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Chronic pain in female breast cancer survivors - prevalence, characteristics and contributing factors: a cross-sectional pilot study

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Abstract

Background While the global incidence of breast cancer is increasing, there is also an increase in the numbers of breast cancer survivors and in survival duration, as early detection programs are implemented, and treatments are optimized. Breast cancer survivors in several countries commonly struggle with a range of symptoms (fatigue, insomnia, depression) with 25–80% of survivors suffering from chronic pain. There is a paucity of literature reporting on breast cancer survivors in South Africa. In this pilot study we aimed to determine the prevalence of chronic pain in female breast cancer survivors attending the breast oncology clinic.

Methods A cross-sectional survey was conducted of all breast cancer survivors attending the Groote Schuur Hospital Breast Unit during one month in 2019. 44 female breast cancer survivors (median age 60.5y) completed a sociodemographic questionnaire, the Brief Pain Inventory, Pain Catastrophizing Scale and measures for neuropathic pain (DN4), health related quality of life (HRQoL; EQ-5d-3 L), physical activity (IPAQ), depression and anxiety (PHQ4), and screening questions to evaluate sleep, happiness and perceived discrimination in the language of their choice.

Results The prevalence of chronic pain (pain on most days for more than three months) was 59% (95%CI 44–72), a significantly higher number than the 18,3% prevalence of chronic pain reported by South African adults. 39% of the women were classified as having neuropathic pain. The median pain severity score was 3.75 (IQR = 2.75-5) and the median pain interference with function score was 4 (IQR = 2.9–5.4). The women were experiencing pain in a median of 2 different body sites (IQR = 1–3). The women with pain were more likely to be unemployed or receiving a disability grant, had significantly worse HRQoL, and significantly worse scores for risk of depression and anxiety.

Conclusion The results of this pilot study suggest that chronic pain may be a significant burden for South African breast cancer survivors. Routine screening for chronic pain in breast cancer survivors is recommended with a larger study indicated to explore this issue further.

Keywords Breast cancer survivor, Chronic pain, Prevalence

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Background

Globally, more women die of breast cancer than any other type of cancer [1]. Approximately 600 000 women died of breast cancer in 2020 with the majority of these women living in sub-Saharan Africa [2]. The incidence of breast cancer is increasing, and it is estimated that over 19 million women will suffer from breast cancer by 2025 [3]. The increasing incidence of breast cancer is associated with increased survival as early detection programs are implemented and treatments are optimized [1]. Breast cancer survival rates are 86% in the USA and although presently only at 40% in sub-Saharan Africa, survival rates are improving. A major new collaborative effort, the Global Breast Cancer Initiative, was introduced in recognition of International Women's Day in March 2021 by the World Health Organization, with the objective of reducing global breast cancer mortality by 2.5% per year until 2040, thereby averting an estimated 2.5 million deaths [4]. Therefore, while there will be a growing number of women developing breast cancer, there will also be a growing number of women surviving breast cancer.

Breast cancer survivors commonly struggle with ongoing symptoms such as fatigue, insomnia, depression and chronic pain [5]. Pain and pain-related disability affect 25–80% of the survivorship population [5]. The prevalence of chronic pain appears to be similar in the limited existing data from South Africa. The neuropathic condition, Post Mastectomy Pain Syndrome, had a 38% prevalence in 92 women who had received treatment at Chris Hani Baragwanath Hospital in South Africa [6]. Literature reporting on the quality of life of African Breast Cancer survivors reports chronic pain as a common symptom negatively impacting quality of life in a wide variety of populations (Nigeria, South Africa and Morocco) [7].

Most concerningly, persistent pain has been reported to be associated with shorter survival time [8] and severe chronic pain is associated with increased risk of mortality, independent of socio-demographic factors [9]. Living with chronic pain (pain that has been present on most days for longer than three months) negatively impacts on quality of life, places greater financial demand on the individual and on the health system and may result in reduced activities and restricted participation in meaningful life roles [10]. Treatment of chronic pain in breast cancer survivors is indicated, not only to decrease the suffering of the individual, but to optimize quality of life and restore patients to their pre-morbid function and their participation in meaningful life roles such as in family, social networks and work.

Numerous biopsychosocial variables have been identified as increasing the risk of developing chronic pain, both in breast cancer survivors and in other populations. Known risk factors for developing chronic pain include: being female; having a lower level of education; lower socioeconomic status; being unemployed; economic insecurity; having low levels of social support; smoking, low levels of physical activity, poor sleep quality, depression, anxiety, and pain catastrophizing [11–13]. In breast cancer survivors specifically, different cancer treatments also have different chronic pain risk profiles [14]. In addition, some studies have shown that younger age at diagnosis of breast cancer is associated with higher prevalence of chronic pain [15]. The majority of these studies have been conducted in breast cancer survivors living in the developed world.

There is a paucity of evidence regarding chronic pain in breast cancer survivors from South Africa. This is concerning as recent literature indicates that the prevalence of breast cancer in sub-Saharan Africa will double by 2050. Describing the prevalence, characteristics and contributing factors to chronic pain in South African breast cancer survivors, will inform strategies to reduce and manage the condition.

The aim of this pilot study was to determine the prevalence of chronic pain in female breast cancer survivors attending the Groote Schuur Hospital (GSH) breast oncology clinic (Breast Unit) during one month in 2019. In addition, the socio-demographic and clinical characteristics and potential contributing factors were explored. These data will be used to guide a larger cross-sectional study to determine the prevalence of chronic pain in female breast cancer survivors in South Africa.

Methods

A cross-sectional cohort descriptive pilot study was conducted during one month in 2019. All female breast cancer survivors being followed up at the GSH Breast Unit during the data collection period were invited to participate in the study. Inclusion criteria included: being female, breast cancer survivor (completed active treatment and in remission i.e. for luminal breast cancer survivors a minimum of four months since completing treatment, for non-luminal, a minimum of six months since completing treatment), and able to speak and understand either English, Afrikaans or isiXhosa. Different time periods were selected for survivors of luminal vs. non-luminal cancer based on GSH Breast Unit policy of following up luminal cancer survivors earlier. Patients with cognitive impairment or intellectual disability were excluded from the study.

For the purposes of this study, a breast cancer survivor was defined as a patient who has completed their active treatment with curative intent and is now being monitored. The sampling frame was female breast cancer survivors who had completed treatment at the GSH Breast Unit and had attended for follow up during one calendar month in 2019. During 2017 and 2018, the Breast Unit

saw an average of 51 new, and 380 follow up patients per month. Based on these data, we estimated that a maximum of 51 breast cancer survivors attend the Breast Unit per month. The sample size required for a cross-sectional survey was calculated using the Yamane formula [16]. The goal was to recruit a minimum of 45 patients for the results to be generalizable to the sampling frame.

Measurement instruments

A sociodemographic questionnaire was developed to capture information previously described as increasing the risk of developing chronic pain including age, marital status, level of education, employment status, economic profile and health literacy. Health literacy was established using the SOS Mnemonic [17]. The IMMPACT group recommend that pain be evaluated using instruments that capture both the complexity and variability of the pain experience as well as the effect of pain on the individual's activities and participation. As it fulfills these criteria, and has been translated and validated for numerous populations, including in South African English, Afrikaans and isiXhosa, the Brief Pain Inventory (BPI) was selected [18]. The BPI generates a Pain Severity Score (PSS), a Pain Interference Score (PIS) and a Pain Management Index (PMI). In addition, the BPI allows participants to indicate different sites of pain on a body chart, facilitating the identification of multiple sites of pain which are an indicator of chronic nociplastic pain [19].

The BPI uses an initial screening question which allows for the identification of chronic pain. The question normalizes daily pain experiences and highlights to patients the difference between chronic pain and "normal daily pains". The question states: "Throughout our lives most of us have had pain from time to time (such as minor headaches, sprains and toothaches). Have you had pain other than these everyday kinds of pain". To establish the presence of chronic pain the question was modified to state "Have you had pain other than these everyday kinds of pain on ***most days during the last three months***?" Participants who responded "Yes" to this question were classified as having chronic pain and completed the full BPI, participants responding "No" were classified as not having chronic pain and did not complete the BPI but did complete all other instruments.

To screen for neuropathic pain we used the Douleur Neuropathique en 4 questionnaire (DN4), a validated clinician-administered questionnaire [20]. The DN4 had been found to be a reliable tool to screen for the presence of neuropathic pain in relevant anatomical areas following chemotherapy administered for the treatment of breast cancer and following surgery for the resection of breast tumours.

The EQ-5D-3 L was used to evaluate health-related quality of life in terms of general health-status and health profile [21]. This assessment tool utilizes five categories: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. The EQ-5D-3 L instrument had been translated and validated in isiXhosa [21] and Afrikaans [22]. Furthermore, it had been used in several studies to assess the quality of life in breast cancer survivors.

We used the International Physical Activity Questionnaire (IPAQ) to assess self-reported physical activity [23]. The Short Version consists of seven core questions, which assesses the respondent's Perceived Physical Activity during the "last seven days" (prior week to completing the questionnaire).

Depression and anxiety have both been consistently associated with chronic pain with some authors suggesting that 50% of patients with a chronic pain condition will also present with a depressive disorder [24]. We used the four-item Patient Health Questionnaire (PHQ-4) to screen for both anxiety and depression [25]. The PHQ-4 includes two questions on depression PHQ-2, and two questions on anxiety.

We used the South African version of the Pain Catastrophizing Scale (PCS) to measure pain catastrophizing [26]. The PCS is available in South African English, Afrikaans and isiXhosa and has been validated for use in English and Afrikaans South African populations. To reduce questionnaire burden, quick screening questions to evaluate sleep, happiness and perceived discrimination were used. A single question from the PHQ-9 was used to screen for the presence or absence of sleep disturbance [27]. A single question to assess Happiness was used based on the work of Calvo [28]: "If you were to consider your life in general these days, would you say you are happy?"

Finally, a single question to assess for perceived discrimination was used as a preliminary screen of perceived discrimination to explore whether this construct is worth evaluating in more depth in a future full study. This question has been validated in women with postpartum depression and presents a simple, low burden method to evaluate for perceived discrimination [29]. The question: "Would you say that during the past 12 months someone treated you unfairly because of your gender, skin colour, the way you dress, your family origin, speech, religious beliefs or something else?" A simple yes/no response was recorded.

On completion of the interview, treatment and process data were collected from the participants' folders. Data recorded included diagnosis, comorbidities, medication, medical and surgical cancer management.

Procedure

The study adhered to the principles of the Declaration of Helsinki throughout with ethical approval granted by the University of Cape Town, Faculty of Health Sciences Human Research Ethics Committee (#766/2018). Subsequently institutional approval was obtained from GSH and the Radiation Oncology Department.

Potential study participants were identified from the weekly Breast Unit appointment list. These patients were contacted by telephone and invited to take part in a study of quality of life in breast cancer survivors during their visit to the Breast Unit the following week. Patients were reassured that participation in the study would in no way affect their ongoing treatment and no members of the data collection team were directly involved in patient care. On attending the GSH Breast Unit, the potential participants who had indicated an interest in participating were approached by the researchers and provided with the study information sheet in their language of choice and given the opportunity to have any questions answered. Participants who consented to take part then completed informed consent.

After agreeing to participate patients were escorted by the researchers into a private room for data collection. Participants were reassured that their place in the queue would not be lost while they were completing data collection. Data were collected by interview with the researchers reading each question from the battery of questionnaires to the participant in the language of their choice and recording their responses. Although the questionnaires were developed for self-administration, and were provided in participants' language of choice, interviews were used to collect data to overcome the known low levels of reading and health literacy [30] and lack of familiarity with reading in an African home language (many patients are verbally fluent on their home language but not fluent in reading and writing) [31]. For the body chart diagram on the BPI, the participants were asked to shade areas of pain themselves. Participants were provided with a drink and snack while they completed the questionnaire. On completion of the questionnaire participants were asked if they would like to be invited to a presentation on completion of the study to learn about the study results. Contact details of participants who wished to attend a presentation were recorded. Participants who reported any pain, depression, anxiety or poor sleep were asked if they would like the researcher to inform the treating doctor. Participants not wanting the doctor to be informed were provided with contact information to relevant support or treatment options.

Raw data were kept in a locked cupboard in the Breast Unit and were collected weekly by the research team. Raw data were entered into an excel spread sheet by the research team and saved in password protected documents on a password protected computer.

Data analysis

Prevalence of chronic pain was determined based on responses to the BPI. Participants were placed into one of two groups: Chronic Pain, or No Chronic Pain. Descriptive statistics were used to summarize the PSS, PMI and PIS of those with chronic pain in addition to summarizing the number of pain sites, type and distribution of pain.

The socio-demographic and health profiles of the participants were summarized for the entire sample and by group. Between group comparisons were performed using the Mann-Whitney U test or Spearman's correlation coefficient calculated to determine differences in categorical variables. Statistical significance was accepted as $p<0.05$.

Results

During the one month of the pilot study, 47 breast cancer survivors were scheduled to attend the Breast Unit and were invited telephonically to participate in the study. One patient declined to participate, and two patients were excluded on attending at the clinic as they did not meet inclusion criteria, leaving a sample of 44 patients (Fig. 1).

Participant characteristics (n = 44)

The 44 women had a median age of 60.5 (IQR = 49.5–67.5). The majority were married, retired, had not completed school, chose to be interviewed in English (n = 42) and had low levels of health literacy (Table 1).

Health Profile (n = 44)

All the participants were breast cancer survivors. Eighteen (41%) of the women were receiving medication for the ongoing management of their breast cancer (4 on Arimidex; 14 Tamoxifen). For the management of their breast cancer, 24 (55%) of the women had been managed with surgery alone. Fourteen (32%) had been treated with surgery, chemotherapy and radiotherapy; 4 (9%) had received surgery and chemotherapy; 1(2%) had received surgery and radiotherapy and 1(2%) had received radiotherapy only. The majority of the women (28, 64%) self-reported that they had previously been diagnosed with other conditions, with 21 (48%) presenting with two or more co-morbidities (median 1, IQR = 0–2) (Table 2).

The participants were receiving a range of medication for the management of their conditions (Table 3).

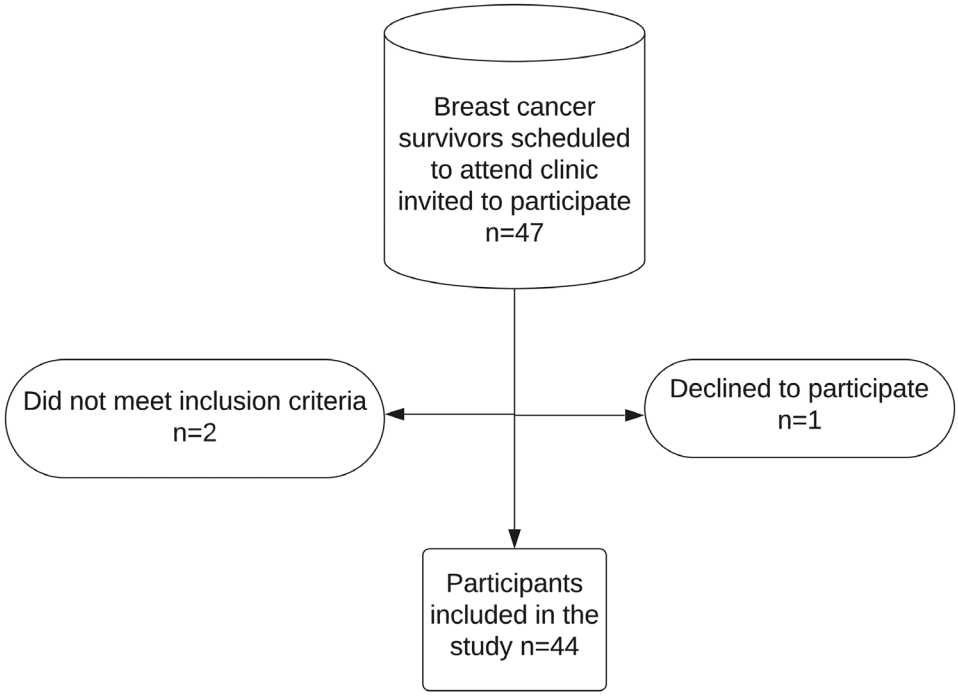

Fig. 1 Participant recruitment

Table 1 Sociodemographic characteristics of the participants (n = 44)

Sociodemographic characteristic	Median (IQR)
Age	60.5 (49.5–67.5)
Marital Status	**Frequency (%)**
Married	20 (45)
Single	10 (23)
Widowed	8 (18)
Divorced	6 (14)
Occupation	
Retired	18 (41)
Employed	11 (25)
Unemployed	12(27)
Disabled (receiving a disability grant)	3 (7)
Highest level of education*	
Did not complete primary school	4 (9)
Completed primary school	1 (2)
Did not complete high school	26 (59)
Completed high school	4 (9)
Tertiary education	9 (21)
Health literacy	
Sufficient literacy	13 (30)
At risk	27 (61)
High risk	3 (7)
Extreme risk	1 (2)

*In South Africa formal school is 12 years, primary school Grades 1–7, high school Grades 8–12

Table 2 Co-morbidities reported by the participants (n = 44)

Condition	Number (percentage)
Hypertension	20 (46)
Diabetes	7 (16)
Ischaemic heart disease	5 (11)
Hypercholesterolaemia	4 (9)
Arthritis	3 (7)
Cerebrovascular Accident	3 (7)
Asthma	2 (5)
Depressive disorder	2 (5)
Epilepsy	1 (2)
Hypothyroidism	1 (2)
Glaucoma	1 (2)
Cardiomyopathy	1 (2)
Hernia	1 (2)
Anxiety disorder	1 (2)
Arrhythmia	1 (2)
Hepatitis B	1 (2)
Cervical cancer	1 (2)

Total is >100% as participants reported more than one co−morbidity

Pain

There was a 59% prevalence of chronic pain (95%CI 44–72%), i.e. 26 of the women had experienced pain which they would not consider normal everyday types of pain on most days for three months or longer. The median pain severity score was 3.75 (IQR = 2.75-5) and the median pain interference with function score was 4 (IQR = 2.9–5.4) (Table 4). The women were experiencing pain in a median of 2 different body sites (IQR = 1–3) (Fig. 2). On the DN4, 17 (39%) of the women with pain were evaluated as presenting with neuropathic pain. However, only one of these women was being treated with medication appropriate for neuropathic

Table 3 Non-cancer related medications

Medication	Number (percentage)
Analgesics	**19 (43)**
Paracetamol/acetaminophen	8 (18)
Tramadol	8 (18)
Acetylsalicylic acid (aspirin)	2 (5)
Morphine	1 (2)
Anti-hypertensives	**26 (60)**
Hydrochlorothiazide	8 (18)
Atenolol	6 (14)
Amlodipine	4 (9)
Losartan	3 (7)
Enalapril	3 (7)
Furosemide	2 (5)
Anti-diabetics	**9 (20)**
Metformin	7 (16)
Insulin	1 (2)
Glimeperide	1 (2)
Thyroid dysfunction	**2 (4)**
Levothyroxine	1 (2)
Calcium carbonate	1 (2)
Other medications	
Warfarin	2 (5)
Simvastatin	4 (9)
Senna glycoside	2 (5)
Lansoprazole	2 (5)
Salbutamol inhaler	1 (2)
Sodium Valproate	1 (2)
Fluoxetine	1 (2)
Tamsulosin	1 (2)
Acrivastine	1 (2)
Vitamin D	1 (2)

Table 4 Pain severity and pain interference scores on the Brief Pain Inventory (n = 26)

Category	Median (IQR)
Pain Severity Score	**3.75 (2.75-5)**
Worst pain	7 (5–9)
Least pain	2 (1–3)
Average pain	4 (2–5)
Pain right now	2 (0–4)
Pain Interference with function	**4 (2.57–5.4)**
General activity	5 (2–6)
Mood	5 (2–7)
Walking ability	2 (0–6)
Normal work	5 (2–6)
Relations with other people	2 (0–5)
Sleep	5 (2–7)
Enjoyment of life	4.5 (1–6)

Scored on a 0–10 scale where 0='no pain' and 10='worst possible pain'.

Pain Severity Score is calculated as the average of the worst, least, average and pain right now.

Pain interference with function is scored as the average of the 7 listed items.

Scores are interpreted as 'mild pain'=0–3; 'moderate pain'=4–6; 'severe pain'=7–10

pain (amitriptyline) with the others prescribed simple analgesics.

The Pain Management Index (PMI) was calculated using the PSS and analgesic information. All of the women in pain were receiving analgesia and therefore had positive PMI scores. The majority of the women scored 2 on the PMI, suggesting that their pain was well managed.

Sociodemographic characteristics and pain

The women with pain were significantly younger than the women without pain [53y (IQR = 48–64) vs. 66.5y (IQR = 56–73); (U = 121; $p < 0.01$)]. There were significant differences between groups in terms of occupation (Spearman r = 0.48; $p < 0.01$). None of the participants without pain were receiving a disability grant and only 2 (11%) were unemployed (Table 5).

Cancer management and pain

Eighteen of the women were on medication for the continued management of their breast cancer. There was no difference in medication between those with pain and without pain. There was also no difference in terms of cancer treatment between those with and without pain (Table 6).

Health Related Quality of Life

On the EQ-5D health related quality of life instrument, the women with pain had significantly worse quality of life [70 (IQR = 50–80)] than the women without pain [85 (IQR = 70–90); U = 132.5; p = 0.01). For the individual health related quality of life domains, the women with pain scored significantly worse in the domains for "usual activities"; "pain/discomfort" and "anxiety/depression" Table 7.

Physical activity

On the IPAQ, there was no difference in the levels of physical activity in the women with pain compared to the women without pain (Spearman r = 0.27; p = 0.07) (Supplementary materials Table S1).

Depression and anxiety

On the PHQ4, the participants with pain had significantly worse scores overall, as well as for the individual items assessing depression and anxiety (Supplementary materials Table S2). The women with pain had mild to moderate symptoms overall, with mild depression and mild to moderate anxiety.

Pain catastrophizing

On the Pain Catastrophizing Scale, there was no difference in scores between those with pain vs. those

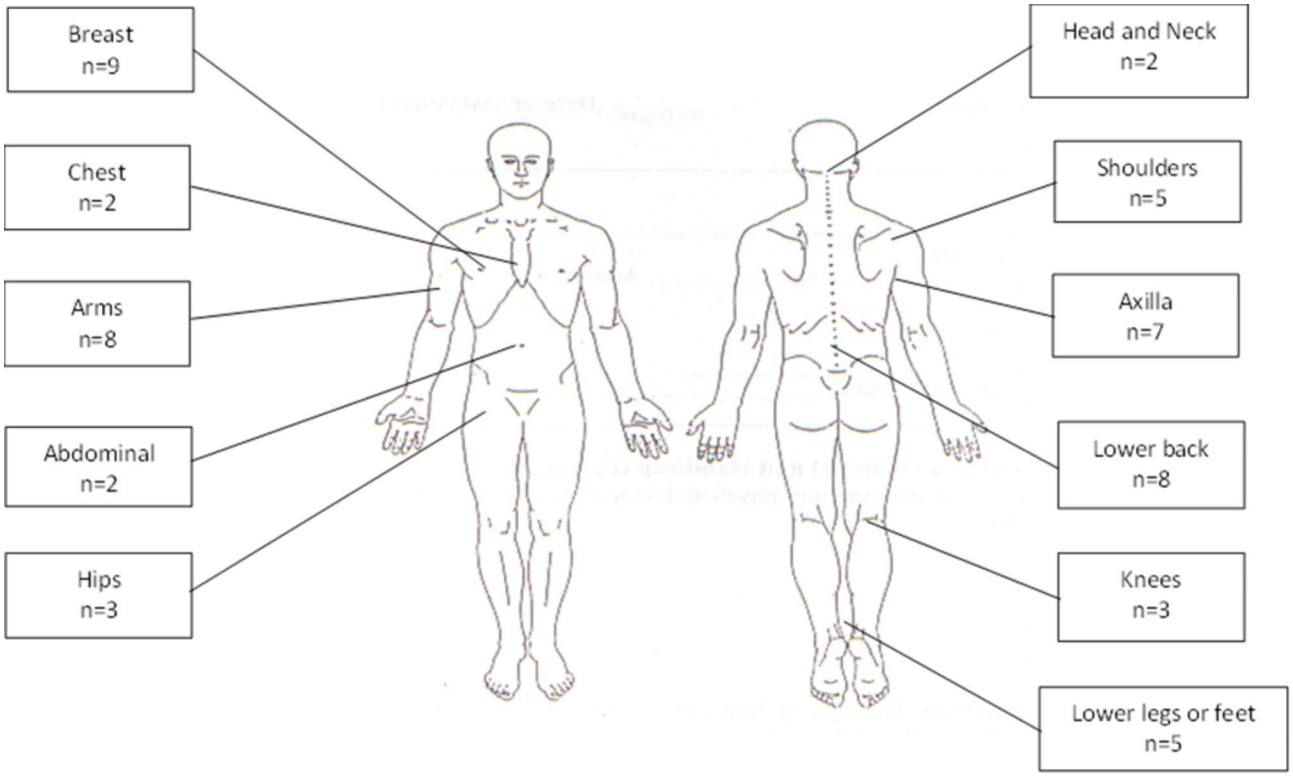

Fig. 2 Sites of pain (n = 26)

without pain [3.5 (IQR=0–8) vs. 0 (IQR=0–12); U=188.5; p=0.28].

Sleep, happiness and perceived discrimination

In response to the question asking whether participants had trouble falling or staying asleep or trouble sleeping too much, there was no difference between those with pain and those without pain (Spearman r=0.22; p=0.15). Overall, 23 of the women (52%) responded having trouble with sleep (16 with pain; 7 without pain).

In response to the question evaluating happiness, there was no difference between those with pain and those without pain (Spearman r=0.23; p=0.14). Overall, 41 of the women responded that they felt happy when considering their life in general (23 of those with pain and all 18 of those without pain).

In response to the question about perceived discrimination and whether they felt that during the past twelve months someone had treated them unfairly because of their gender, skin colour, the way they dress, family origin, speech or religious beliefs, there was no difference between those with pain and those without pain (Spearman r=0.19; p=0.20). Overall, 6 of the women responded feeling discriminated against in the past year, 5 of those with pain and 1 woman without pain.

Discussion

We conducted a pilot study on the prevalence, characteristics and contributing factors to chronic pain in 44 breast cancer survivors. The majority of the women in our study were married (48%) and retired (43%). Most had not completed high school and had low levels of health literacy. The median age of these women was 60,5 (50–68), typical of women survivors of breast cancer internationally [32]. Similar to studies of breast cancer survivors elsewhere reporting high numbers of co-morbidities in this population, most of the women in our study had co-morbidities, with 21 (46%) presenting with two or more conditions [33]. In this setting, where the majority of patients present late in the course of their disease, management should include neoadjuvant chemotherapy or hormonal therapy to enable surgical resection. In this group of women, surgical management included mastectomy (18.39%), lumpectomy (4.9%) and wide local excision (1.2%). Subsequently, 18 (39%) of these women received chemotherapy and 16 (35%) were treated with radiotherapy.

The prevalence of chronic pain in this pilot study of breast cancer survivors was 59% (95% CI 44–72%), a significantly higher number than the 18.3% prevalence of chronic pain in adults reported in the South African demographic household survey [34]. While there is a wide variation in chronic pain prevalence estimates in

Table 5 Differences in Sociodemographic Characteristics between those with pain and without pain

Sociodemographic characteristic	Women with pain n = 26	Women without pain n = 18	Statistical analysis
Marital Status	**Frequency (%)**	**Frequency (%)**	Spearman r = 0.19; p = 0.21
Married	11 (42)	9 (50)	
Single	10 (39)	0 (0)	
Widow	3 (12)	5 (28)	
Divorced	2 (8)	4 (22)	
Income classification			Spearman r = 0.25; p = 0.10
H0	9 (35)	8 (44)	
H1	15 (58)	4 (22)	
H2	2 (8)	5 (28)	
Occupation			Spearman r = 0.48; p < 0.01
Retired	6 (23)	12 (67)	
Employed	7 (27)	4 (22)	
Unemployed	10 (38)	2 (11)	
Disabled (receiving a disability grant)	3 (12)	0(0)	
Highest level of education*			Spearman r = 0.17; p = 0.26
Did not complete primary school	1 (4)	3 (17)	
Completed primary school	0 (0)	1 (6)	
Did not complete high school	18 (69)	8 (44)	
Completed high school	3 (12)	1 (6)	
Tertiary education	4 (15)	5 (28)	
Health literacy			Spearman r = 0.09; p = 0.53
Sufficient literacy	7 (27)	6 (33)	
At risk	17 (65)	10 (56)	
High risk	1 (4)	2 (11)	
Extreme risk	1 (4)	0 (0)	

*indicates significance with p<0.05

Table 6 Cancer management in those with pain and without pain

	Women with pain n = 26	Women without pain n = 18	Statistical analysis
Medication	**Frequency (%)**	**Frequency (%)**	Spearman r = 0.19; p = 0.45
Arimidex	2 (8)	2 (11)	
Tamoxifen	10 (38)	4 (22)	
Cancer management			Spearman r = 0.22; p = 0.14
Surgery	17 (65)	7 (39)	
Surgery, chemotherapy, radiotherapy	8 (31)	6 (33)	
Surgery, radiotherapy	1 (4)	0 (0)	
Surgery, chemotherapy	0 (0)	4 (22)	
Radiotherapy	0 (0)	1 (6)	

Table 7 Problems in health-related quality of life domains in women with pain and women without pain

Health related quality of life domain	Women with pain n = 26	Women without pain n = 18	Statistical analysis
Mobility			Spearman r = 0.16; p = 0.29
No problems	18	15	
Some problems	8	3	
Unable to mobilise	0	0	
Self-care			Spearman r = 0.10; p = 0.51
No problems	23	17	
Some problems	3	1	
Extreme problems	0	0	
Usual activities			Spearman r = 0.37; p = 0.01*
No problems	12	15	
Some problems	14	3	
Extreme problems	0	0	
Pain/Discomfort			Spearman r = 0.45; p < 0.01*
No pain	3	11	
Moderate pain	22	7	
Extreme pain	1	0	
Anxiety/Depression			Spearman r = 0.54; p < 0.01*
None	6	14	
Moderate	19	4	
Extreme	1	0	

*indicates significant difference between groups with p<0.01

breast cancer survivors, chronic pain prevalence appears to be consistently higher than in population samples [35]. This higher prevalence has been reported in breast cancer survivors from high-income countries such as the United States, (34.6% prevalence, near double the general population) [36], Denmark (42% prevalence) and Israel (74% prevalence of chronic pain) [37]; and from low- and middle-income countries including India (44% prevalence of chronic pain) [38] and Brazil ([39].

In our cohort, there was a correlation between low levels of income and the prevalence of chronic pain. The social determinants of health, including the multiple aspects of poverty (low levels of income, low levels of education, poor access) have been demonstrated to contribute to the prevalence of chronic pain in a range of populations [40]. These findings support the need for attention to be given to the social determinants of health for breast cancer survivors to reduce burden on the individual and on the system. This will have to include other aspects beyond the health systems such as at the policy level and engagement with the

distribution of resources and wealth. In a 2016 USA National Health Interview Survey, 20% of the population reported chronic pain with 8% of those having high impact chronic pain (chronic pain that frequently limits life or work activities) [40]. Chronic pain and high impact chronic pain were more prevalent in women; older adults; those unemployed and those living in poverty. The women receiving treatment at the Breast Unit are mostly from disadvantaged backgrounds and mostly from single income households. The majority were H1 classified which means that their treatment is subsidised by the government with patients paying a nominal fee of <ZAR1000 (US$53) for their treatment. To be classified as H1, patients must be earning less than ZAR70000 (US$3731) as single income or ZAR100000 (US$5331) family income per year. This income level is below the South African poverty line, clearly illustrated when the cost of a loaf of bread (US$0.75) or a litre of milk (US$1) are considered. These data suggest that the majority of these women struggle to make ends meet, thus making them more vulnerable or at high risk of developing chronic pain.

The women with pain were younger than those without, a finding previously reported in other studies of breast cancer survivors [41]. We hypothesise that younger breast cancer survivors may be more at risk for chronic pain due to the combined psychosocial challenges of self-stigma related to changes in body image, and the fear and anxiety of living with a potentially terminal condition from a young age.

The women with chronic pain had poorer health related quality of life than those without pain. They reported worse mobility in their usual activities, and pain or discomfort. This pushes us to strive to put measures in place to enhance the quality of life of cancer survivors [42]. A clear shift needs to be made by all members of the health team treating breast cancer beyond survival towards optimising quality of life. This extends beyond pain to mental health disorders. The women with chronic pain had more symptoms of depression and anxiety compared to the women without chronic pain. We did not explore whether the participants had received or pursued any non-pharmacological treatments for their pain, information which would be valuable to obtain in future studies. Depression and anxiety are recognised as risk factors for chronic pain [12], however, it may also be proposed that feeling depressed or anxious following treatment for breast cancer with ongoing pain illustrates a bidirectional relationship between depression/anxiety and chronic pain. Depression and anxiety may not be causative of the chronic pain but it certainly increases suffering and needs to be considered in treatment [43].

There were several strengths and weaknesses identified in this study which will inform a future larger study of chronic pain in breast cancer survivors. We were fortunate to be able to recruit enough candidates to provide adequate power for this pilot study. The selected measuring tools were easily understood and administered apart from the IPAQ. The IPAQ was particularly challenging to administer in this patient group with patients struggling to understand the wording of the questions and not relating to the questions. If levels of physical activity are to be evaluated in the larger study, an alternative measure such as the Yale Physical Activity Survey is recommended [44]. In addition, gender-specific body charts will be used as part of the BPI to enhance communication with participants.

The protocol for identifying potential participants and recruitment will be revised. The process of identifying eligible participants based on chart review alone was insufficient with interview checking of eligibility also required. The protocol required verbal telephonic consent to be obtained prior to approaching potential participants at the clinic. However, contacting patients telephonically prior to their clinic appointment was challenging with numerous potential participants not contactable thus reducing the potential sample. In-person recruitment on attendance at clinic would obviate this problem.

Conclusion

The results of this pilot study suggest that chronic pain may be a significant burden in breast cancer survivors. A larger study in South African and African Breast Cancer survivors appears feasible and is indicated to explore this issue. We recommend that clinicians managing breast cancer survivors routinely assess for chronic pain at each clinical consultation using the Brief Pain Inventory to optimise the quality of life of these patients.

Supplementary Information

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Supplementary Material 1

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Authors' contributions

NS and MC contributed equally to study conceptualization and design, data collection, data analysis and drafting of the manuscript.RP, TT and UW &

contributed equally study conceptualization and design, data analysis and drafting of the manuscript.

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Data Availability
The datasets generated and analyzed during the current study are not publicly available due to patient confidentiality and hospital policy but are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
Ethics approval for this study was granted by the University of Cape Town, Human Research Ethics Committee of the Faculty of Health Sciences (Ref: (#766/2018). All participants provided informed consent.

Consent for publication
Not applicable.

Competing interests
U.W. serves on the External Consultant Board for the "NIH Preclinical Screening Platform for Pain", a novel pre-clinical pain therapy screening platform that has been launched at the National Institute for Neurological Disorders and Stroke in the U.S. In her capacity as a special government employee of the US Food and Drug Administration (FDA), she has served as a voting member of the FDA Anesthetic and Analgesic Drug Products Advisory Committee. In the past 3 years she has received compensation for serving on advisory boards or for consulting activities for Aphrodite Health Inc., Wilmington, DE, Avenue Therapeutics Inc., New York, NY, Bayer Aktiengesellschaft, Leverkusen, Germany, Biohaven Pharmaceuticals, New Haven, CT and Syneos Health, Morrisville, NC, all unrelated to the submitted work. The remaining authors declare that they have no competing interests.

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