

RESEARCH ARTICLE

## The Influence of Cancer Stage and Primary Cancer Location on the Occurrence of Breakthrough Pain (BTP) in Cancer Patients at Haji Medan Hospital

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**Abstract: Background :** The International Agency for Research on Cancer (IARC) in 2022 reported 20 million cancer patients worldwide. IARC also reported that the incidence of cancer in Indonesia reached 408,661 new cases in 2022. As many as 66% of cancer patients usually experience cancer pain as a complaint experienced by patients. Breakthrough Pain (BTP) generally occurs in patients with cancer cases, 40% to 93% of cancer patients experience BTP. **Objective:** To determine the effect of cancer stage and primary location of cancer on the incidence of BreakThrough Pain (BTP) in cancer patients at the Haji Medan Hospital. **Results:** of the 62 total respondents, 51 experienced cancer pain and 34 experienced (BTP). The majority of respondents who experienced BTP were women with primary cancer locations in the mammary glands and were already in the final stages of cancer. **Conclusion:** A significant relationship was found between cancer stage and primary location of cancer with the incidence of BTP at the Haji Medan Hospital.

**Keywords:** Primary location of cancer, cancer stage, Breakthrough Pain

### INTRODUCTION

IARC reported that the incidence of cancer in Indonesia reached 408,661 new cases in 2022. The three cancers with the highest number of new cases were breast cancer, lung cancer, and cervical cancer<sup>1</sup>. This was also reported in the results of the 2023 Indonesian Health Survey, which recorded a cancer prevalence of 1.2% in Indonesia<sup>2</sup>.

Among the various complaints experienced by cancer patients, one of the most frequent and bothersome is cancer pain. Approximately 66% of cancer patients

typically experience pain as a symptom.<sup>3</sup> *Breakthrough Pain* (BTP) umumnya terjadi pada pasien dengan kasus kanker, 40% hingga 93% pasien kanker mengalami BTP<sup>4</sup>. Breakthrough Pain (BTP) commonly occurs in patients with cancer, with 40% to 93% of cancer patients experiencing BTP<sup>4</sup>. There are two impacts felt by patients experiencing BTP. The first is the direct impact of BTP, which is defined as the discomfort and suffering experienced by patients due to the severe pain they feel. The second is the indirect impact, which is the influence of BTP on patients' quality of life because varying

levels of pain prevent patients from carrying out daily activities like normal people.<sup>5</sup>

As pain is the most frequent complaint experienced by cancer patients, causing discomfort and reducing their quality of life, this study aims to determine the influence of cancer stage and primary cancer location on the occurrence of BreakThrough Pain (BTP) in cancer patients at Haji Medan Hospital.

## METODE

This research was conducted in accordance with the research ethics code and is registered under certificate number 1369/KEPK/FKUMSU/2024.

This research is an analytical study with a cross-sectional research design and uses a questionnaire. As for the sample data collection method in this study, it is non-random sampling and purposive sampling, with a sample size of 62 samples. Data was obtained by conducting direct interviews with cancer patients undergoing treatment and follow-up at Haji Medan Hospital for 1 month who met the following criteria: 1) Patients diagnosed with cancer based on medical records at Haji Medan Hospital 2) Patients experiencing cancer pain 3) Willingness to participate as research respondents. The prospective respondents were previously informed about the research to be conducted. If they were willing, the respondents would sign the informed consent form provided by the researcher. The researcher would then conduct a direct interview to inquire about the cancer pain and BTP experienced by the respondents. Finally, the researcher would

access the medical records to document the primary cancer location experienced by the respondents. After the data is obtained, it will be processed using a statistical test, namely the chi-square test.

## RESULT

In this study, all the data obtained will be separated between respondents who experience cancer pain and those who do not.

**Table 1** Prevalence of patients with cancer pain

cancer pain	n	%
Experiencing pain	51	82,3
No pain experienced	11	17,7
<b>Total</b>	<b>62</b>	<b>100</b>

Based on Table 1, the majority of cancer patients experienced cancer-related pain, totaling 51 people (82.3%).

Then, from the respondents experiencing cancer pain, a distinction will be made between those with cancer pain who experience BTP and those who do not.

**Table 2** Frequency distribution of cancer pain patients with breakthrough pain

BreakThrough Pain	n	%
Experiencing BTP	34	66,7
Not experiencing BTP	17	33,3
<b>Total</b>	<b>51</b>	<b>100</b>

Out of the 51 people experiencing cancer pain, the majority, 34 individuals (66.7%), experienced BTP.

The characteristics of respondents with cancer pain experiencing BTP are presented in Table 3.

**Table 3 Frequency distribution of breakthrough pain characteristics**

<b>Respondent Data</b>	<b>n</b>	<b>%</b>
<b>Gender</b>		
Male	5	14,7
Woman	29	85,3
<b>Age</b>		
30-40	6	17,7
41-50	8	23,5
51-60	13	38,2
61-70	6	17,7
71-80	1	2,9
<b>Cancer Location</b>		
Colon	2	5,9
Mammae	27	79,4
Nasopharyngeal	1	2,9
Ovarium	1	2,9
Pulmo	1	2,9
Rectum	1	2,9
Non-Hodkin	1	2,9
Lymphoma		
<b>Cancer Stadium</b>		
Early Stadium	0	0
Late Stadium	34	100
<b>BTP Intensity</b>		
Mild Pain	10	29,4
Moderate Pain	9	26,4
Severe Pain	15	44,1
<b>Pain Character</b>		
Pulsating	26	76,5
Electrified	5	14,7
Depressed	3	8,8
<b>BTP Location</b>		
Behind The Ear	1	2,9
Leg	3	8,8
Neck	1	2,9
Arm	2	5,9
Breast	18	52,9

Stomach	2	5,9
Waist	5	14,7
Shoulder	2	5,9
<b>The Initiator of BTP</b>		
Cough	2	5,9
Being Active	11	32,4
None	21	61,8
<b>Duration of BTP</b>		
< 5 minute	15	41,2
10 minute	2	11,8
15 minute	4	11,8
> 30 minute	13	35,3
<b>BTP Episode</b>		
1x/day	15	44,1
2x/day	2	5,9
3x/day	4	11,8
>4x/day	13	38,2
<b>Activity Impairment</b>		
Disturbed	18	52,9
Not Disturbed	16	47,1
<b>Appetite Disorders</b>		
Disturbed	18	52,9
Not Disturbed	16	47,1

With a total of 34 cancer patient respondents experiencing BTP at Haji Medan Hospital, the majority were female with 29 people (85.3%), and the most frequent age group was 51-60 years old with 13 people (38.2%). The highest number of respondents experiencing BTP were breast cancer patients, totaling 27 people (79.4%). 100% of respondents experiencing BTP were in the final stage, with 15 people (44.1%) experiencing severe intensity. The majority of respondents felt throbbing pain when experiencing BTP, with 26 people (76.5%) reporting this. The most common location of pain for respondents experiencing BTP was in the breasts, with 18 people (52.9%)

reporting this. Additionally, some respondents also felt BTP pain in their lower back, with 5 people (14.7%) reporting this. Out of the 34 respondents who experienced BTP, 21 people (61.8%) experienced BTP without any trigger. The most frequent occurrence experienced by respondents was 1x/day by 15 people (44.1%), with a duration of <5 minutes by 14 people (41.25%), making it the most common duration experienced by respondents with BTP. 18 (52.9%) of the respondents with BTP experienced activity disturbances and appetite disturbances, and 23 (67.6%) experienced sleep disturbances..

The subsequent analysis was performed using the Fisher's exact test to find the relationship between the primary cancer location and BTP, as presented in Table 4.

**Table 4** Table 4 Relationship between primary cancer location and Breakthrough Pain

Lokasi Primer		BTP			Nilai P
		Ya	Tidak	Total	
Colon		2	1	3	0,029
		(66,7)	(33,3)	(100)	
Mammae		27	9	36	
		(75)	(25)	(100)	
Nasopharingeal		1	0	1	
		(100)	(0)	(100)	
Non-Hodkin Lymphoma		1	0	1	
		(100)	(0)	(100)	
Ovarium		1	4	5	
		(20)	(80)	(100)	
Pankreas		0	1	1	
		(0)	(100)	(100)	
Pulmo		1	0	1	
		(100)	(0)	(100)	
Rektum		1	0	1	
		(100)	(0)	(100)	
Tiroid		0	2	2	
		(0)	(100)	(100)	
Total		34	17	51	
		(66,7)	(33,3)	(100)	

The Fisher's exact test results showed a significant value (p-value) of 0.029, which is <0.05. This indicates a significant relationship between the primary cancer location and the occurrence of BTP in cancer patients at Haji Medan Hospital.

The final analysis was performed using the chi-square test to determine the relationship between cancer stage and BTP, as presented in Table 5.

**Table 5** Relationship between cancer stage and Breakthrough Pain

Stadium kanker		BTP			Nilai P
		Ya	Tidak	Total	
Stadium awal		0	6	6	0,029
		(0)	(100)	(100)	
Stadium akhir		27	9	36	
		(75)	(25)	(100)	
Total		34	17	51	
		(66,7)	(33,3)	(100)	

The chi-square test results showed that the significance value (p-value) was 0.001, which is <0.05. This indicates a significant relationship between cancer stage and the occurrence of BTP in cancer patients at Haji Medan Hospital..

## DISCUSSION

From the research results, it was found that 51 out of 62 respondents (82.3%) experienced cancer pain. This is in line with Sebastiano Mercadante's statement in 2019, which revealed that more than half of cancer patients generally experience pain symptoms<sup>6</sup>. In Carmen Rodriguez's 2019 study, it was found that 69% of cancer patients experienced pain symptoms of moderate to severe intensity<sup>7</sup>. Cancer pain

occurs due to two pathophysiologies: nociceptive pain and neuropathic pain. Nociceptive pain results from damage to tissues other than nerve tissue, which is further divided into somatic and visceral pain. Neuropathic pain, on the other hand, occurs due to damage to the somatosensory nervous system. However, in cancer patients, mixed pain often occurs, combining both nociceptive and neuropathic elements<sup>3</sup>. Cancer pain occurs due to two pathophysiologies: nociceptive pain and neuropathic pain. Nociceptive pain results from damage to tissues other than nerve tissue, which is further divided into somatic and visceral pain. Neuropathic pain, on the other hand, occurs due to damage to the somatosensory nervous system. However, in cancer patients, mixed pain often occurs, combining both nociceptive and neuropathic elements..

In this study, it was also found that out of 47 respondents experiencing cancer pain, 34 (72.3%) experienced BTP. A study conducted by Sebastiano Mercadante in 2015 revealed that the prevalence of cancer pain patients experiencing BTP was 75%, which is consistent with the findings of this study.<sup>8</sup> A similar finding was also reported by Xue-Bin Yan in 2016, with data showing that 83% of cancer patients experience BTP.<sup>9</sup> By Arvind Narayana in 2019, it was stated that 80% of cancer patients undergoing adequate opioid therapy still experience BTP.<sup>10</sup> Pain can occur in cancer patients due to tumors invading healthy tissue, which triggers pain. BTP can

also arise from the therapies cancer patients undergo, such as surgery, chemotherapy, or radiotherapy.<sup>11</sup>

In this study, the age group most affected by BTP was found to be 51 – 60 years old. This is consistent with the findings of Aida Sri Rachmawati in 2020, who stated that 62% of cancer patients at Jasa Kartini Hospital in Tasikmalaya City were adults compared to the elderly, toddlers, and adolescents.<sup>12</sup> Also, research conducted at Sanglah General Hospital in Bali in 2020 stated that the highest number of breast cancer patients were in the age range of 41 years to >50 years.<sup>13</sup> Also, research conducted at Sanglah General Hospital in Bali in 2020 stated that the highest number of breast cancer patients were in the age range of 41 years to >50 years. Research conducted at Sanjiwani General Hospital in Gianyar in 2015 also stated that 72.4% of colorectal cancer patients were over 50 years old.<sup>14</sup> This relates to Yeonju Kim's statement in 2015 that women in Asia have a younger average age of breast cancer onset compared to Caucasian women<sup>15</sup>. Research by Joseph Arthur in 2022 found that younger patients (<65 years old) experienced pain related to the psychological distress caused by their illness.<sup>16</sup>

The findings of this study also show that the cancer patients who experienced BTP were those with breast cancer, with a percentage of 79.4%. A study at Jasa Kartini Hospital in 2020 found that breast cancer was the most common type of cancer among patients<sup>12</sup>. In a 2015 study by Yeonju Kim, it

was also stated that Southeast Asia ranks 2nd in the world for breast cancer incidence, with Indonesia being the country with the highest prevalence in Southeast Asia.<sup>15</sup> In a 2015 study by Yeonju Kim, it was also stated that Southeast Asia ranks 2nd in the world for breast cancer incidence, with Indonesia being the country with the highest prevalence in Southeast Asia.<sup>17</sup>

The majority of respondents in this study experienced severe pain during their BTP episodes. This is consistent with the findings at Oslo University Hospital, which stated that patients experiencing BTP reported a higher intensity of severe pain.<sup>18</sup> In patients with poor clinical conditions, this affects their mental burden, leading to more severe pain.<sup>19</sup>

In this study, the majority of respondents experienced disruptions in daily activities, sleep disturbances, and appetite changes. This aligns with previous research stating that the majority of patients experiencing BTP stopped their activities during BTP attacks.<sup>20</sup> Research conducted in Spain also found that complaints such as fatigue, sleep disturbances, and loss of appetite frequently occur in patients experiencing BTP.<sup>21</sup> This can happen because of the pain and discomfort experienced by the patient, leading not only to pain symptoms but also to disruptions in daily activities, sleep disturbances, and appetite changes.

The results of the Fisher's exact test analysis in this study showed a significant

value (p-value) of 0.029, which means a significant relationship was found between the primary cancer location and the occurrence of BTP. In a study conducted in Spain by Conceptio Perez-Pernandez, it was revealed that patients with primary cancer located in the pancreas had the highest incidence of BTP, followed by colorectal cancer. Tumors in solid organs tend to cause more pain than blood cancers, which is related to tumor infiltration into the surrounding healthy tissue.<sup>22</sup>

The results of the Pearson chi-square analysis in this study showed a significant value (p-value) of 0.001, which is  $<0.05$ . This indicates a significant relationship between cancer stage and BTP occurrence. This finding aligns with the results of a study conducted in Spain by Conceptio Perez-Hernandez, which found that 57% of patients with advanced-stage cancer experienced BTP<sup>22</sup>. This is also recorded in the results of a study conducted in China by Rongrong Fan, which stated that 55% of patients with metastasis experienced BTP more frequently<sup>20</sup>. Patients with advanced stages will experience more severe background pain, which will also affect the characteristics of breakthrough pain experienced by cancer patients with advanced stages<sup>20</sup>. background: Untreated pain leads to the release of excitatory neurotransmitters like glutamate, which causes BTP<sup>3</sup>. However, the 11 individuals with advanced stages in this study did not experience BTP. The researchers assumed that this phenomenon was related to

the effectiveness of the therapy the respondents were undergoing.

### CONCLUSION

The results of this study show that 82.3% of cancer patients at Haji Medan Hospital experience cancer pain symptoms. Of the 51 patients who experienced cancer pain, 72.3% experienced breakthrough pain. A significant relationship was found between the primary location of cancer and the occurrence of breakthrough pain. A significant relationship was found between cancer stage and the occurrence of breakthrough pain.

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