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# Assessing oral Health-Related quality of life in women undergoing chemotherapy for breast Cancer in Karachi Pakistan

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**Introduction.** In Pakistan, women undergoing chemotherapy are usually unaware of the potential impact of the treatment on their oral health related quality of life. This study aims to assess the impact of chemotherapy on oral health related quality of life. **Method.** A cross-sectional study was conducted among 160 breast cancer (BC) patients on chemotherapy coming to Aga Khan Hospital and Jinnah Postgraduate medical center. Data collection was performed using a validated questionnaire for sociodemographic variables, types and frequency of oral hygiene measures, oral mucositis (OM) and oral health related quality of life (OHRQoL) and oral examination was performed. Data was analyzed using simple linear regression method. **Results.** Among these females, 119 were married, with a mean age of  $47.64 \pm 10.89$  years. OM was present in 88, 25 used miswak/dentonic, 33 did not receive care by dentists/nurses, 15 reported moderate to severe gingival inflammation, and 85 were at stage 3 BC. OHRQoL was significantly associated with OM, women's age, marital status, gingival status, and platelet count. **Conclusion.** This multi-center cross-sectional study highlights poor OHRQoL among BC patients undergoing chemotherapy. These findings highlight the need for comprehensive oral health care for these patients to improve their quality of life and treatment outcomes. **Word Count:** 201.

**Keywords** Breast Cancer, Oral health and hygiene, Oral mucositis, Oral health related quality of life, Chemotherapy

Breast cancer (BC) is the most frequent cancer among women worldwide and the primary cause of cancer-related mortality for women<sup>1</sup>. Based on population patterns, an estimated 2.2 million newly diagnosed cases of BC are projected to exist worldwide yearly<sup>2</sup>. The threefold increase in incident cases of BC during the last few decades may be attributed to population growth, age-specific incidence rates rising, and a change in the age makeup of the population<sup>3</sup>. Although incidence has increased, BC death rates have decreased by 40% since their peak, most likely as a result of effective early detection programs and developments in adjuvant therapy<sup>4</sup>. However, the prevalence of BC in Pakistan has risen over the last few years with one in every nine Pakistani women diagnosed with BC at some point in their life<sup>5</sup>.

Numerous treatments, including chemotherapy, radiotherapy, and long-term hormonal adjuvant therapy with aromatase inhibitors (up to 8 years), are used to treat cancer and encourage disease-free survival with radiotherapy and surgery being the most common treatment option for oligometastatic breast cancer<sup>6,7</sup>. For a long time, it was considered that patients diagnosed with relapsed cancer cannot be cured. For such patients, only available treatment of choice was systemic chemotherapy. However, advancements in cancer treatment have expanded the range of therapeutic options, providing hope for improved outcomes<sup>8</sup>. Common chemotherapeutic drugs for early breast cancer include anthracycline such as doxorubicin and epirubicin, as well as taxanes like docetaxel and paclitaxel<sup>9</sup>. These are frequently administered alongside other chemotherapy agents such as carboplatin, cyclophosphamide, and fluorouracil<sup>9</sup>. Unfortunately, these medicines have a variety of unfavorable side effects that are harmful to health and have negative impact on quality of life<sup>10,11</sup>. Oral health and hygiene amongst all is one of the most impacted region by chemotherapy regimen<sup>10,12</sup>. During or after BC therapy, there is a higher incidence of xerostomia, mucositis, tooth loss, and gingival bleeding<sup>12</sup>. Chemotherapy also impacts

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the nutritional condition of patients<sup>13</sup>. Neglecting to assess and monitor the ongoing treatment status of both soft and hard oral tissues and to implement sufficient precautions can significantly impact therapy outcomes<sup>13</sup>. All these factors are associated with poor Oral health related quality of life (OHRQoL)<sup>14</sup>.

Examining OHRQoL alongside standard measures provides a more comprehensive insight into how oral disorders affect the daily lives of BC patients<sup>15</sup>. OHRQoL is stated as a “multidimensional construct that reflects people’s comfort with their oral health as well as their comfort when eating, sleeping, and interacting with others”<sup>15</sup>. Poor oral health can have a negative impact on one’s physical, social, and psychological well-being. A person’s quality of life might be affected by their oral health. Since oral health and the resulting quality of a person’s life are crucial to overall health and wellbeing, the World Health Organization has identified oral health as a key component of its Global Oral Health Program<sup>16</sup>. The oral health impact profile (OHIP) is an instrument used to measure quality of life in relation to oral health. It has been observed that the OHIP-14 short form is a valuable instrument with good validity, reliability, and accuracy for use in a clinical environment<sup>17</sup>. The questionnaire is based on a conceptual oral health model and is intended to measure self-reported dysfunction, discomfort, and impairment attributable to oral disorders<sup>18</sup>.

Chemotherapy has reduced the mortality rate of cancer patients; however, oral complications experienced by women during their chemotherapy cycles such as xerostomia, oral mucositis, tooth loss, and gingival bleeding affect their overall OHRQoL hindering cancer treatment and care<sup>10,12</sup>. Understanding the impact of these oral health issues on patients’ quality of life is essential for providing comprehensive care and support during cancer treatment. By employing validated instruments like the Oral Health Impact Profile (OHIP-14), this study aims to quantify the physical, social, and psychological burden of oral health problems among breast cancer patients undergoing chemotherapy. Pakistani women undergoing chemotherapy for breast cancer treatment are usually unaware regarding the potential impact of chemotherapy on oral health impacting their OHRQoL, therefore this study aims to assess the impact of chemotherapy and factors associated with to assess OHRQoL using OHIP-14 score in women undergoing chemotherapy for BC after at least 1 cycle of chemotherapy at AKUH & JPMC in Karachi, Pakistan.

## Materials & methods

### Study design and setting

A cross-sectional study design was employed to assess OHRQoL amongst women undergoing chemotherapy for BC with or without oral mucositis after at least one cycle of chemotherapy at the Aga Khan Hospital and Jinnah Postgraduate Medical Centre Karachi.

### Study population, sampling technique, and sample size

All participants visiting Oncology departments of Aga Khan University Hospital (AKUH) and Jinnah Postgraduate Medical Centre (JPMC) from July 20th to October 20th, 2021, were enrolled in the study.

Permission was taken from the oncology department of the two hospitals. Women meeting the eligibility criteria were approached for the informed consent and recruited after it was obtained. After informed consent, patients were interviewed without intervening the pace of clinics. Data collection included in person interviews and oral examination, both were done by principal investigator and research associate.

This study builds upon our previously published study “Oral mucositis & oral health related quality of life in women undergoing chemotherapy for breast cancer in Karachi, Pakistan: A multi-center hospital based cross-sectional study”<sup>19</sup>. All women diagnosed were above 18 years with early-stage breast cancer planned to receive neo-adjuvant or adjuvant systemic chemotherapy. These patients had undergone at least one cycle of chemotherapy and gave consent to participate in the study. Patients were excluded if they had history of other malignancy or recurrence of breast cancer and receiving chemotherapy.

Participants were recruited through non-probability purposive sampling technique. Around 174 patients were approached, six patients refused to participate and eight were excluded due to other malignancy and stage four breast cancer diagnosis (Fig. 1). A minimum sample of 160 women diagnosed with breast cancer were needed to achieve the study objectives. Sample size was calculated using OpenEpi software keeping the frequency of BC women of 40%, 5% level of significance, 80% power and adjusting for 10% non-respondent<sup>15</sup>. The patients who gave consent were approached for interviews and oral examination.

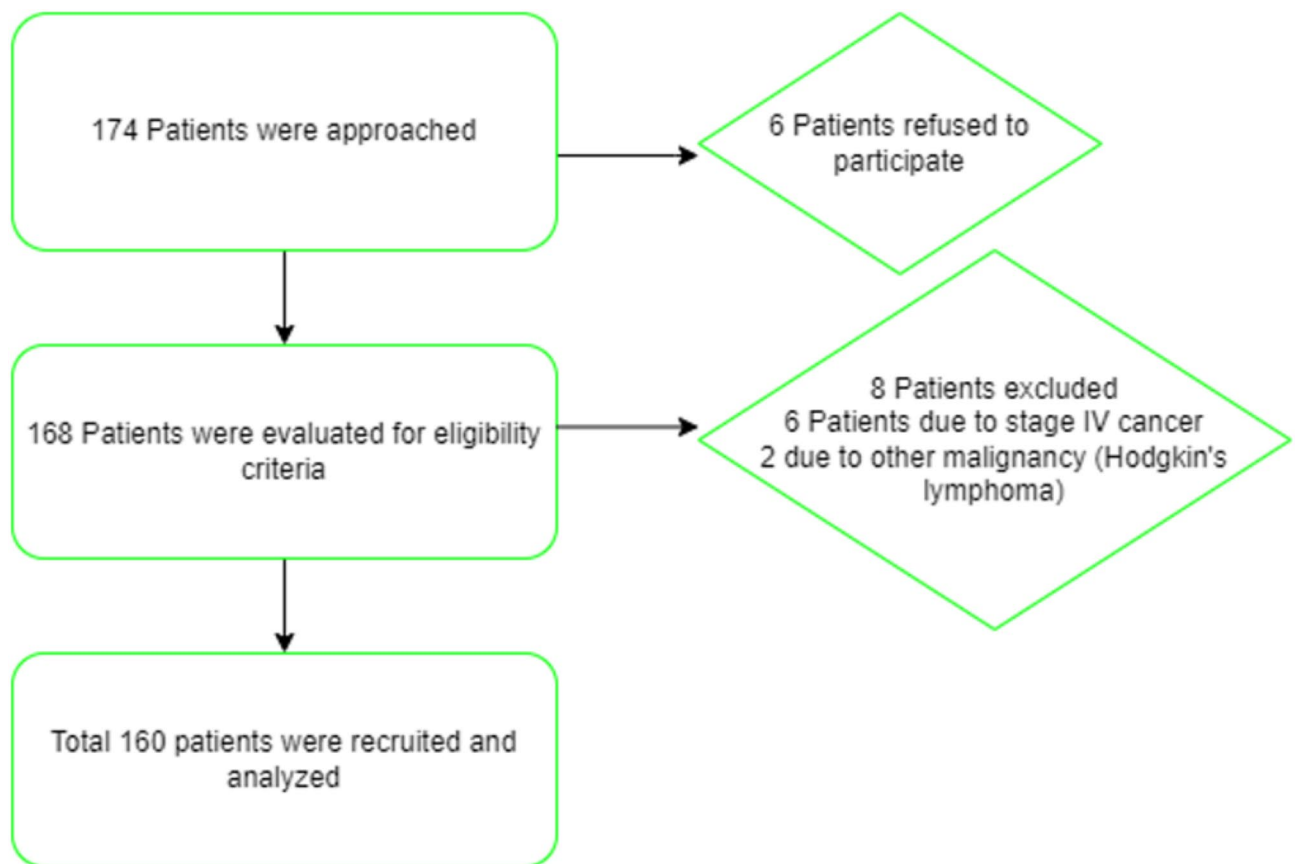
### Variables and data collection tools

Data were collected using a self-administered questionnaire and oral examination of patients. The author (Asad Allana) of the manuscript created the questionnaire for the present study. Structured Questionnaire included multiple sections regarding sociodemographic variables, types of oral health hygiene measures and frequency of oral hygiene measures. Oral mucositis was assessed using WHO OM tool, OHRQoL were assessed using OHIP-14 and gingival status was assessed using Loes and Silness gingival index. Oral examination was performed using facemasks, torch, gloves and disposable dental examination kits. During oral examination patient’s oral hygiene, presence or absence of oral Mucositis, Decayed, Missing, Filled teeth (DMFT), gingival status and presence or absence of dental prosthesis were assessed.

### Outcome variable

#### Oral health related quality of life (OHRQoL)

OHRQoL is compromised among patients diagnosed with breast cancer and undergoing chemotherapy. For assessment of OHRQoL, a structured OHIP 14 questionnaire was used to assess these participants (Fig. 2). This questionnaire is a shorter version of OHIP-49 scale by Slade and Spencer. This scale consists of seven dimensions including Functional limitation, physical pain, psychological discomfort, physical disability, psychological



**Fig. 1.** Patient flow chart.

disability, social disability and impairment<sup>20</sup>. A Likert scale is followed with coding 0 as never, 1 as hardly ever, 2 as occasionally, 3 as fairly often, and 4 as very often. The scores ranges from 0 to 56<sup>21</sup>. The score of > 11.0 shows overall poor OHRQoL and the score of < 9.3 is considered a good score for overall OHRQoL<sup>22</sup>. The tool has been used in both English and Urdu languages in multiple studies with reliability of 0.84 and 0.7 respectively<sup>20,22,23</sup>.

### Exposure variable

#### *Oral mucositis*

Oral Mucositis (OM) is a common and serious side effect of cancer chemotherapy treatment, and despite the use of a number of treatments, it remains a significant source of further illness and discomfort<sup>24,25</sup>. It has been observed that the quality of life among women diagnosed with breast cancer, suffering from OM, is significantly affected<sup>26</sup>. For assessment of OM, the World Health Organization (WHO) grading scale for OM was utilized. The scale is based on clinical features and functionality of the participant (Fig. 3). This scale is dependent upon the variables which can be both objective and subjective in nature<sup>27</sup>. It measures components that are anatomical, symptomatic and functional related to OM<sup>27</sup>.

### Demographic and health related variables

Sociodemographic variables including age, educational level, and socioeconomic status were gathered. Socioeconomic status was analyzed using Modified KUPPUSWAMY scale<sup>28</sup>. The scale has three items including occupation, education and total monthly income of the family<sup>28</sup>. In previous studies, it was observed that people diagnosed with cancer and low socioeconomic status had poor oral health conditions<sup>29</sup>. According to the scores, value of ≤ 10 indicates lower class, 11 to 25 range indicates middle class, and 26 to 29 range indicates upper class<sup>29</sup>.

Health related outcomes include menopausal status, frequency of oral hygiene measures used, gingival status, smokeless tobacco consumption, white blood count levels, type of chemotherapy and number of cycles of chemotherapy.

To assess gingival inflammation, the study employed the “Löe and Silness Gingival Index”, a widely recognized tool for measuring gingival health based on visual signs and bleeding tendency (Fig. 4). This index categorizes gingival status into four scores: Score 0 indicates normal gingiva with a natural coral pink color and no signs of inflammation, score 1 represents mild inflammation with slight changes in color and slight edema without bleeding on probing, score 2 denotes moderate inflammation with redness, edema, glazing, and bleeding upon

**Box 2 OHIP-14 questionnaire**

Dimension	Question
Functional limitation	Have you had trouble <i>pronouncing any words</i> because of problems with limitation your teeth, mouth, or dentures?
	Have you felt that your <i>sense of taste</i> has worsened because of problems with your teeth, mouth, or dentures?
Physical pain	Have you had <i>painful aching</i> in your mouth?
	Have you found it <i>uncomfortable to eat any foods</i> because of problems with your teeth, mouth, or dentures?
Psychological discomfort	Have you been <i>self-conscious</i> because of your teeth, mouth, or dentures?
	Have you <i>felt tense</i> because of problems with your teeth, mouth, or dentures?
Physical disability	Has your <i>diet been unsatisfactory</i> because of problems with your teeth, mouth, or dentures?
	Have you had to <i>interrupt meals</i> because of problems with your teeth, mouth, or dentures?
Psychological disability	Have you found it <i>difficult to relax</i> because of problems with your teeth, mouth, or dentures?
	Have you been a bit <i>embarrassed</i> because of problems with your teeth, mouth, or dentures?
Social disability	Have you been a bit <i>irritable with other people</i> because of problems with your teeth, mouth, or dentures?
	Have you had <i>difficulty doing your usual jobs</i> because of problems with your teeth, mouth, or dentures?
Handicap	Have you felt that life in general was <i>less satisfying</i> because of problems with your teeth, mouth, or dentures?
	Have you been <i>totally unable to function</i> because of problems with your teeth, mouth, or dentures?

**Fig. 2.** Oral Health Impact Profile (OHIP-14) to measure OHRQoL.

probing, and score 3 indicates severe inflammation characterized by marked redness, edema, ulceration, and spontaneous bleeding<sup>30,31</sup>.

#### Data collection procedure

The principal investigator hired a data-collecting officer with dental expertise for a time of three months. The data collector was trained for consent, recruitment, oral examination, outcome assessment and data collection methods. For facilitation in consistency of study implementation a manual of operations was shared with data

Grade	Description
0 (none)	None
I (mild)	Oral soreness, erythema
II (moderate)	Oral erythema, ulcers, solid diet tolerated
III (severe)	Oral ulcers, liquid diet only
IV (life-threatening)	Oral alimentation impossible

Fig. 3. WHO tool to measure OM.

Scores	Gingival Status	Criteria
0	Normal gingiva	Natural coral pink gingival with no e/o inflammation
1	Mild inflammation	Slight changes in color, slight edema. No bleeding on probing
2	Moderate inflammation	Redness, edema and glazing. Bleeding upon probing
3	Severe inflammation	Marked redness and edema/ ulceration/tendency to bleed spontaneously

Fig. 4. . Gingival index of Loe and Silness to measure Gingival inflammation.

collecting officer. The data collector had to report to PI at the end of each week about patient enrolment and interview forms.

**Ethical clearance**

The Departmental Review Committee (DRC) initially conducted ethical review. After receiving an approval from DRC, the proposal was sent to Ethical Review Committee (ERC) of both AKUH and JPMC [ERC # 2021–5895-17872]. The study began after receiving approvals. Training sessions for data collector were held in order to regulate the study in an ethical manner.

**Statistical analysis**

The outcome variable, oral health related quality of life (OHRQoL) is a continuous variable and calculated on the basis of scores. Multiple linear regression analysis was performed using STATA version 17 software. The descriptive statistics of all independent variables and outcome variable was conducted. For all normally distributed continuous variables like age, mean and standard deviations were reported. Median and Interquartile ranges (IQR) of all skewed continuous variables like cycles of chemotherapy were provided. All categorical variables like marital status, level of education, socioeconomic status, menopause status, oral hygiene measures used, frequency of oral hygiene used, use of smokeless tobacco, oral care provision by doctors/nurses, DMFT, gingival status, stage of cancer, type of chemotherapy, WBC counts, neutrophil counts, platelets count, and oral mucositis status were summarized using frequencies and percentages.



The univariate analysis was performed using simple linear regression analysis. Each variable was regressed separately with OHRQoL. Linear regression coefficients, standard errors and 95% confidence intervals were reported. The significance was assessed at a p-value of  $\leq 0.25$ . Such variable with p-values greater, were removed and other variables with significant p-values were included in multivariable analysis. In multivariable analysis, all variables that were significant at univariate analysis level, these were assessed using stepwise multiple linear regression analysis. All variables with a p-value  $\leq 0.05$  were included in the model. The presence of biologically plausible interaction and confounding was also assessed. The final model was evaluated for adequacy by normal probability plots.

### Data management

The Principal Investigator (PI) on regular basis reviewed the data collected by the data collector. Questionnaires were rigorously reviewed for completeness, logical data entry, and consistency. After finishing the full data collection, PI performed the last editing of the data to achieve an accurate data entry process. Data editing and cleaning was performed on site using different color pens. The responses received by the participants were then entered into google form to get the data in a spreadsheet. Data cleaning was performed to thoroughly inspect the content, discover errors and wild code entries. It was done to assess missing information and rectify errors.

In order to ensure that the data were not misplaced, backup files were created. To ensure confidentiality, backup files didn't have participant's name and contact details. Data were stored in such a manner that each participant was provided with unique ID numbers. The Electronic data have been secured with a password and this data will be discarded after seven years of completion of the study as per university policy. Strict measures were taken to minimize the data handling and movement.

### Results

A total of 160 women having BC, participated in this study. Among them, 12 (7.50%) were single, 119 (74.38%) were married, and 29 (18.13%) were separated or widowed. The mean age of the participants was  $47.64 \pm 10.89$  years.

Out of 160 women, 25 (15.63%) reported using miswak/dentonic as an oral hygiene measure, while 135 (84.38%) reported using brushing. Regarding the frequency of oral hygiene practices among the women, 41 (25.63%) reported using oral hygiene products occasionally, 88 (55%) reported using them once daily, and only 31 (19.38%) reported using them twice daily. Additionally, among these women, 33 (20.63%) did not receive oral care provided by doctors/nurses, while 127 (79.38%) received such care. Among the total women participated, 83 (51.88%) had no gingival inflammation, 62 (38.75%) reported mild gingival inflammation and only 15 (9.38%) reported moderate to severe gingival inflammation.

Out of 160 women participated, 7 (4.38%) were at stage 1, 68 (42.50%) were at stage 2, and 85 (53.13%) were at stage 3. Additionally, the median and interquartile range (IQR) of cycles of chemotherapy was 7 (8). Significant differences were observed among the types of chemotherapy received by the participants, where 41 (25.63%) received Taxanes only, 31 (19.38%) received AC only, and 88 (55%) received both Taxanes and AC. The mean OHIP-14 score of 160 BC women was  $15.55 \pm 0.67$  as shown in Table 1.

Out of the total participants, 33 women (26.3%) had a mild form of OM classified as Grade 1, 32 women (20%) had a moderate form of OM classified as Grade 2, and 23 women (14.4%) had a severe form of OM classified as Grade 3. However, for the purpose of analysis in our study, OM was treated as a binary variable, with 88 women (55%) classified as having OM present and 72 women (45%) as having OM absent, as shown in Table 2.

In the final model, oral mucositis, Age of women, marital status, gingival status, and platelet count were significant factors (p-value  $< 0.05$ ). These independent variables collectively explained 30.14% of the variability in the quality of life among breast cancer women. The final model indicated that the estimated mean scores of OHRQoL, as measured by OHIP-14, increased by 0.11 ( $-0.001$  0.22) units with every one-year increase in women's age. It is important to note that in the OHIP-14 scale, an increase in the score indicates a worsening quality of life. Furthermore, the estimated mean scores of quality of life among breast cancer women with oral mucositis was 5.97 (3.6 8.29) units higher compared to those without oral mucositis (Table 3).

### Discussion

This study assessed the Oral Health-Related Quality of Life (OHRQoL), and the factors linked to it among breast cancer women. Our results showed that the mean OHIP-14 score was 15.5, this mean score was quite close to a study conducted in Karachi Pakistan in a tertiary care hospital which showed that the mean OHIP-score of patients was 18.9<sup>17</sup>. Our study showed that for women with OM, the overall OHIP score increases by 5.97 (95% CI: 3.65–8.29) indicating decrease in overall OHRQoL. These results were in line with a study conducted by Qamar et al. in Karachi Pakistan which showed high score of for OHRQoL ( $25.3 \pm 15.6$ ) was observed in patients with moderate to severe OM<sup>32</sup>. Another study conducted by Sahni et al. showed that patients with oral alterations such as OM, Lichenoid reaction, vesiculobullous disease following chemotherapy had a significantly higher overall OHIP-14 score ( $12.4 \pm 7.4$ ) compared to their OHIP-14 score prior to chemotherapy ( $4.0 \pm 7.7$ )<sup>15</sup>.

Our results showed that for every one-year increase in age, the overall OHIP score increases by 0.11 (95% CI:  $-0.001$  to 0.22), indicating a decline in overall Oral Health-Related Quality of Life (OHRQoL). Although age was only marginally significant (p-value 0.052), it was retained in the final model due to its biological plausibility. This finding aligns with a study by Zucoloto et al. conducted in Araraquara, Brazil, which showed that among the age was the significant predictor of poor OHRQoL. Their results also showed that health-related quality of life deteriorates with increasing age<sup>33</sup>. Similar findings have been reported in another study conducted by Uliniski et al. in Brazil, which demonstrated a negative impact of age on OHRQoL. The study showed that as age

Characteristics	Frequency	Percentages
<b>Age* (in years)</b>	47.64	10.89
<b>Marital status</b>		
Single	12	7.50
Married	119	74.38
Separated /widowed	29	18.13
<b>Level of education</b>		
Schooling /matric Low Middle High	109	68.13
Intermediate	17	10.63
Graduate/post-graduation	34	21.25
<b>Employment status</b>		
Un-employed	146	91.25
Employed	14	8.75
<b>Socio-economic status</b>		
Low	95	59.38
Middle	40	25
High	25	15.63
<b>Menopause status</b>		
Pre-menopausal	78	48.75
Post-menopausal	82	51.25
<b>Oral hygiene measures used</b>		
Miswak /Dentonic	25	15.63
Brush	135	84.38
<b>Frequency of oral hygiene used</b>		
Occasionally	41	25.63
Once daily	88	55.00
Twice daily	31	19.38
<b>Use of smokeless tobacco</b>		
No	139	86.88
Yes	21	13.13
<b>Oral care provided by doctors/nurses</b>		
No	33	20.63
Yes	127	79.38
<b>DMFT</b>		
Low (0.0–2.6)	30	18.75
Moderate (2.7–4.4)	7	4.38
High (4.5 & > )	123	76.88
<b>Gingival status</b>		
No inflammation	83	51.88
Mild inflammation	62	38.75
Moderate to severe inflammation	15	9.38
<b>Stage of cancer</b>		
Stage 1	7	4.38
Stage 2	68	42.50
Stage 3	85	53.13
<b>Cycles of chemotherapy**</b>	7	8
<b>Type of chemotherapy</b>		
Taxanes only	41	25.63
AC only	31	19.38
AC + Taxanes	88	55
<b>WBC Counts</b>		
Low (< 4.5 × 10 <sup>9</sup> /L)	31	19.38
Normal (4.5 × 10 <sup>9</sup> /L to 11 × 10 <sup>9</sup> /L)	122	76.25
High (> 11 × 10 <sup>9</sup> /L)	7	4.38
<b>Neutrophil count</b>		
Low (< 50%)	14	8.75
Normal (50–75%)	135	84.38
High (> 75%)	11	6.88
<b>Platelet count</b>		
Low(400 × 10 <sup>9</sup> /L)	6	3.75
Normal(140 × 10 <sup>9</sup> /L-400 × 10 <sup>9</sup> /L)	124	77.50
High(> 400 × 10 <sup>9</sup> /L)	30	18.75
<b>OHIP-14 score</b>	15.55	0.67
DMFT: Decayed, missing, filled Teeth AC: Adriamycin cyclophosphamide WBC: white blood cells *Mean ± SD **Median (IQR)		

**Table 1.** Percentage distribution of socio-demographic, personal habits, oral hygiene measure, clinical characteristics & OHIP-14 scores among 160 breast cancer women in a multi-center study, Karachi, Pakistan.

Characteristics	Frequency	Percentages
Oral Mucositis grading	72	45
None (Grade 0)	33	20.63
Mild (Grade 1)	32	20
Moderate (Grade 2)	23	14.37
Severe (Grade 3)		
Oral Mucositis*	72	45
Absent	88	55
Present		

**Table 2.** Percentage and severity distribution of oral mucositis among 160 breast cancer women in a multi-center study, Karachi, Pakistan. \* Oral Mucositis was classified as a binary variable with two categories: Present and Absent.

Characteristics	Unadjusted $\beta$ (95% CI)	Adjusted $\beta$ (95% CI)
Oral mucositis	Ref	Ref
Absent	6.24 (3.73 8.74)	5.97 (3.65 8.29)
Present		
Frequency of oral hygiene used	4.27 (0.33 8.22)	
Occasionally	4.88 (1.43 8.34)	
Once daily	Ref	
Twice daily		
Age	0.19 (0.07 0.31)	0.11 (−0.001 0.22)
Marital status	Ref	Ref
Single	6.88 (1.92 11.84)	6.44 (2.08 10.79)
Married	9.78 (4.16 15.40)	9.27 (4.12 14.43)
Separated /widowed		
Level of education	−0.87 (−4.16 2.42)	
Schooling /matric	−5.24 (−10.20 −0.27)	
Intermediate	Ref	
Graduate/post-graduation		
Employment status	2.88 (−1.83 7.59)	
Un-employed	Ref	
Employed		
Menopause status	Ref	
Pre-menopausal	2.44 (−0.21 5.09)	
Post-menopausal		
Gingival status	Ref	Ref
No inflammation	1.09 (−1.62 3.81)	−0.03 (−2.47 2.42)
Mild inflammation	9.12 (4.58 13.66)	6.21 (2.12 10.30)
Moderate to severe inflammation		
Platelet count	Ref	Ref
Normal( $140 \times 109 /L$ – $400 \times 109 /L$ )	9.15 (2.27 16.03)	7.18 (1.15 13.21)
Low( $400 \times 109 /L$ )	−2.52 (−5.87 0.83)	−1.93 (−4.85 0.98)
High( $> 400 \times 109 /L$ )		

**Table 3.** Comparison of unadjusted and adjusted  $\beta$ - coefficient with 95% CI for factor associated with quality of life among breast cancer women in a multi-center study, Karachi, Pakistan. \*Ref: reference category taken for the variable

increased, the OHIP-14 scores decreased, likely due to the greater impact of oral and systemic diseases on elderly individuals. This suggests that older adults may experience a decline in their oral health-related quality of life as they age, highlighting the importance of addressing oral health issues in this population<sup>34</sup>.

Our study found that women experiencing moderate to severe gingival inflammation had an overall increase in the OHIP score by 6.21 (95% CI: 2.12–10.30), indicating a decline in their overall oral health-related quality of life (OHRQoL). These findings are supported by a study conducted by Oliveira et al., which showed that greater levels of full-mouth gingival inflammation (RR = 1.23; 95% CI: 1.06–1.44;  $p = .004$ ) and gingival inflammation confined to the anterior region (RR = 1.29; 95% CI: 1.11–1.51;  $p \leq .001$ ) were significantly linked to poorer OHRQoL<sup>35</sup>. The reduction in Oral Health-Related Quality of Life (OHRQoL) due to gingival inflammation can be explained by the increase in redness, swelling, bleeding, tenderness, and enlargement of the gums. These signs and symptoms can lead to psychological challenges, such as negative social interactions and dissatisfaction with one's appearance, especially when they occur in the front teeth. Additionally, experiencing bleeding during everyday activities like brushing teeth may affect one's perception of their oral health, thereby contributing to the observed association<sup>36,37</sup>.

Our study showed that for women who are separated or widowed the overall OHIP score increases by 9.27 (95% CI: 4.12 14.43) and for women who are married the overall OHIP score increases by 6.44 (95% CI: 2.08 10.79) compared to women who are single indicating decrease in OHRQoL in both groups. For married women similarly, a study conducted by Beşiroğlu et al. on a Turkish population found that marital status is associated with periodontal status. The study showed that married individuals exhibited poorer periodontal health and



lower OHRQoL, as reflected by OHIP-14 scores, compared to single individuals. Additionally, the rate of regular brushing twice or more daily was lower among married individuals than single individuals<sup>38</sup>. Another cross-sectional study of a Spanish population by Aguilera et al. also found that married individuals had higher OHIP-14 scores than single individuals and more than half of the individuals with “stress-related” oral problems were married<sup>39</sup>. For separated or widowed women, several factors contribute to the decline in OHRQoL. Emotional stress and loneliness following separation or widowhood can negatively impact oral health habits and routines. Financial difficulties might limit access to dental care and proper oral hygiene products. Additionally, the loss of social support can lead to neglect of self-care practices, including oral health maintenance. These factors collectively contribute to the deterioration of oral health and overall quality of life in separated or widowed women.

Our result showed that in women with low platelet count the overall OHIP score increases by 7.18 (95% CI: 1.15–13.21), indicating a decline in their overall oral health-related quality of life (OHRQoL). A low platelet count, or thrombocytopenia, can impair these processes, making the mucosal tissues more susceptible to injury and increasing the likelihood of bleeding. This vulnerability can exacerbate the severity of oral mucositis, a common and painful side effect of chemotherapy that involves inflammation and ulceration of the oral mucosa. These findings align with the study conducted by Khelif et al., which reported that patients with persistent/chronic immune thrombocytopenia (cITP) not only have low platelet counts and an increased risk of bleeding and bruising but also often suffer from a reduced OHRQoL. Treatments for cITP can enhance OHRQoL by elevating platelet counts, however they may also induce side effects that adversely affect health-related quality of life, underscoring the necessity for balance in managing this condition<sup>40</sup>. One factor contributing to reduced OHRQoL in individuals with platelet disorders could be their hesitation to brush and floss regularly due to the fear of bleeding. This reluctance may lead to higher rates of cavities and periodontal (gum) disease among these individuals compared to the general population<sup>41</sup>.

Our results also showed that around 68% of the BC women had low educational status, having completed only primary, secondary schooling, or matriculation. These findings support the association between low education and poor OHRQoL. A low level of education negatively impacts OHRQoL by limiting access to information about proper oral hygiene, constraining financial resources for dental care, reducing health literacy, and influencing health behaviors negatively. Individuals with less education often adopt poor oral health habits, face economic barriers to accessing dental services, and have lower health literacy, which affects their ability to follow dental care instructions and recognize early dental issues. Additionally, they may live in environments with fewer health resources and receive less social support for maintaining oral health, further exacerbating their risk of dental problems and overall poorer OHRQoL<sup>42</sup>.

Our results also showed that approximately 51% of the women with breast cancer were in the postmenopausal stage. However, menopausal status was statistically insignificant in our study. These results were quite contrast to a study conducted by Kim YH et al. which showed that post menopause can significantly impact oral health, affecting the overall quality of life of individuals<sup>43</sup>. Post menopause significantly impacts oral health, often leading to conditions such as dry mouth, gum disease, bone loss, burning mouth syndrome, and altered taste sensations. The consequences of these oral health issues extend beyond physical discomfort; they can diminish self-esteem, hinder social interactions, and impair daily functions like eating and speaking, ultimately reducing the overall quality of life<sup>43</sup>.

This study has several notable strengths. First, it not only measured the overall OHRQoL scores but also assessed all associated factors in detail with OHRQoL in BC patients. Another notable strength is the multi-center design, which included both public and private hospital settings. This diverse sampling increased the generalizability of the results across different socio-economic statuses. Additionally, the study included patient counseling and education on oral hygiene practices, such as brushing techniques, and prescribed mouthwashes and gels in the government hospital, demonstrating a practical application of findings to improve patient care.

Despite its strengths, the study has several limitations. The cross-sectional design introduces inherent biases such as recall bias and non-response bias and limits the ability to establish temporality between different exposures such as OM, age, marital status, platelet count and the outcome (OHRQoL). A longitudinal follow-up study would provide more robust results by tracking patients over time, allowing for a more accurate measurement of the effects of chemotherapy type and number of cycles on OHRQoL. Furthermore, the lack of stratification according to the hospital setup (government vs. private) may have resulted in an overestimation of OHRQoL issues. Most patients were from the government hospital, and a weighted sample size should have been calculated to account for the potential differences in OHRQoL between the two settings.

Future research should consider longitudinal designs to establish causal relationships between chemotherapy, oral health complications, and OHRQoL over time. There is a need for intervention studies to develop and evaluate strategies to mitigate the oral health side effects of chemotherapy and improve OHRQoL among breast cancer patients. Expanding the study to include patients from various geographical regions, including rural areas, would enhance the generalizability of the findings. Integrating dental care with oncology services could be explored to provide comprehensive care and improve the overall quality of life for breast cancer patients undergoing chemotherapy.

## Conclusion

This multi-center cross-sectional study highlights the significant impact of OHRQoL among women undergoing chemotherapy for BC in Karachi, Pakistan. Oral mucositis, age, marital status, gingival status, and platelet count were identified as key factors affecting OHRQoL. Oral mucositis notably emerged as a substantial determinant, significantly lowering OHRQoL. Increasing age, severe gingival inflammation, and low platelet count were also associated with decreased quality of life. Although education level and menopausal status were not statistically significant, they are important factors influencing overall well-being. These findings underscore the importance

of comprehensive oral health care for breast cancer patients undergoing chemotherapy. Patients should maintain consistent oral hygiene and have regular dental check-ups to minimize complications. Treating physicians are encouraged to integrate dental care into oncology services to improve overall treatment outcomes and quality of life.

## Data availability

The datasets generated and analyzed during the current study are not publicly available due to individual privacy could be compromised but are available from the corresponding author on reasonable request.

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## Author contributions

Conception or design: AA, US. Execution of Project: AA, AI, MAK, US, YR, FRK and SR. Questionnaire & Data Collection: AA. Data Analysis and interpretation: AA and AI. Drafting the Article: AA, AI and MAK. Table formulations: AA and AI. Critical review: AA and MAK. Final approval: AA and MAK.

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## Declarations

## Competing interests

The authors declare no competing interests.

## Ethics approval

Ethical approval was obtained from Ethical Review Committee of the Aga Khan University Hospital, Karachi, Pakistan (Ref no. 2021-5895-17872). Written informed consent was obtained from all the study participants. All methods were performed in accordance with the Declaration of Helsinki.

## Consent for publication

Consent was obtained from the participants of the study to publish the study results, online in a scientific journal.

## Informed consent

Before data collection, all participants were asked to sign a form of consent to be included in this study.

## Author disclosure statement

No competing financial interests exist.

## Additional information

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