RESEARCH ARTICLE

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Work Ability, Anxiety, and Depression among Long-Term Breast Cancer Survivors of Northern Kerala, India; A Historical Cohort Study

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Abstract

Background: Increasing number of breast cancer cases, and improved survival due to advancements in early detection, and treatment resulted in an increase in women living beyond a cancer diagnosis. Survivors have to face long-term physical effects as well as psychosocial issues post-treatment. This study aims to study survivourship in terms of work ability, anxiety and depression. **Methods:** Retrospective cohort study on female breast cancer survivors from Hospital Based Cancer Registry (HBCR) of a Tertiary Cancer Centre (TCC). Data from 2016 (n=534) were collected from the medical records, and a follow-up survey (n=209) was conducted in 2022 to study their survivorship issues. **Results:** In 2022, the mean age of the cohort (n=209) was 55.45 ± 9.36. The mean work ability score was 40.7±5.73 (95% CI 39.92 to 41.48). In the multivariate binary logistic regression model, those who were married (OR 7.15, 95%CI 2.61 to 19.55), disease-free (OR 15.27, 95% CI 2.36 to 98.7), employed (OR 9.09, 95%CI 1.12 to 73.5), having no fatigue (OR 2.6, 95% CI 1.05 to 6.48), no pain (OR 3.11, 95% CI 1.16 to 8.35), and no depression (OR 6.58, 95% CI 1.82-23.8) were found to have optimal work ability. Anxiety (OR 4.93, 95% CI 1.76 to 13.76), and sub-optimal work ability (OR 4.22, 95% CI 1.39 to 12.77) were predictors of depression among survivors. Disease status and fatigue were associated with all three dimensions of survivorship in our study. **Conclusion:** Understanding survivorship will help improve health outcomes in this population. In our study, work ability, anxiety, depression, and their associated factors were found to be interrelated. Interventions in these areas can go a long way in improving breast cancer survivorship.

Keywords: Breast cancer- work ability- Kerala- survivor

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Introduction

Breast cancer is leading globally in 2020 with more than two million cases [1]. Advanced treatment and early detection have improved five-year survival, leading to an increasing number of individuals living beyond breast cancer treatment [2]. While treatment is one side of the coin, the other side is the post-treatment consequences experienced by the survivor [3]. The term 'survivorship' refers to the experience of living with, through and beyond, a cancer diagnosis and the person is known as a 'survivor' [4]. The term 'survivor' was first used by Dr Mullan in his article "Seasons of Survival; Reflections of a Physician with cancer", where he told the world that cancer survivors have common experiences which are specific to them, that are different from the general population [5]. In Asia, breast cancer is diagnosed at much younger ages than in Western countries [6], the registry data from South India also confirming the same [7]. Cases are diagnosed in the early stages in Kerala as opposed to other parts of India [8, 9]. Early diagnosis results in better survival. This, in turn, has resulted in an increasing number of young survivors living beyond treatment in that region. While the physician is more cautious about the immediate side effects of cancer treatment and signs of recurrence, the survivor is more concerned about the hindrances to day-to-day activities caused by post treatment lymphedema, fatigue, pain, hot flashes, and so on [10]. Survivorship research is gaining importance in the presently, as the difficulties and challenges faced by these women can no more be ignored [11].

Breast cancer treatment has a multimodality approach, which has medical as well as psychosocial long-term and late effects [3]. The survivor also have issues related to their social roles, return to work, body image concerns, and sexual functions [12]. Work ability, is an important factor affecting her return to work [13], financial status, mental happiness, social relations and productivity [14]. Due to young age at diagnosis, work ability, anxiety, and depression are described as challenges to breast cancer

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survivorship [13].

In survivorship research, participants are identified either from registry or from the hospital outpatient departments. Fewer studies have enrolled cohorts of survivors, and followed them longitudinally through the survivorship continuum. Studies on survivors based on registry are scarce, moreover studies on survivors of breast cancer are also few in India [15], and there are no such studies from Northern Kerala. Studies on work ability of breast cancer survivors are also few in Asia [13]. The aim of the study was to understand the work ability, anxiety and depression among breast cancer survivors from Northern Kerala and associated factors.

Materials and Methods

This is a retrospective cohort study on breast cancer survivors identified from the HBCR of 2016. The study was conducted in a Tertiary Cancer Centre (TCC) in Northern Kerala, which has a Hospital Based Cancer Registry (HBCR), containing data of all cancer patients who registered there in that particular year. The detailed protocol regarding the phases of the study, sample size, sample selection, variables, data source, and data collection methods are described elsewhere [16].

All female breast cancer patients registered in the TCC in 2016 (n=534) were included in the phase 1 of the study. From 2016 to 2022, the number of survivors who were lost to follow up (n=147), and those who succumbed to the disease(n=113) brought changes in the cohort size. All survivours diagnosed in 2016, who were traceable in 2022 and gave consent for the study were included in phase 2. those with a history of anxiety or depression or on treatment for the same were excluded. The final sample size was 209.

For Phase 1, data was collected from the HBCR. For Phase 2, a follow up survey was done by administering the questionnaire directly by the principal investigator, to the survivors after getting consent, during their follow up at TCC, taking time to explain the questions and clarifying doubts if any. Data collection was done in a separate room near OPD with adequate privacy.

The questionnaire consisted of sociodemographic details, questions related to long term and late health effects of treatment, present disease status, and scales for measuring work ability, depression and anxiety among survivors. Work ability, is the ability to perform work, as per demands of the job, in relation to his/ her health and mental resources. In this study, work ability is measured using the Work Ability Index (WAI) [17], a valid and well accepted tool for perceived work ability of individuals. It includes seven items, with scores ranging from 7-49 with further categorisation into poor (7-27), moderate (28-36), good (37-43), and excellent (44-49) [18]. The seven dimensions include current work ability compared to lifetime best, current work ability in relation to demands of the work, number of comorbidities, current work impairment due to the disease, absenteeism, own prognosis of work ability two years from now, and estimate of their mental resources. Linguistic validity was done by forward and backward translation methodology, and reliability by using internal consistency approach (Cronbach's alpha 0.8). For assessing anxiety and depression in this study, we used the GAD 7 and PHQ 9 scales respectively, which were recommended instruments for screening by American Society of Clinical Oncology [19, 20]. The responses were scored as "not at all" (score 0) to "nearly every day" (score 3). The total score was 0 to 21(GAD 7) and 0 to 27 (PHQ 9) [20, 21]. Cut-off points of 5, 10, and 15 represent mild, moderate, and severe levels in both scales. Validated, published Malayalam versions are used in this study [22]. Scores less than five almost always signified the absence of depression [23], hence, a cut-off point of five was used for further categorisation [24].

Data was analysed and categorical variables were given as frequencies and proportions, and continuous variables as mean and standard deviations. Bivariate analysis of categoric variables was performed by contingency tables and Chi square statistics or Fischer's exact test with significant alpha level taken as .05. Binary logistic regression was performed with the dichotomised work ability, anxiety, and depression scores as dependent variable. The most predictive model for each was formulated by purposeful selection of covariates with significant associations and through a process of model refitting and verifications.

The qualitative information from open ended question as to 'what the participants felt were their causes of anxiety' was analysed. The responses of participants were first coded deductively, and as they started showing a kind of pattern, they were converted to themes and listed. The study received approval from the Institutional Ethics Committee of the institution where the principal investigator is a research scholar (SCT/IEC/1711/AUGUST/2021), and Institutional Ethics committee of TCC where the study was conducted (1617/IRB-IEC/13/MCC/26-05-2021/2).

Results

The study participants registered in the TCC in 2016 was 534, from six districts of northern Kerala. The mean age of the cohort in 2016 was 53.8 ±12.1 (25 to 85 years). Two-fifths of the participants were less than 50 years of age. Three fourth were married and more than 60% were educated above fifth standard. Majority were home makers (85%). Post-menopausal women accounted to 67.6%. Sixty percentage presented in early stages.

The mean age of study participants in 2022 included in phase 2(n=209) was 55.45 ± 9.36, with majority (68.4%) 50 years and above. Employed women constituted 18.7%. As per disease status, 95.2% were presently disease free, and 4.8% (n=10) progressed to advanced stages. In comparison with 2016, nine women were widowed and one got divorced, seven women lost their job, while two started new jobs.

The long-term and late physical effects of cancer treatment as reported by the survivors ('yes' or 'no' responses) were collected (Table 1). Treatment induced menopause and mood changes following menopause were seen in nearly half of the women, followed by fatigue (30%).

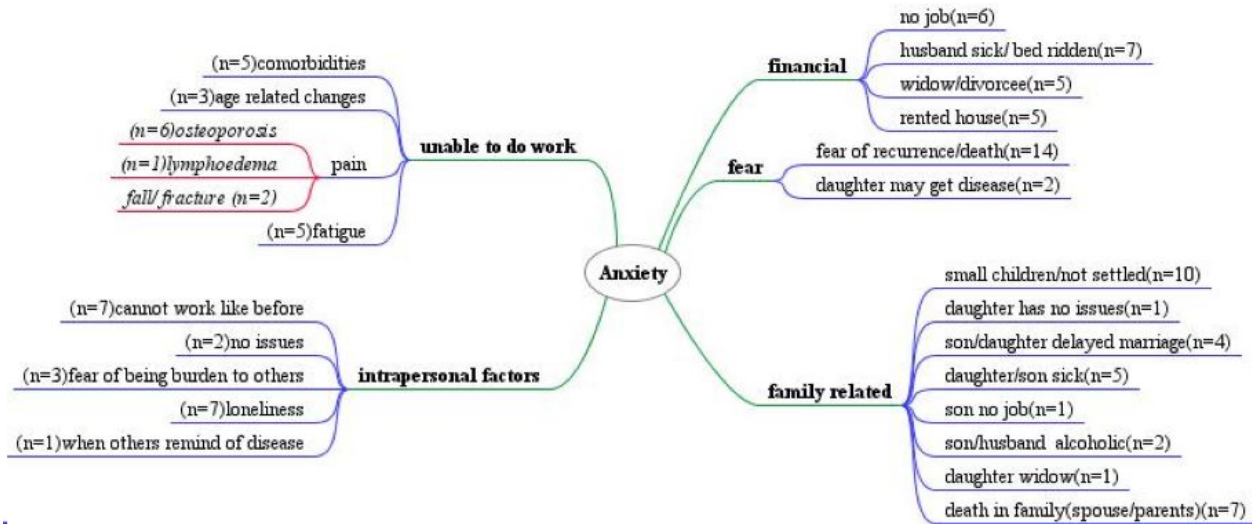

Figure 1. Causes of Anxiety among Long Term Breast Cancer Survivors as Reported in Responses to the Open-Ended Question "What do you think are the cause of your increased anxiety?"

Table 1. Long Term and Late Physical Effects of Treatment among Breast Cancer Survivors (n=209)

	n (%)
Fatigue	
Yes	64 (30.6)
No	145 (69.4)
Pain	
Yes	42 (20.1)
No	167 (79.9)
Lymphoedema	
Yes	58 (27.8)
No	151 (72.2)
Numbness /weakness of upper limb	
Yes	56 (26.8)
No	153 (73.2)
Cognition issues	
Yes	53 (25.4)
No	156 (74.6)
Osteoporosis related symptoms	
Yes	60 (28.7)
No	149 (71.3)
Weight gain	
Yes	23 (11.0)
No	186 (89.0)
Hot flushes	
Yes	40 (19.1)
No	169 (80.9)
Mood changes	
Yes	89 (42.6)
No	120 (57.4)
Menstrual changes	
Chemotherapy induced menopause	95 (45.5)
Others	114 (54.5)

The mean WAI score was 40.7±5.73 (95% CI, 39.92 to 41.48). Excellent work ability was seen in 37%, good in 45%, moderate in 13% and poor in 5% of women. For further analysis, this was categorized into 'sub optimal'(poor and moderate, score 7-36) and 'optimal'(good and excellent, score 37-49) [13]. About 82% of the survivors had 'optimal' and 18% had 'sub optimal' work ability. While 18.2% (n=38) of women reported no hindrance to daily work, 43.5% (n=91) of women had difficulty in carrying out their work due to some symptoms, 43% (n=90) had to either slow down their work or change their routine methods, 2.9% (n=6) could do only part time work, and 1% (n=2) were entirely unable to do any work. On bivariate analysis, sociodemographic factors like marital status and job, long-term effects of treatment like fatigue, pain, and treatment-induced menopause, present disease status, anxiety, and depression were factors significantly associated with work ability. Binary logistic regression was performed with the dichotomised work ability scores as dependent variable to understand the predictors. The indicator showing the correct fitness of the model was the Hosmer and Lemeshow test not being significant ($\chi 2(7) = 6.613$, $p=0.47$). The independent variables contributing to the model include marital status, present disease status, employment, fatigue, pain, and depression. (Table 2) Being in a marital relationship, disease free status and being employed were significantly associated with optimal work ability and having pain, fatigue, and depression were associated with reduced work ability. Majority of women (n=199) were disease free, with only ten survivors living with the disease in 2022. The high OR values here are to be interpreted with caution.

The prevalence of depression among survivors was 9.6% (mild to moderate (9.1%), and severe (0.5%)). On bivariate analysis, depression was significantly associated with fatigue, menopause-associated mood changes, present disease status, present work ability, and anxiety. Binary logistic regression was performed with

Table 2. Summary of Binary Logistic Regression Analysis for Work Ability and Predictive Factors among Breast Cancer Survivors (n=209)

Variables	Workability		Unadjusted		Adjusted	
	Suboptimal (score7-36) n (%)	Optimal (score 37-49) n (%)	OR (95% CI)	p value	OR(95%CI)	p value
Marital status						
Married	23 (13.9)	143 (86.1)	3.33 (1.55-7.17)	<0.001*	7.15 (2.61-19.55)	<0.005*
Others	15 (34.9)	28 (65.1)			reference	
Disease status						
Disease free	31 (15.6)	168 (84.4)	12.65 (3.10-51.57)	0.003	15.27 (2.36-98.7)	<0.001*
With disease	7 (70)	3 (30)			reference	
Job						
Employed	1 (2.6)	38 (97.4)	10.57 (1.40-79.59)	0.005	9.09 (1.12-73.5)	0.003*
Homemaker	37 (21.8)	133 (78.2)			reference	
Fatigue						
Yes	20 (31.3)	44 (68.8)	3.21 (1.56-6.61)	0.001	reference	0.04*
No	18 (12.4)	127 (87.6)			2.6 ((1.05-6.48)	
Pain						
Yes	15 (35.7)	27 (64.3)	3.48 (1.61-7.51)	0.001	reference	0.02*
No	23 (13.8)	144 (86.2)			3.11 (1.16-8.35)	
Depression						
No depression	24 (12.7)	165 (87.3)	16.04 (5.63-45.74)	<0.001	6.58 (1.82-23.8)	0.004*
Depression	14 (70.0)	6 (30.0)			reference	
Menopausal Status						
Treatment induced menopause	11 (11.6)	84 (88.4)	2.37 (1.11-5.08)	0.02	-	-
Others	27 (23.7)	87 (76.3)				
Anxiety						
No anxiety	22 (12.9)	148 (87.1)	4.68 (2.15-10.20)	<0.001	-	-
Anxiety	16 (41.0)	23 (59.0)				

*, p value <0.05; OR, Odds ratio; CI, Confidence Interval

dichotomised depression scores "No depression" (score <5) and "depression" (score ≥5)) as the outcome. The correct fitness of the model was indicated by the Hosmer and Lemeshow test ($\chi 2(6) = 1.933$, $p=0.926$). As per the model, sub optimal work ability, and anxiety were found to be the predictors of depression in survivours (Table 3).

The prevalence of anxiety among survivours was 18.6%; mild to moderate (18.1%), and severe (0.5%). It was further categorized to "No anxiety" (score<5), and "anxiety" (score≥5) [24]. On bivariate analysis, marital status, fatigue, mood changes, numbness or weakness of arms, work ability, present disease status, and depression were significantly associated with anxiety in our study (Table 4). It was found that 85%, women in a marital relationship and 86% of those without fatigue had no anxiety. Binary logistic regression was tried but a good fit model could not be obtained.

The themes which emerged on analysis of responses to open ended question include financial issues, family, intrapersonal factors, fear, and worry regarding the inability to do daily work (Figure 1). Each child node explained the respective parent node and their ultimate link to anxiety. No job for self, husband being bedridden or deceased, living in rented house all lead to financial issues and subsequent anxiety. The purpose was to substantiate the quantitative findings and not to explore the unknown. Findings show that women were worried more about other factors than the disease itself.

Dimensions of survivourship and associated factors as synthesis

We tried to analyse SURVIVORSHIP in the realm of its dimensions of work ability, anxiety and depression. Present disease status and fatigue were associated with all three. Mood changes due to treatment-induced premature menopause was associated with both anxiety and depression. Marital status was associated with work ability and anxiety. Work ability was associated with both anxiety and depression. As evidenced from the results, there were several factors which were common for the three dimensions of SURVIVORSHIP studied.

Table 3. Summary of Binary Logistic Regression Analysis for Variables Predicting Depression among Breast Cancer Survivors (n=209)

Variables	Category		Unadjusted		Adjusted	
	No depression (score<5)	Depression (score≥5)				p value
	n (%)	n (%)	OR (95% CI)	p value	OR (95%CI)	
Anxiety						
No anxiety	160 (94.1)	10 (5.9)	5.52 (2.11-14.43)		reference	
Anxiety	29 (74.4)	10 (25.6)		<.001*	4.93 (1.76-13.76)	0.002*
Present disease status						
Disease free	184 (92.5)	15 (7.5)	12.27 (3.19-47.16)	<.001*	-	-
With disease	5 (50.0)	5 (50.0)				
Present work ability						
Sub optimal	24 (63.2)	14 (36.8)	16.04 (5.63-45.74)	<.001*	4.22 (1.39-12.77)	0.01*
Optimal	165 (96.5)	6 (3.5)			reference	
Mood changes						
Yes	75 (84.3)	14 (15.7)	3.55 (1.31-9.64)	0.009*	-	-
No	114 (95.0)	6 (5.0)				
Fatigue						
Yes	51 (79.7)	13 (20.3)	5.03 (1.90-13.30)	<.001*	-	-
No	138 (95.2)	7 (4.8)				

*, p value <0.05; OR, Odds ratio; CI, Confidence Interval

Discussion

The five-year survival of breast cancer is increasing due to early detection, increased life span and advanced treatment, so are the number of women living long after treatment. Women have to accept their new normal life and move forward, amidst a spectrum of posttreatment effects, the price they have to pay for their survivorship [3, 25].

Table 4. Sociodemographic and Other Factors associated with Anxiety among Breast Cancer Survivors (n=209)

Variables	No Anxiety (score<5) n (%)	Anxiety (score≥5) n (%)	Chi-square p-value
Marital status			
Married	141 (84.9)	25 (15.1)	0.008*
Others	29 (67.4)	14 (32.6)	
Fatigue			
Yes	46 (71.9)	18 (28.1)	0.01*
No	124 (85.5)	21 (14.5)	
Mood changes			
Yes	63 (70.8)	26 (29.2)	0.007*
No	107 (89.2)	13 (10.8)	
Numbness/ weakness of arms			
Yes	37 (66.1)	19 (33.9)	<0.001*
No	133 (86.9)	20 (13.1)	
Work ability			
Sub optimal	22 (57.9)	16 (42.1)	<0.001*
Optimal	148 (86.5)	23 (13.5)	
Present disease status			
Disease free	167 (83.9)	32 (16.1)	<0.001*†
With disease	3 (30.0)	7 (70.0)	
Depression			
No Depression	160 (84.7)	291 (5.3)	0.002*
Depression	10 (50.0)	10 (50.0)	

†, Fischer's exact test; *, p value <0.05

This study had many challenges like lost to follow-up, non-traceability due to improper or non-updated address, non-availability of mortality related information, similar to other registry-based studies [26]. In our study, we could trace 47.8% (n=209) survivors during follow up, which was higher than other registry based studies in Germany [27] and Norway [28].

In the present study about 60% were in early stage which is consistent with other studies from Kerala [29, 8], and in contrast to Northern parts of India where only 46% presented in early stages [9].

In our study the most frequent post treatment long term physical effects reported were fatigue, numbness/ weakness of arms, lymphoedema, cognitive issues, premature menopause. and mood changes. The prevalence of fatigue and lymphoedema in our study was found to be similar to other studies [30, 15, 31]. Pain, as reported in our study was higher than in other studies [32, 15].

In our study 82% had optimal work ability as opposed to 64% in another study among breast cancer survivors, while those with poor workability was similar [13]. This may be due to the fact that, majority were in early stages and were below 50 years at diagnosis in our study. Being married [33], and being employed [34] were found to be associated with good work ability as in our study. Majority were married and the support from family may be the reason for good work ability in our study. Even among unemployed general population, physical activity was associated with good work ability [35]. This shows how important work is to a survivor, whether it be household

chores or paid job, as good work ability is associated with good productivity, and better quality of life [13, 34].

Though fatigue affects functional capacity in breast cancer patients undergoing treatment [36], our study found that fatigue, pain and depression were significantly associated with decreased work ability among survivors too, which is in confirmation with other studies [13, 28, 37]. Cognition changes causing decreased work ability [28], was not found in our study, as cognition issues were reported by only one fourth of participants compared to other studies (40%) [3].

Studies report that a significant number of survivors had to make adjustments and modifications in both household chores and employment [33, 14]. Our study, also reports about two fifth of survivors either slowing down their work or changing the way in which they worked earlier or losing their job. Lymphoedema [28] was not significantly associated with work ability in our study. Treatment induced menopause was associated with reduced work ability in our study, menopause related bodily changes was reported to reduce work ability even in general population [38], and is described as cause of poor emotional functioning in younger survivors [39].

Mastectomy was associated with poor work ability [33]. Good work ability was seen in 90% of those with breast-conserving surgery (BCS) in our study also, though not statistically significant.

Various studies reported prevalence of depression ranging from 1% to 56% depending upon the study population, type of scales and post treatment duration [40, 41], consistent with our study. Fatigue was associated with depression in our study, in confirmation with other studies [42, 41]. Treatment-induced menopause and hot flashes were associated with depression in studies [42], but not found statistically significant in our study. Menopause induced mood changes had significant association with depression in our study as in other studies [43]. Depression and anxiety were associated with present disease status in our study. Other studies also reported that disease progression was associated with both [11, 40, 44]. Higher level of anxiety was associated with depression among survivors in our study as reported in a US based study [45]. Higher levels of depression was associated with poor work ability score in our study which was similar to a study conducted at Singapore [13].

Prevalence of anxiety in various studies were from 22% to 38% [42, 46, 47]. Prevalence of anxiety among our study participants (18.7%) was slightly less. In our study being married was associated with less anxiety, as in other studies [44]. Comorbidities like diabetes causing fatigue and hindering day to day activities led to anxiety as reported by survivors in the open-ended questions. (Figure 1) Increased symptom burden leading to decreased physical functioning found among survivors with recurrence, in our study was in confirmation with other study [44].

Fatigue, comorbidities and having children was associated with both anxiety and depression among cancer patients [48]. In our study only fatigue was associated with both. Having small children was also described as cause of anxiety by our survivors. Disease recurrence was associated with both anxiety and depression in our study, as reported in previous studies [48]. In our study prevalence of anxiety was much more than depression which also is in confirmation with other studies [46].

The post treatment period is a crucial period of transition from 'cancer patient' to a 'survivor' [41]. The factors that contribute to better survivorship like improving work ability by managing fatigue, depression and anxiety at the right time will improve their quality of life [44]. On synthesis, work ability, anxiety, depression, and the associated factors were found to be interrelated. Hence, they can be considered as the three dimensions of survivorship, and improving any one factor may result in better health outcomes.

Strength and limitations: Though this study may have limitations of a hospital- based study, that maximum survivors could be recruited can be mentioned as the strength of the study. There were only ten traceable survivors living with the disease in our study. This has influenced the OR as well, which has to be interpreted with caution.

Author Contribution Statement

Conceptualization: NAP, SK; Design: NAP, SK; Literature search: NAP; Data acquisition: NAP; Data analysis: NAP, SK; Manuscript preparation: NAP; Manuscript editing: NAP, SK; Manuscript review: SK..

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Ethics committee approval

Approval was obtained before starting the study from Institutional Ethics Committee of Malabar Cancer Centre (1617/IRB-IEC/13/MCC/26-05-2021/2) and, Sree Chitra Tirunal Institute for Medical Sciences and Technology

(SCT/IEC/1711/AUGUST/2021).

Conflict of interest

The authors of this paper declare no conflict of interest.

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