RESEARCH ARTICLE

Editorial Process: Submission:03/24/2022 Acceptance:09/22/2022

Adherence to Chemotherapy among Women with Breast Cancer Treated at Tikur Anbessa Specialized and Teaching Hospital, Addis Ababa, Ethiopia

Fatuma Hassen[1,2]*, Fikre Enquselassie[3], Ahmed Ali[3], Adamu Addissie[3], Girma Taye[3], Mathewos Assefa[4], Aster Tsegaye[2]

Abstract

Background: Adherence is important for women with breast cancer because it is a primary determinant for effectiveness of treatment and optimum clinical benefit. Though Breast cancer is the leading cancer in Ethiopia,adherance to chemotherapy is not investigated in Ethiopian women. **Objective:** This study aimed to assess adherence to chemotherapy among women with breast cancer treated at Tikur Anbessa specialized and Teaching Hospital. **Methods:** Cross-sectional study was conducted among 164 breast cancer patients with chemotherapy. After eligible participants were identified, data were collected using face-to-face interviews, card reviews and telephone interviews. Adherence was calculated as the number of doses taken divided by number of recommended or expected doses. Pearson chi-square test was used to evaluate predictors of adherence. **Results:** Among a total of 164 breast cancer patients, majority, 119, (72.6%) of them were urban residents. The mean age of study participants was 41.99 + 10.9 years. The majority 149, (90.9%) of patients were married. More than half 94, (57.3%) of the women were literate. In this study, 137 out of 164 (83.5%) women were adherent to their chemotherapy. Of the 27 non adherent participants. he reason for non-adherence to chemotherapy was unknown for 7, (25.9%) of women. Among different identified reasons for non-adherent, sever illness prevents patients to receive chemotherapy. Based on Pearson chi square test, distance from referral center and treatment regimen were significantly associated with non-adherence rate. **Conclusion:** The present study the results showed that the majority 137, (83.5%) of patients were in good adherence to their chemotherapy. The most identified factor of non-adherence was inability to come for their therapy as a result of severity of illness. Therefore, expansion of cancer diagnosis and treatment centers should be encouraged in order to maximize patient's access and adherence to chemotherapy.

Keywords: Breast cancer- adherence- Non adherence

Asian Pac J Cancer Prev, **23 (9)**, 3035-3041

Introduction

Breast cancer is the most commonly diagnosed cancer in women. Globally, 24.2%, of all new cancer cases identified in women is breast cancer. It is also the leading cause of cancer death in women, which accounts for15.0% of cancer deaths (WHO, 2018). Adherence can be defined as the extent to which patients follow the instructions they are given for prescribed treatments. This definition was somewhat extended by the WHO as 'the extent to which a person's behavior taking medication, following a diet and/or executing lifestyle changes corresponds with agreed recommendations from a health care provider' (Sabaté, 2003). A Retrospective cohort study of 5,861 women with breast cancer at the Brazilian National Cancer Institute from 2004 to 2010 was conducted to identify factors associated with adherence to hormone therapy. The result revealed that the proportion of adherent patients was 76.3%. There was lower likelihood of adherence among younger women (<40 years), women who were alcohol drinkers, or smokers, and among those who were diagnosed at a non-curable stage. There was also a higher likelihood of adherence among women who had completed second grade or higher education, and among women with a family history of cancer (Claudia et al., 2014).

A population based retrospective observational study conducted in Italy to see the adherence to long-term pharmacological treatment for breast cancer showed that over 46% of patients demonstrated poor/moderate

*[1]School of Public Health, College of Health Sciences, Addis Ababa University, Addis Ababa, Ethiopi. [2]Department of Medical Laboratory Sciences, College of Health Sciences, Addis Ababa University, Addis Ababa, Ethiopia. [3]School of Public Health, College of Health Sciences, Addis Ababa University, Addis Ababa, Ethiopia. [4]Department of Oncology, School of Medicine, College of Health Sciences, Addis Ababa University, Addis Ababa, Ethiopia. *For Correspondence: fatuma.hassen@aau.edu.et*

adherence, 20% good and only 34% showed an excellent adherence. During the 5 years of follow-up only one woman in every two carried out the adjuvant treatment (Marianna et al., 2013). According to study conducted in South Karnataka, India showed that, even though the treatment options were expensive, family income was not identified as a significant predictor of adherence to treatment. A logistic regression analysis with adherence and different demographic, treatment and disease variables found that spouses support and distant /organ metastasis at the time of diagnosis were significant predictors of adherence to treatment (Nagappa et al., 2012).

Astudy done on adherence to Intravenous Chemotherapy in African-American and Caucasian Women with Early Stage breast cancer found that, 84, (90%) of the sample was adherent to their chemotherapy regimen and only 9(10%) of the sample discontinued chemotherapy prior to completion. For the 44 Caucasian participants, 42, (87.5%) were adherent and 2, (4.3%) were non-adherent. For the 49

African-America participants, 42, (82.4%) were adherent and 7, (13.7%) were non-adherent. No racial difference was found in adherence to chemotherapy between African-American and Caucasian women. Between these two groups, those who were <100% adherent to chemotherapy regimens reported lower income ($p < .001$) (Wells et al., 2015).

Similar study conducted at a breast cancer clinic in Nigeria during a 5-year period (2004-2008) also showed that of the 275 study patients, 79 (28.7%) refused a biopsy sample needed for a definitive diagnosis. Of those who agreed to provide a biopsy sample, 28 patients (10.2%) did not return for a follow-up visit. Mastectomy was offered to 140 patients, 67 of them (47.9%) refused surgery. Of the 53 patients diagnosed with locally advanced lesions offered neo-adjuvant chemotherapy, 15 patients (28.3%) completed the recommended therapy. Of the 44 patients offered adjuvant chemotherapy, 38.6% (17 patients) completed the recommended therapy (Stanley et al., 2011). Among many factors for adherence lack of, getting social support, and thorough therapeutic communication were strongly linked with adherence to them (Wakoet al., 2021). Astudy done in Aira Hospital, rural Ethiopia to assess the feasibility of and adherence to tamoxifen therapy found that among a total of 101 breast cancer patients, 66 (65%) patients were HR+ and were eligible for tamoxifen treatment. However, 15 of the HR+ patients died before tamoxifen became available. Of the remaining 51 HR+ patients, 26 (51%) initiated tamoxifen but only 9 of them (35%) adhered to therapy (medication possession rate ≥80%, median observation 16.2 months). After 1 year, 52% of the patients were still adherent, and 9 patients had discontinued therapy. The reasons for non-initiation of tamoxifen included patient factors, including financial hardship or lack of transportation, and health care provider factors (Reibold et al., 2021).

Even though the trend of breast cancer is increasing in Ethiopia, there is scarcity of data on the adherence of breast cancer patients in order to provide evidence based intervention. Therefore, the aim of this study was to assess the level of adherence to chemotherapy and associated factors among breast cancer patients at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia.

Materials and Methods

Study setting

This study was conducted in Addis Ababa at Tikur Anbessa Specialized Hospital (TASH) oncology departments. The oncology center which is located and part of TASH and it is the only institution that provides radiotherapy service in Ethiopia. With the support of Ethiopia's governmental institutions, Non-Governmental Organizations (NGOs) and international partners, the hospital is hoping to develop a comprehensive program, including cancer registry, early detection, prevention, standard treatment and palliative care. The hospital has one CT scanner and one MRI scanner. The hospital has 700 beds, of which 18 are allocated for cancer treatment. Of the 201 physicians in the hospital only 2 are hematologists, 4 are medical oncologists, 4 are radiotherapists, 2 are surgical oncologists and one is a pediatric oncologist. Three palliative pain specialists also work at the hospital. Only 26 of the TASH's 627 nurses are dedicated oncology nurses (INCTR, 2015). Tikur Anbessa Specialized Hospital (TASH) was selected for the study, as it it was the only referral center for cancer treatment during the time of data collection.

Study design and population

Hospital based cross-sectional study design was conducted from September 2018 to June 2019. Even though we identified a total of 230 patients, 24, (10.4%) patients were excluded due to incomplete information. In addition, 7(3.0%) patients were considered to be ineligible because of moved to other regional chemotherapy centers and private health facilities and 17, (7.3%) patients were planned for chemotherapy, but they did not start their treatment. Similarly 16, (6.9%) of patients were ineligible because patients were die before initiation of chemotherapy and during the follow-up period. Therefore, the final sample consisted of 164 participants who had complete information.

Data collection, analysis and management

Participants were identified, based on the required criteria, and data were collected by trained oncology nurses during the 3rd, 5th and 7th cycle depending on the type of treatment regimen. In addition card review and telephone interview were applied in order to get complete data. Breast cancer chemotherapy adherence was calculated as the number of doses taken divided by the number of recommended or expected dose. A patient was considered to be non- adherent if she did not present for two consecutive doses of chemotherapy. Patients who had dose reduction and/ or omission due to inadequate hematological profile or poor clinical condition, unplanned public holidays were not included as non-adherent. The patients or patients' family members were contacted via phone calls to supplement the collected data. Some patients were excluded since some patients were moved to private and public health facilities which provide chemotherapy

services in different regions of the country. In addition, some patients, medical records had either incomplete or information totally unavailable, thus Finally, for some patients and their condition was unknown. Finally a total of 164 women with breast cancer were included in this analysis. Bivariate analysis was conducted in order to see the association between different independent variables with adherence. Regarding factors associated with adherence analysis was made based on baseline characteristics. Clinical stage at diagnosis was assigned to each patient based on American Joint Committee on Cancer (TNM) classification scheme , which had indicated that Size and extent of tumor (T), node (N), and metastasis (M).

Ethical consideration and quality assurance

Ethical approval was obtained from Addis Ababa University, College of Health Sciences Institutional Review Board with protocol number 073/17/SPH. Permission was obtained from the Oncology department of TASH. Written informed consent was obtained from each respondent. Confidentiality and privacy were maintained throughout the study. Each interview was transcribed precisely and anonymized to ensure confidentiality by removing any details that might identify any patient or their family. This study was conducted based on research requirements, regulations and policies that safeguard the wellbeing of study participants and to ensure the reliability and integrity of this finding. Therefore, all methods were carried out in accordance with relevant guidelines and regulations.

Results

Socio demographic Characteristics of study participants

In this study a total of 164 breast cancer patients were included of which, total of 119, (72.6%) of the patients were urban residents. The mean age of study participants was 41.99 + 10.9 years. Nearly half, 79, (48.2 %) of women were less than 40 years of age. The majority 149, (90.9%) of patients were married. More than half 94, (57.3%) of the women were literate. The study also showed, majority 119, (72.6%) of women were unemployed. Regarding income, more than half 39 (52.0%) of women earn monthly income of less than 2000 Ethiopian Birr. The result also showed that, more than half, 91, (55.5%) of women were premenopausal. For the majority, 81, (49.3%) of women distance from the referral cancer center is greater than 100 kilometer.

According to the result of Pearson Chi square test, there was no significant difference in the level of adherence based on place of residence and age group of study participants. However, all, 15 (100%) of never married women were adherent to their chemotherapy. In this case the chi-square test showed nearly significant association, (P =0.071). There was also no significant difference in adherence with educational status, employment status, income and menopausal status of women. However, there was significant association between adherence to chemotherapy and distance from the referral cancer center (P = 0.015). Patients who come from a long distance had a significantly lower level of adherence (Table 1).

Distribution of personal characteristics of study participants

In this study 11, (6.7%) of patients had a family history of breast cancer. Even though there was no significant association, patients with a family history of breast cancer were more adherent as compared to those women with no family history of breast cancer. Regarding smoking, only, 3 (1.8%) of breast cancer patients had a history of smoking cigarettes. However, 28, (17.1%) of women had a history of drinking alcohol. Regarding exercise in this study almost one fourth, 39, (23.8 %) of the study participants had experience of moderate exercise. On the other hand only, 12 (7.3%) of women had experience of strenuous exercise before they had been diagnosed with breast cancer. Among a total of 39 women who had experience of moderate exercise, majority, 35 (89.7%) of women adhere to their treatment as compared with only 4 (10.3) women who did not adhere to their treatment. In general there was no statistically significant difference between adherence to chemotherapy with family history, cigarette smoking, alcohol consumption and physical activity (Table 2).

Clinical characteristics of study participants

In this study, 12, (7.3%) of women underwent previous breast surgery, and the adherence level was almost the same between women who underwent previous breast surgery and who had not underwent surgery. The finding also showed that the majority, 73, (44.5%) of women had stage III tumor at diagnosis. Similarly, the commonest pathological diagnosis among the patients was invasive ductal carcinoma, 144, (87.8%). In general there was no statistically significant difference between level of adherence with different stages of tumors and pathological diagnosis. This study also found that, more than half, 104 (63.44%) of patients were planned for eight course of chemotherapy, while 52, (31.7%) and 8, (4.9%) of patients were planned for six and four course regimens of chemotherapy respectively. Based on the Pearson chi-square test, there was a significant difference between the level of adherence and recommended chemotherapy regimen. (Table 3).

Factors associated with non-adherence to chemotherapy

In this study the reason for non-adherence to chemotherapy was unknown for 7, (25.9%) of women. Among different identified reasons for non-adherent cases. Severity of disease /pain was most frequent encountered for 9. (33.3%) of the patients to receive chemotherapy. In addition financial constraints 4, (14.8%), security or distance from cancer referral center, 3, (11.1%) were also identified as factors for non adherence (Table 4).

Discussion

In this study a total of 164 breast cancer women were participated. Based on residence, majority, 72.6 % of women were from urban, which was not comparable with a study done in rural Ethiopia, were only (21%) from urban area, (Reiboldet al., 2021). This difference between studies

Table 1. Socio-demographic Profile of Breast Patients Attending Chemotherapy at Tikur Anbessa Specialized Hospital, Addis Ababa Ethiopia, 2020 (n=164)

Variable	Adherent	None adherent	Total (%)	X^2	P- Vlue
Residence	Frequency (%)	Frequency (%)			
Urban	102 (85.7)	17 (14.3)	119 (72.6)		
Rural	35 (77.8)	10 (22.2)	45 (27.4)	1.49	0.221
Age group (years)					
Less than 40	65 (82.3)	14 (17.7)	79 (48.2)	1.98	0.576
40-49	37 (82.2)	8 (17.8)	45 (27.4)		
50-59	17 (81.0)	4 (19.0)	21 (12.8)		
60 and above	18 (94.7)	1 (5.3)	19 (11.6)		
Marital status					
Ever married	122 (81.9)	27 (18.1)	149 (90.9)	3.25	0.071
Never married	15 (100)	0 (0.0)	15 (9.1)		
Education level					
Illiterate	59 (84.3)	11 (15.7.)	70 (42.7)	0.05	0.823
Litrate	78 (83.0)	16 (17.0)	94 (57.3)		
Occupation					
Employed	37 (82.2)	8 (17.8)	45 (27.4)	0.078	0.78
Unemployed	100 (84.0)	19 (16.0)	119 (72.6)		
Income (n=75)					
<2000	32 (82.1.)	7 (17.9)	39 (52.0)	0.23	0.632
> 2000	31 (86.1)	5 (13.9)	36 (48.0)		
Menopausal status					
Premenopausal	74 (81.3)	17 (18.7)	91 (55.5)	0.731	0.392
Post menopauses	63 (86.3)	10 (13.7)	73 (44.5)		
Distance from referral cancer center					
Near the cancer center	63 (92.6)	5 (7.4)	68 (41.5)	10.46	0.015
< 100 KM	14 (93.3)	1 (6.7)	15 (9.1)		
100-500 Km	44 (74.6)	15 (25.4)	59 (36.0)		
> 500 KM	16 (72.7)	6 (27.3)	22 (13.4)		

X^2, Chi square; %, Percent

Table 2. Personal Characteristics and Level of Adherance among Breast Patients Attending Chemotherapy at Tikur Anbessa Specialized Hospital, Addis Ababa Ethiopia, 2020 (n=164)

Variable	Adherent	None adherent	Total	X^2	P- Value
	Frequency (%)	Frequency (%)			
Family history of breast cancer					
No	127 (83.0)	26 (17.0)	153 (93.3)	0.466	0.495
Yes	10 (90.9)	1 (9.1)	11 (6.7)		
Smoking Cigarettes					
No	134 (83.2)	27 (16.8)	161 (98.2)	0.602	0.438
Yes	3 (100)	0 (0.0)	3 (1.8)		
Alcohol intake					
No	113 (83.1)	23 (16.9)	136 (82.9)	0.116	0.733
Yes	24 (85.7)	4 (14.3)	28 (17.1)		
Moderate exercise					
No	102 (81.6)	23 (18.4)	125 (76.2)	1.43	0.231
Yes	35 (89.7)	4 (10.3)	39 (23.8)		
Strenuous exercise					
No	126 (82.9)	26 (17.1)	152 (92.7)	0.622	0.43
Yes	11 (91.7)	1 (8.3)	12 (7.3)		

X^2, Chi square; %, Percent

Table 3. Clinical Characteristics and Level of Adherence among Breast Cancer Patients Attending Chemotherapy at Tikur Anbessa Specialized Hospital, Addis Ababa Ethiopia, 2020

Variable	Adherent Frequency (%)	None Adherent Frequency (%)	Adherent Total Frequency (%)	X^2	P- Value
Patient with previous breast surgery					
No	127 (83.6)	25 (16.4)	152 (92.7)	0	0.984
Yes	10 (83.3)	2 (16.7)	12 (7.3)		
Stage at diagnosis					
I&II	35 (79.5)	9 (20.5)	44 (26.8)		0.926
III	63 (86.3)	10 (13.7)	73 (44.5)		
IV	39 (83.3)	8 (17.0)	47 (28.7)		
Histology type					
Ductal	121 (84.0)	23 (16.0)	144 (87.8)	0.796	`0.850
Lobular	6 (85.7)	1 (14.3)_	7 (4.3)		
Mixed	5 (83.3)	1 (16.7)	6 (3.7)		
Other/unspecified	5 (71.4)	2 (28.6)	7 (4.3)		
Course of recommended therapy					
Eight	93 (89.4)	11 (10.6)	104 (63.4)	8.5	0.014
Six	37 (71.2)	15 (28.8)	52 (31.7)		
Four	7 (87.5)	1 (12.5)	8 (4.9)		

X^2, Chi square; %, Percent

might be due to the focus of that study being on the rural part of Ethiopia. The mean age of study participants was 41.99 + 10.9 years which was lower than a study done in Northwest Iran where the mean age of study participants was 50.4 years (Dolatkhah et al., 2020). This could be due to the large proportion of women being found at a young age as described in previous studies done in Ethiopia (Tadele, 2015, Abate et al., 2016, Kantelhardtet al., 2014). Nearly half (48.2%) of women were less than 40 years of age, which was also comparable with previous studies done in Ethiopia (Tadele, 2015, Abate et al., 2016, Kantelhardt et al., 2014). It was found that 90.9 % of women were married, which was comparable with study done in rural Ethiopia, (93%) (Reibold et al., 2021), Nigeria (70%) (Ali-Gombe et al., 2021).

In this study, 137 out of 164 (83.5%) of women were adherent to their chemotherapy and 27 (16.5%) women's discontinued their chemotherapy before completion because of different reasons. This finding was lower than a study done on adherence to intravenous Chemotherapy in African-American and Caucasian Women, which was revealed that 90% of breast cancer women were adherent to their chemotherapy (Wells et al., 2015). This difference could be due to that in African-American and Caucasian women study was done among early stage breast cancer patients which might increase patients willingness due to higher probability of good outcome for early stage cancer. The other possible reason could be the study participants might have better chance to get treatment access within a short time due to better infrastructure and adequate health facilities. However this study finding was comparable with the same study done on Caucasian participants, which was 87.5% and 82.4% for African America participants (Wells et al., 2015). On the other hand, this finding was lower than another study done in USA, which had revealed that (88.1 %) completed the prescribed therapy, this difference could be due to the better infrastructure of the study setup and the study was focused on early discontinuation of chemotherapy in women with breast cancer (Neugut et al., 2016). However, this study was comparable with a

Table 4. Factors Associated with Non-adherence to Chemotherapy among Breast Cancer Patients Attending Chemotherapy at Tikur Anbessa Specialized Hospital, Addis Ababa

Variable	Frequency	Percent
Unknown/No response	7	25.9
Severity of disease /pain	9	33.3
Financial constraint	4	14.8
Security issue or distance	3	11.1
Did not believe in chemo/ visit holly water	1	3.7
Pregnancy	1	3.7
Comorbidity	1	3.7
Feels well	1	3.7
Total	27	100

study done in USA, which was found that among a total of 7,399 patients, 1,222 (16.5%) were non adherent cases (Barcenas et al., 2012).

In this study level of adherence was higher among never married women. It was also found that 52.0 % of women earn less than 2000 Ethiopian Birr per month. However, there was no significannt difference in the level of adherence based on monthly income. Regarding menopausal status 55% of women were premenopausal status, which was comparable to study done in rural Ethiopia (47%) (Reibold et al., 2021). The level of adherence was higher among post-menopausal women. This study also found that level of adherence was significantly lower among women who come from long distances from the referral cancer center. This could be due to lack of transport and accommodations. Regarding personal factors, level of adherence was higher among women who had family history of breast cancer as compared to women who did not have a family history of breast cancer. This might be due to women who had family history of breast cancer might have adequate information about the severity of the disease and the importance of treatment. It was also found that there was no statistically significant difference in the level of adherence among women who had a history of smoking as well as drinking alcohol. However level of adherence was higher among women who had experience of moderate as well as extraneous physical exercise.

Regarding clinical characteristics of the current study participants, the majority of women (44.5%) were found to be stage III tumor at diagnosis. Besides, ductal carcinoma was the commonest histology finding. This study finding was comparable with a previous study done in Ethiopia (Kantelhardt et al., 2014). However there was no difference in the level of adherence across tumor grade and tumor pathology/histology. In this study, the majority, 104, (63.4%) of patients recommended eight course chemotherapy, which was not comparable with study done in Nigeria (21.0%). This difference might be due to the different clinical condition of patients. In this study factors related to non-adherence to chemo therapy were assed. However the reason for non-adherence was unknown for a significant number 25.9% of patients. This is because it was difficult to access the patients through their phones in order to know their reason for non-adherence and their current status. Among a total of 27 non adherent women, the majority, 9 (33.3) of women did not adhere their treatment regimen due to the severity of their illness. On the other hand, 3 out of 27 (11.1%) of women did not adhere their treatment. This finding was not comparable with study done in Nigeria, which revealed that financial constraints were the main reasons for non-adherence to chemotherapy for 61% of the patients (Ingwu et al., 2019). This difference could be due to the focus of the Nigeria study was among 100 non adherent women which might explore the potential reasons for non-adherence. Even though their number is limited there were women who did not attend their chemotherapy as a result of financial constraints. Because there was a significant number of patient's living in rural areas, the long distance might prevent them from obtaining health service. Their information about towards breast cancer could also be limited as compared to urban patients.

As a limitation of this study, since it was difficult to get non adherent women, we could not explore different personal and health service related factors which can affect the adherence level of breast cancer patients. There would be potential bias in the data collected using telephone interview and imprecise answers about adherence by relatives of deceased patients. In addition Factors associated with non-adherence were analyzed based on the baseline data which is mainly focused on patient related factors.

In conclusion, the results showed that the majority 137, (83.5%) of patients were in good adherence with their chemotherapy. The most identified factors were inability to come for their therapy as a result of the severity of illness and the residences of patients were long distance from the cancer referral center. For non adherence, distance from referral center and course/regimen of chemotherapy were significantly associated with non-adherence. Therefore, Health care providers should provide adequate information for their patients and establish certain mechanisms for those patients who had withdrawn from their treatment in order to identify reasons for non-adherence and to take appropriate action.

Author Contribution Statement

Conceptualization and design, Data acquisition, Data analysis and interpretation, Critical revision of the manuscript: Fatuma Hassen, Fikre Enquselassie, Aster Tsegaye, Mathewos Assefa, Ahmed Ali, Adamu Addissie, Girma Taye. Supervision and and final approval: Fatuma Hassen, Aster Tsegaye, Mathewos Assefa, Ahmed Ali, Adamu Addissie, Girma Taye.

Acknowledgments

The authors would like to thank the Addis Ababa University, School of Public Health for funding and facilitating the overall research activity. The Department of Oncology and the study participants are gratefully acknowledged for their cooperation.

Funding

This study was funded by Addis Ababa University and principal investigator. The university had no role in the study design, data collection and data analysis, decision to publish and manuscript preparation. Since the fund was given for an academic exercise by the university, there was no an award/grant number.

Ethics approval

This study was approved by Institutional Review Board of College of Health Sciences of the Addis Ababa University with protocol number 073/17/SPH.

Patient consent

Informed written consent form was signed by the participants.

Data sharing statement

Due to privacy and ethical concerns, supporting data cannot be made openly available.

Conflict of Interests

All authors declare that there is no conflict of interests regarding the publication of this paper manuscript.

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