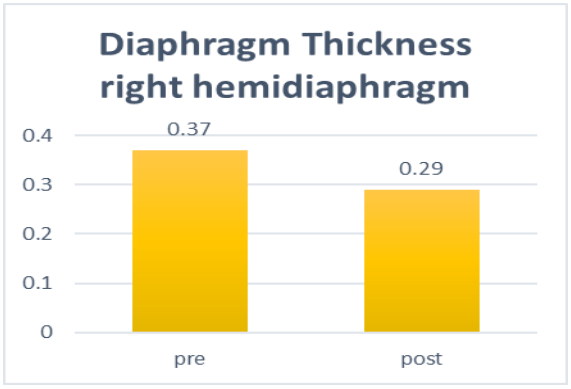

Figure 3 shows the mean of pre and post values of right hemidiaphragm thickness during deep inspiration

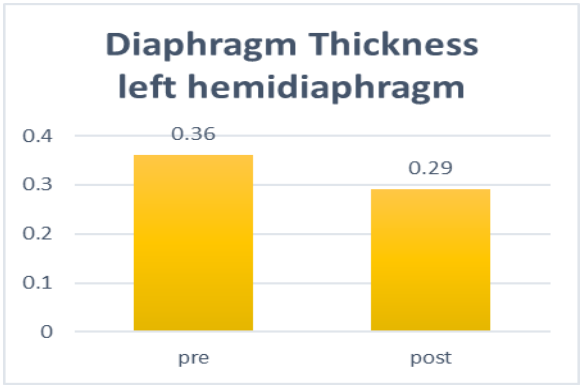

Figure 4 shows the mean of pre and post values of left hemidiaphragm thickness during deep inspiration

Interpretation:

Figure 3 and figure 4 compares the values of right and left hemidiaphragm thickness during deep inspiration before and after 5 weeks of chemotherapy respectively.

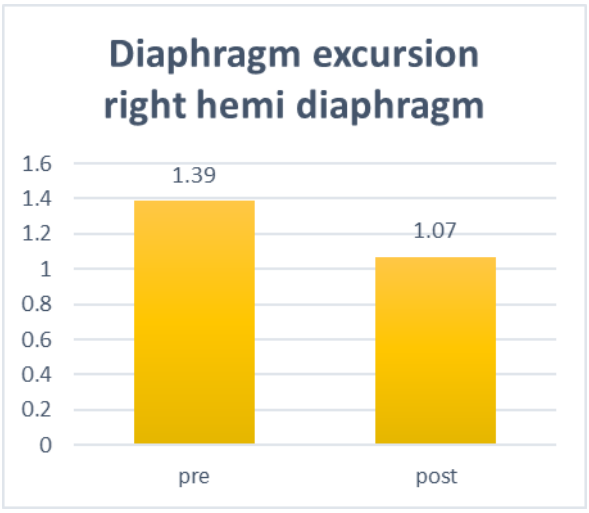

Figure 5 shows the mean of pre and post values of right hemidiaphragm excursion during quiet breathing

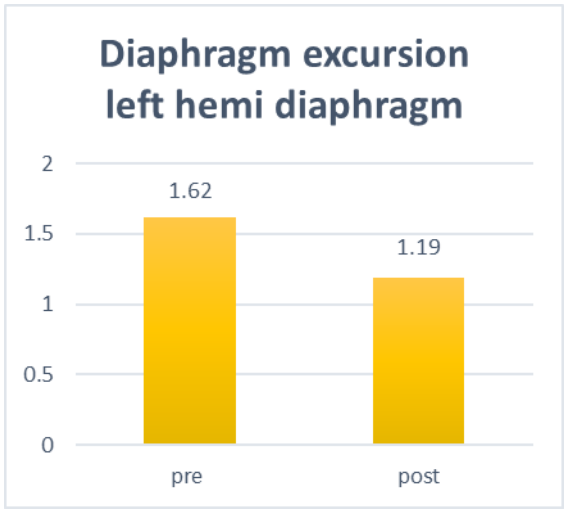

Figure 6 shows the mean of pre and post values of left hemidiaphragm excursion during quiet breathing

Interpretation:
Figure 5 and figure 6 compares the values of right and left hemidiaphragm excursion during quiet breathing before and after 5 weeks of chemotherapy respectively.

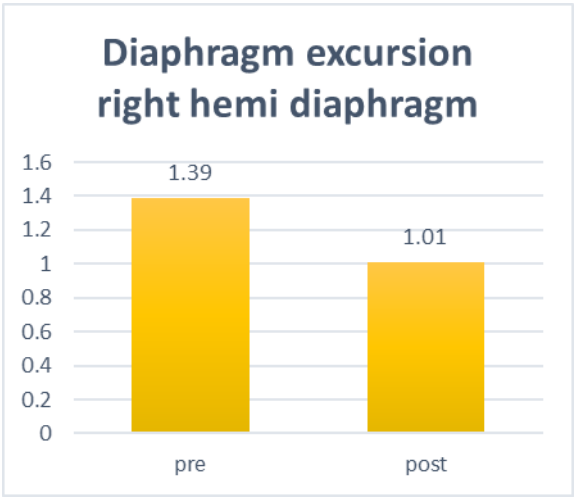

Figure 7 shows the mean of pre and post values of right hemidiaphragm excursion during deep inspiration

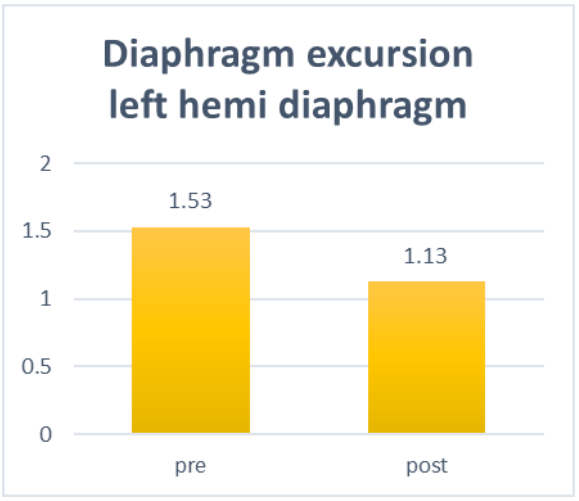

Figure 8 shows the mean of pre and post values of left hemidiaphragm excursion during deep inspiration

Interpretation:
Figure 7 and figure 8 compares the values of right and left hemidiaphragm excursion during deep inspiration before and after 5 weeks of chemotherapy respectively.

DISCUSSION

Breast cancer is a compilation of distinct malignancies that manifests in the mammary glands[11]. Breast cancer is known to be the most commonly diagnosed cancer among female patients and is the leading cause of cancer-related death. The treatments of breast cancer include surgery, chemotherapy, radiotherapy (RT), endocrine therapy, targeted therapy, and immunotherapy. The current optimal chemotherapy regimen is taxane with or without anthracycline, given in sequence or combination, both in NAC and AC settings. The application of anthracyclines remains controversial, but it seems to be essential in high-risk patients, such as triple-negative and HER-2 positive subtypes[12]. Most

commonly Doxorubicin IP, chemotherapeutic drug, also decreases the weight and cross-section of diaphragm fiber bundles. Loss of muscle mass confirms prior reports in the literature[9].

Still, there is a lack of evidence about the effect of chemotherapy drugs on diaphragm mobility and diaphragm thickness in breast cancer patients. Thus, the current study helps to determine the effect of chemotherapy on diaphragm mobility and thickness in breast cancer patients.

In the present study of 30 patients, the mean age group was 50.23±12.31, height 157.03±5.18, weight 56±6.0. In our study, we found a result showing statistically significant changes in diaphragm mobility and diaphragm thickness in breast patients.

The mean values of pre and post diaphragm mobility of right hemidiaphragm during quiet breathing is 1.39 and 1.07 and during deep inspiration is 1.39 and 1.01 respectively whereas the mean values of pre and post diaphragm mobility of left hemidiaphragm during quiet breathing is 1.62 and 1.19 and during deep inspiration is 1.53 and 1.13 respectively.

The mean values of pre and post diaphragm thickness of right hemidiaphragm during quiet breathing is 0.35 and 0.29 and during deep inspiration is 0.37 and 0.29 respectively whereas the mean values of pre and post diaphragm mobility of left hemidiaphragm during quiet breathing is 0.34 and 0.28 and during deep inspiration is 0.36 and 0.29 respectively.

The findings of our study are in accordance with a study conducted by Macrina D'souza et al that reported decline in diaphragmatic thickness, mobility[13]. We found statistically significant decline in diaphragm thickness and mobility on quiet breathing after 5 weeks of chemotherapy. In comparison to the diaphragm thickness and mobility measured during quiet breathing, statistically significant changes were seen in the diaphragm mobility which was measured during deep inspiration.

The decline in diaphragm mobility and thickness might be because of administration of the chemotherapy drugs consisting of corticosteroids as stated by Peter Gilbar[10]

In the present study we found significant decrease in diaphragm mobility and thickness in breast cancer patients after 5 weeks of chemotherapy

CONCLUSION

Breast cancer can be effectively treated by chemotherapy, although there can be adverse effects of chemotherapy on structural aspects of diaphragm leading to reduced diaphragm mobility and its thickness. We conclude that after administration of 5 weeks of chemotherapy, there is decline in diaphragm mobility and thickness of right and left hemidiaphragm.

Limitation

The present study did not consider the effect of surgery on diaphragm excursion and diaphragm thickness.

Declaration by Authors

Ethical Approval: Approved

Acknowledgement: I would like to thank my parents. I am highly grateful to Dr. Archana Nagargoje, Dr. Pranali Gaikwad and my colleagues for helpful feedback and guidance.

Source of Funding: None

Conflict of Interest: The authors declare no conflict of interest.

REFERENCES

1. Spyropoulou D; Leotsinidis M; Tsiamita M; Spiropoulos K; Kardamakis D; Pulmonary function testing in women with breast cancer treated with radiotherapy and chemotherapy. U.S. National Library of Medicine; 2009; 23: 867-873.
2. Sathishkumar K, Chaturvedi M, Das P, Stephen S, Mathur P. Cancer incidence estimates for 2022 & projection for 2025: result from National Cancer Registry Programme, India. Indian Journal of Medical Research. 2022 Oct 1; 156(4&5):598-607.
3. Arnold M, Morgan E, Rumgay H, Mafra A, Singh D, Laversanne M, Vignat J, Gralow

JR, Cardoso F, Siesling S, Soerjomataram I. Current and future burden of breast cancer: Global statistics for 2020 and 2040. The Breast. 2022 Dec 1;66:15-23.
4. Ding L, Wang L, Yin J, Fan Z, He Z. Effects of neoadjuvant chemotherapy on respiratory function in patients with breast cancer. Chinese Journal of Cancer Research. 2020 Feb;32(1):36.
5. Shah R, Rosso K, Nathanson SD. Pathogenesis, prevention, diagnosis and treatment of breast cancer. World journal of clinical oncology. 2014 Aug 8;5(3):283.
6. Katsura C, Ogunmwonyi I, Kankam HK, Saha S. Breast cancer: presentation, investigation and management. British Journal of Hospital Medicine. 2022 Feb 2;83(2):1-7. Dubé BP, Dres M. Diaphragm dysfunction: diagnostic approaches and management strategies. Journal of clinical medicine. 2016 Dec 5;5(12):113.
7. Park SS, Park HS, Jeong H, Kwak HB, No MH, Heo JW, Yoo SZ, Kim TW. Treadmill exercise ameliorates chemotherapy-induced muscle weakness and central fatigue by enhancing mitochondrial function and inhibiting apoptosis. International neurourology journal. 2019 Feb;23(Suppl 1):S32.
8. Gilliam LA, Moylan JS, Callahan LA, Sumandea MP, Reid MB. Doxorubicin causes diaphragm weakness in murine models of cancer chemotherapy. Muscle Nerve. 2011 Jan;43(1):94-102. doi: 10.1002/mus.21809. PMID: 21171100; PMCID: PMC3057655
9. Gilbar P, McPherson I. Severe hiccups during chemotherapy: corticosteroids the likely culprit. Journal of Oncology Pharmacy Practice. 2009 Dec;15(4):233-6.
10. Feng Y, Spezia M, Huang S, Yuan C, Zeng Z, Zhang L, Ji X, Liu W, Huang B, Luo W, Liu B. Breast cancer development and progression: Risk factors, cancer stem cells, signaling pathways, genomics, and molecular pathogenesis. Genes & diseases. 2018 Jun 1;5(2):77-106.
11. Wang J, Wu SG. Breast cancer: an overview of current therapeutic strategies, challenge, and perspectives. Breast Cancer: Targets and Therapy. 2023 Dec 31:721-30.
12. D'souza M, Samuel S, Rai S, Alaparthi GK, Saxena PP, Nagaraja R. Diaphragm thickness, mobility and respiratory muscle strength in patients with head and neck cancer receiving chemoradiation therapy: A longitudinal pilot study. F1000Research. 2022 Mar 10;11(294):294.

How to cite this article: Apurva Bipin Joshi, Abhijit Diliprao Diwate, Arijit Kumar Das. Effect of chemotherapy on diaphragm mobility and diaphragm thickness in breast cancer patients: an observational study. *Int J Health Sci Res.* 2024; 14(10):319-325. DOI: *https://doi.org/10.52403/ijhsr.20241034*

******