ISSN No:-2456-2165

The Relationship of Pain at the Depression Level of PHQ - 9 (Patient Health Quistionnaire - 9) to the Degree of VAS (Visual Analog Scale) for Pain in Cancer Patients in Haji Adam Malik Hospital Medan

Mirza Arya Putra Nasution, Akhyar Hamonangan Nasution, Muhammad Ihsan
Department of Anesthesiology and Intensive Care, Medical Faculty, North Sumatera University,
Haji Adam Malik General Central Hospital, Medan, Indonesia

Abstract:-

- ***Introduction:***

Pain and depression are both often found in cancer patients and the relationship between these symptoms has been widely investigated.

- ***Objective:***

This study aimed to determine the relationship of depression level (Patient Health Questionnaire – 9) to the degree of pain (Visual Analog Scale) in cancer patients in Haji Adam Malik Hospital, Medan.

- ***Method:***

This study is a quantitative analytic study with a cross-sectional design. The study was conducted at Haji Adam Malik Hospital (RSUP HAM) from March to April 2019. The total sample obtained was 107. Data collection used the PHQ – 9 and VAS questionnaires.

- ***Results:***

From the results, the most severe PHQ – 9 depression scores were found to have severe pain levels of 80% and for moderate to severe depression also had the most severe pain levels at 60%. Whereas for minimal depression, mild depression, and moderate depression were had the moderate pain level with each 87.5%, 60%, and 52.3%. Statistically there is a significant relationship of depression level (patient health questionnaire – 9) to the degree of pain (visual analog scale) in cancer patients with a value of p = 0.008 (<0.05).

- ***Conclusions:***

There is a strong correlation between the level of depression (patient health questionnaire – 9) to the degree of pain (visual analog scale) in cancer patients with values.

Keywords:- *Depression (Patient Health Questionnaire – 9), Degree of Pain (Visual Analog Scale), Cancer*

I. INTRODUCTION

Cancer is a kind of disease that involves the growth of abnormal cells that have the potential to attack or spread to other parts of the body. This is different from a benign tumor, which does not spread to other parts of the body. The possible signs and symptoms may include lumps, abnormal bleeding, long-term coughing, unexplained weight loss, strong pain in almost throughout the body and the change in bowel movements. Although these symptoms indicate cancer, they may have other causes. More than 100 types of cancer affect humans. Cancer is also the second leading cause of death globally and is responsible for 8.8 million of deaths in 2015. Almost 1 in 6 deaths are caused by cancer. (WHO, 2018)

Cancer is a health problem in the community with an increased incidence due to longer life expectancy. Nationally, the prevalence of cancer in the population of all ages in Indonesia in 2013 was 1.4 per mile, but it became to 1.8 per mile in 2018. Province D.I. Yogyakarta has the highest prevalence of cancer, which is 4.1 per mile that changed to 4.9 per mile in 2018. North Sumatra Province had a prevalence for cancer, of 1.0 per mile or estimated at around 13,391 people (Riskesdas, 2018; Yildirim *et. al*., 2009)

At the Haji Adam Malik Hospital in Medan, data on cancer patients in 2016 was 760 patients, and in 2017 it was 1071 patients Psychological problems in cancer patients are estimated to have different degrees. Sometimes this problem can arise as a reaction to a cancer diagnosis to the patient. However, psychological problems in most patients may be caused by the cessation of therapy, symptoms of the disease that cannot be controlled, delay in hospitalization and unexpected treatment defiance. The rate of psychiatric morbidity in cancer patients has been reported to be between 9 and 60%, but studies using standardized interviews and diagnostic criteria have reported that the rate of psychiatric morbidity in cancer patients is around 10-30%. Depression is the most common psychiatric condition in cancer, occurring in about a quarter of advanced cancer patients (Hong and Tian, 2014). Depression is also four times more common in cancer patients than in populations that do not have cancer and are

ISSN No:-2456-2165

often undiagnosed (Prasertsri *et. al*., 2011; Miyata *et. al*., 2004; Tavoli *et. al*., 2007; Hong and Tian, 2014)

More than 50% of cancer patients with metastasis and more than 90% of patients with advanced cancer experience pain. Cancer pain has a negative impact on the physical, mental status, and social ability of patients, thus damaging the quality of life. It has been found that cancer patients regard pain as an indicator of progressive disease and as a sign of death upcoming, these bad thoughts cause despair and hopelessness in patients causing increasingly severe depression (Ozkan, 2010; Kuzeyli *et. al*., 2005).

Pain in cancer can arise from tumors that suppress or infiltrate adjacent body parts; from treatment management and diagnostic procedures; or from the skin, nerves and other changes caused by hormonal imbalances or immune responses. Most chronic pain (long-term) is caused by disease and most acute pain (short-term) is caused by medication or diagnostic procedures. However, radiotherapy, surgery, and chemotherapy can be painful conditions that last long after treatment ends. The presence of pain depends mainly on the location of cancer and the stage of the disease. At any given time, about half of all people diagnosed with malignant cancer experience pain, and two-thirds of those with advanced cancer experience pain with such intensity that it adversely affects sleep, mood, social relationships, and daily life activities. With competent management, cancer pain can be eliminated or controlled properly in 80% to 90% of cases, but almost 50% of cancer patients in developed countries receive less than optimal treatment. Worldwide, nearly 80% of people with cancer receive little or no painkillers. Adequate pain management can sometimes slightly improve the standard of life for patients in advanced stages. (Hanna, Magdi; Zylicz, Zbigniew, 2013)

A cancer diagnosis can have a big impact on most patients and families. Depression, anxiety, and fear are very common and are a normal response to the change of life experiences. Patients often feel sad because of changes in the state of the body in undergoing daily activities. Physical symptoms such as pain, nausea, or extreme fatigue are also more likely to cause emotional stress. Patients also fear death, suffering, and pain. (American Cancer Society, 2016)

Depression develops more frequently in patients who experience severe pain than patients with milder pain, and depression is reported to increase the pain. Pain and depression are both often found in cancer patients and the relationship between these symptoms has been widely investigated. Epidemiological studies showed that depression and pain often appear together. There was also physiological evidence that supports this theory that the area in the cerebellar cortex that processes pain is also involved in the process of depression. Pain in cancer patients is influenced by many variables including cancer stage, the extent of disease and treatment. A prevalence survey showed that about 90% of cancer patients experience pain (Caraceni dan Portenoy, 1999; Spiegel, 1983; Spiegel *et. al*., 1994; Caraceni and Portenoy, 1999; Lloyd *et. al*., 2004; Bair *et. al*., 2004; Giesecke *et. al*., 2005; Andersen and Sjogren, 1998).

The Patient Health Questionnaire (PHQ-9) is an instrument that is widely used to see the state of depression in patients in clinical research. The first goal of this study was to test psychometric PHQ-9 in cancer patients. The second objective was to calculate unbiased estimation of the burden of depression for several cancer groups by considering the age and sex distribution. It was expected that the mean PHQ-9 value of the general population sample allows a fair comparison of various groups of cancer patients. The difference between the expected mean score (coming from the general population) and the standard mean score of cancer subsamples was reported to give a better estimation of the burden of depression. The results confirmed that PHQ-9 performs well in testing depression in cancer patients. Regression coefficients can be used to make unbiased comparisons between cancer groups (Andreas Hinz, 2016)

VAS (Visual Analogue Scale) is a tool used to assess the intensity of certain sensations and feelings, such as pain, anxiety, and depression. visual analog scale for pain is a straight line with one end which means there is no pain and the other end means the worst pain imaginable. The patients mark a point on the line that matches the amount of pain they feel. This can be used to help choosing the right dose of pain medication. (NCI, 2018)

There are various kinds of problems and sufferings faced by cancer patients. One of them is an unexplained fear of death, which is an existential problem. In a study that investigated the relationship between death anxiety and its correlation in cancer patients. It was found that anxiety of death is not considered as a natural consequence of suffering from cancer; this is related to unresolved psychological and physical disorders. (Journal of Pshycosocial Oncology, 2012)

In an effort to develop a practical assessment methodology for advanced-stage cancer patients, Visual Analogue Scales (VAS) for pain, depression and anxiety compared to the standard size of patients suffering from cancer that is related to pain. There were supports found for the validity of VAS-Pain and VAS-Depression but not for VAS-Anxiety. Studies showed that VAS-Pain and VAS-Depression provide a practical and valid method for assessing sensory and affective components of cancer-related pain. (Ahles TA, 2014)

Based on the background explained above, the researchers wanted to know whether there was a relationship between the level of depression (Patient Health questionnaire-9) to the degree of pain (Visual Analog Scale) in cancer patients at Haji Adam Malik Hospital Medan.

ISSN No:-2456-2165

II. RESEARCH METHODS

A. Research Design

This study was a quantitative analytical study with a cross-sectional design to see and find out the relationship between the level of depression (Patient Health Questionnaire - 9) with the degree of pain (Visual Analog Scale) in cancer patients at H Adam Malik Hospitalk

B. Place and Time of Research

This study was conducted at the Haji Adam Malik Hospital. It started after ethical clearance and the research permit from Haji Adam Malik Hospital was issued until the sample was fulfilled.

C. Research Population and Samples

The population was all patients suffering from cancer in Haji Adam Malik Hospital Medan who fulfilled the inclusion and exclusion criteria. In this study, consecutive sampling was used. Where the entire population that met the inclusion and exclusion criteria in the study was a sample.

D. Sampling Technique

The sampling technique used was nonprobability sampling with consecutive sampling. Consecutive sampling is a sample selection technique in which all subjects who come and meet the selection criteria are included in the study until the number of subjects needed is fulfilled.

E. Criteria for Inclusion And Exclusion

➢ *Inclusion Criteria*

1. Willing to participate in research
2. Aged 18-60 years old.
3. Compos Mentis Cooperative Awareness
4. Able to express or interpret feelings towards cancer that is suffered.
5. Patients who have received standard operating procedure (SOP) protocol for pain therapy from the palliative division and consulted with the anesthesiologist.
6. Patients with VAS values > 4

➢ *Exclusion Criteria*

1. Patients who experience other diseases besides cancer that can cause pain.
2. Patients with type 1 and type 2 diabetes mellitus
3. Patients with speech and hearing impairments
4. Patients with schizophrenia
5. Have received anti-depression therapy

F. Procedures

1. This study was first approved by the research ethics commission in the health field of the Faculty of Medicine, University of North Sumatra and Haji Adam Malik Hospital Medan.
2. The cancer patients then gave informed consent to undergo treatment in the Inpatient Room of H. Adam Malik Hospital, Medan.
3. All samples to be studied have met the requirements determined according to the needs of this study.
4. The patients were explained about the purpose of the study, possible follow-up plans to be taken, and the benefits of this study.
5. After the patients agreed, the patients were interviewed according to the PHQ-9 questionnaire and asked about the assessment of the pain scale according to the VAS score.
6. The questionnaires were then numbered and tabulated, for further analysis of the data

G. Management Plan and Data Analysis

After all the required data had been collected, the data was then checked again regarding the completeness before the tabulation and processing. After that, the data were coded to facilitate tabulation. Data were tabulated into the master table using SPSS software. Data were carried out by univariate analysis, bivariate test and correlation test to see the relationship between variables

III. RESEARCH RESULT

➢ *Sample Characteristics*

This research was conducted for 2 months, March - April 2019 at the Haji Adam Malik Hospital in Medan. This study aimed to determine the relationship of depression level (patient health questionnaire-9) to the degree of pain (visual analog scale) in cancer patients at Haji Adam Malik Hospital, Medan. The samples obtained in this study were 107 samples and in accordance with the inclusion and exclusion criteria. Sample characteristics are shown in Table 1.

Characteristics		**p *value***
Sex, n (%)		
Male	66 (61,7)	0.09
Female	41 (38,3)	
Age, mean (SD)	49.77±1.40	0.66
hemodynamic, mean (SD)		
TDS	123.17±1.2	0.113
TDD	88.01±6.7	0.257
HR	83.84±0.9	0.414
RR	19.82±0.58	0.189
BMI, mean (SD)	21.31±0,4	0.135
PHQ-9, n (%)		
Minimal/normal depression	8 (7,5)	
Mild depression	35 (32,7)	
Moderate depression	44 (41,1)	0.212
Moderate-severe depression	15 (14,0)	
Severe depression	5 (4,7)	
VAS, n (%)		
Moderate pain	58 (54.2)	0.362
Severe pain	49 (45.8)	
Total	107 (100.0)	

Table 1:- Sample Characteristics

ISSN No:-2456-2165

Table 1 shows the distribution of sample characteristics in this study. It is obtained that the characteristic data in this study were normally distributed, with a value of p > 0.05. In addition, in this study, the samples were mostly male with 66 samples (61.7%) and a mean age of 49.77 years old. The hemodynamic status of the sample in this study was overall stable with TDS of 123.17 mmHg, TDD of 88.01 mmHg, HR of 83.84 times per minute, RR of 21.3 times per minute. The mean of body mass index (BMI) in the sample was 21.31 kg/m2 which showed normoweight. While for the PHQ-9 value in the overall sample, mostly was moderate PHQ-9 value of 44 samples (41.1%). While the highest VAS values were at moderate pain level with 58 samples (54.2%).

type of cancer	Frequency (n)	Percentage (%)
Bladder cancer	6	5.6
Bone cancer	1	0.9
Breast cancer	8	7.5
Buli cancer	1	0.9
Cervix cancer	6	5.6
CNS cancer	2	1.9
Colonorectal cancer	10	9.3
Endometrium cancer	2	1.9
Gaster cancer	2	1.9
Genital cancer	3	2.8
Head and neck cancer	24	22.4
Hepar cancer	6	5.6
Kidney cancer	3	2.8
Lung cancer	8	7.5
Non melano skin cancer	1	0.9
Ovarium cancer	3	2.8
Pankreatic adenocarcinoma cancer	2	1.9
Prostate cancer	10	9.3
Unknown of origin cancer	9	8.4

Table 2:- Description of the type of cancer

Based on Table 2 it was found that the most types of cancer in this study were head and neck cancer of 24 cases (22.4%), followed by colonorectal cancer and prostate cancer, each of which was 10 cases (9.3%) and 10 cases (9.3%). The breast cancer case in the study was 8 cases (7.5%) and lung cancer (7.5%). While the least types of cancer were bone cancer, bladder cancer, gaster cancer, laryngeal cancer, mandibular cancer, non melano skin cancer, and sinonasal cancer which were 1%. While for the case of the unknown origin cancer, it was classified as high, amounting to 9 cases (8.3%)

➢ *Hemodynamic status based on the degree of pain with VAS*

Description of hemodynamic status based on the degree of pain with VAS is shown in Figure 4.1.

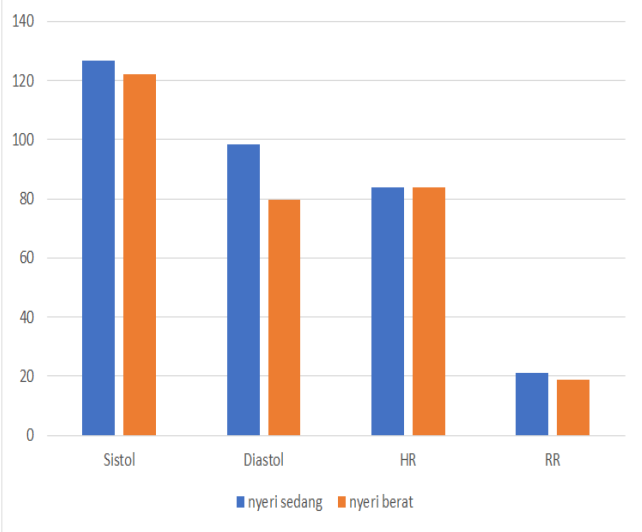

Fig 1:- Hemodynamic status based on the degree of pain with VAS

Based on Figure 1 it was found that the hemodynamic status based on the degree of pain with VAS showed a stable hemodynamic status. However, the highest TDS and TDD values were found in patients with moderate degrees of pain. Meanwhile for HR and RR hemodynamic status relatively had almost the same mean value.

➢ *Hemodynamic status based on degree of depression with PHQ-9*

Description of hemodynamic status based on degree of depression with PHQ-9 is shown in Figure 2.

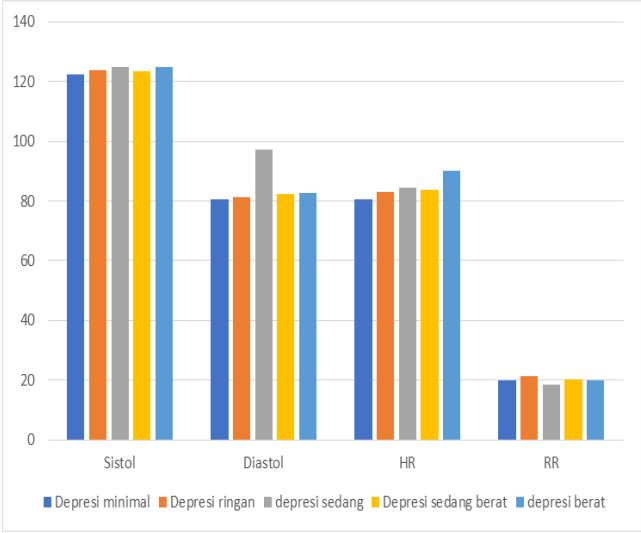

Fig 2 Hemodynamic status based on degree of depression with PHQ-9

Based on Figure 2 it was found that the hemodynamic status based on the degree of depression with PHQ-9 showed a stable hemodynamic status. However, the highest mean TDD was found in moderate depression, while the highest mean HR was found in major depression.

Relationship between depression level (patient health questionnaire-9) with the degree of pain (visual analog scale) The relationship of the depression level (patient health questionnaire-9) with the degree of pain (visual analog scale) is shown in Table 3.

		Moderate pain n (%)	Severe pain n (%)	Total	P value
PHQ-9	Minimal depression	7 (87,5)	1 (12,5)	8	0,008
	Mild depression	21 (60)	14 (40)	35	
	Moderate depression	23 (52,3)	21 (47,7)	44	
	Moderate-severe depression	6 (40)	9 (60)	15	
	Severe depression	1 (20)	4 (80)	5	
	Total	**58**	**49**	**107**	

Table 3:- Relationship of depression level (patient health questionnaire-9) with the degree of pain (visual analog scale) (Chi-square test, α<005)

Based on table 3, it was found that the most severe PQH-9 depression was found to have severe pain levels of 80% and for moderate to severe depression also had the highest degree of severe pain by 60%. Whereas for minimal depression, mild depression, and moderate depression had moderate pain with 87.5%; 60%; and 52.3%. Statistically, there is a significant relationship between the level of depression (patient health questionnaire) and the degree of pain (visual analog scale) in cancer patients with a value of p=0.008 (<0.05).

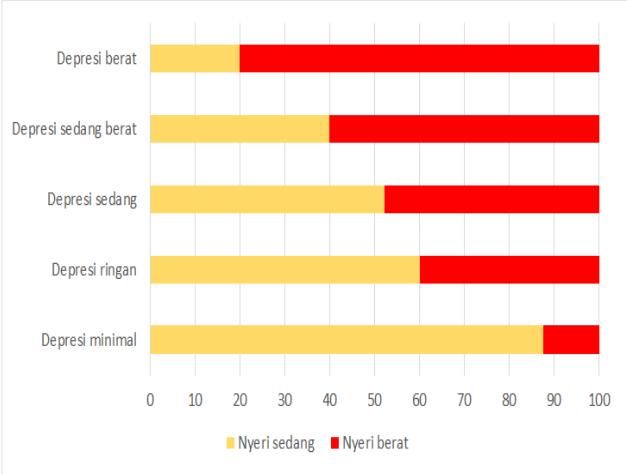

Fig 3:- Level of Depression (Patient Health Questionnaire-9) to the Degree of Pain (Visual Analog Scale)

Based on figure 3, it was found that the degree of pain increased with the increasing degrees of depression. This shows that there is a tendency to increase the scale of pain in patients with severe degrees of depression. In depression, at least more than 80% of patients experienced moderate pain, whereas in severe depression only 20% experienced moderate pain.

Variable	Mean±SD	Correlation (r)	P value
VAS	6.6 ± 0.76	**0.71***	**0.009**
PHQ-9	11.02 ± 9.45		

Table 4:- Correlations of Depression level (patient health questionnaire-9) with the degree of pain (visual analog scale) *Pearson Correlation Test

Based on table 4 it was found that there was a strong correlation between the level of depression (patient health questionnaire-9) and the degree of pain (visual analog scale) in patients suffering from cancer with a value of p = 0.71 and a significant of p (0.009) < 0.005.

IV. DISCUSSION

This study was conducted to determine the relationship of depression level (patient health questionnaire-9) with the degree of pain (visual analog scale) in cancer patients at Haji Adam Malik Hospital, Medan. Depression conditions in cancer patients are thought to increase the degree of pain in patients so that cancer patients with pain can also have depression that needs to be treated.

Based on Table 1, the samples were mostly male with 66 samples (61.7%) and a mean age of 49.77 years old. The results of this study are consistent with the research conducted by Tuck *et. al.* (2018) who also assessed PHQ-9 scores with VAS scores that got a mean age of 59.2 years old and mostly male samples with 52.8% (Tuck et al., 2018). Whereas for the PHQ-9 value in the overall samples, most of them had PHQ-9 values with moderate depression of 44 samples (41.1%). While for VAS values, most of them were at a moderate pain level of 58 samples (54.2%) and no samples with mild pain were found

Based on Table 2 it was found that the most types of cancer in this study were head and neck cancer of 24 cases (22.4%), followed by colonorectal cancer and prostate cancer, each of which was 10 cases (9.3%) and 10 cases (9.3%). The breast cancer case in the study was 8 cases (7.5%) and lung cancer (7.5%). While the least types of cancer were bone cancer, bladder cancer, gaster cancer, laryngeal cancer, mandibular cancer, non melano skin cancer, and sinonasal cancer which were 1%. While for the case of the unknown origin cancer, it was classified as high, amounting to 9 cases (8.3%). This result is different from the report by Bray *et. al.* (2018) from the International Agency for Research on Cancer (IARC) in 2018 that globally, there were the estimation of 18.1 million cases of lung cancer (17.0 million excluding nonmelanoma skin cancer) and 9.6 million deaths from cancer (9.5 million excluding nonmelanoma skin cancer) in

2018. Lung cancer was the most commonly diagnosed cancer with a total case of 11.6% and contributing 18.4% of deaths caused by cancer, followed by female breast cancer (11.6%), prostate cancer (7.1%), and colorectal cancer (6.1%)

Based on Figure 1 it was found that the hemodynamic status based on the degree of pain with VAS showed a stable hemodynamic status. However, the highest TDS and TDD values were found in patients with moderate degrees of pain. Meanwhile for HR and RR hemodynamic status relatively had almost the same mean value. Based on Figure 4.2 it was found that the hemodynamic status based on the degree of depression with PHQ-9 showed a stable hemodynamic status. However, the highest mean TDD was found in moderate depression, while the highest mean HR was found in major depression. While for the hemodynamic status of TDS and RR there was no difference in mean values. The results of this study were in accordance with Schonberger *et. al.* (2014)that there were no differences in hemodynamic status assessed with increasing depression assessed by PHQ-9 and the degree of pain assessed by VAS (Schonberger et al., 2014).

Based on table 3, it was found that the most severe PQH-9 depression was found to have severe pain levels of 80% and for moderate to severe depression also had the highest degree of severe pain by 60%. Whereas for minimal depression, mild depression, and moderate depression had moderate pain with 87.5%; 60%; and 52.3%. Statistically, there is a significant relationship between the level of depression (patient health questionnaire) and the degree of pain (visual analog scale) in cancer patients with a value of p=0.008 (<0.05). This is consistent with the theory that each pain and depression are related and often occur together although the underlying interactions between pain and depression are not fully understood. their presence has been shown to cause additional side effects in patients, including deteriorating function and reduced response to treatment (Rayner et al., 2016) This can be shown that pain can occur in cancer patients with depressive symptoms in about 10%-25% of them. These symptoms have a large detrimental effect on functional status and quality of life, and have a poor prognosis in advanced cancer, including the desire to speed up death. In addition, both depression and pain are often underdiagnosed in cancer patients, and more than half of cancer patients feel depressed during one follow-up year. Unfortunately, cancer pain is often not addressed (Kurt, 2010).

Indiana Cancer Pain and Depression (INCPAD) Study was a clinical trial involving patients from oncology practices from communities suffering from depression or cancer-related pain. This study stated that pain and depression in patients with cancer have an independent and synergistic relationship with increased pain severity, and also estimated pain and depression are associated with increased use of health care (Kroenke et al., 2010) This is also supported by findings that depression often occurs in cancer patients and can lead to a reduced quality of life, inadequate treatment, physical, social, family disorders, and reduced desire to live. So that Depression can cause an increase in the patient's perception of pain, decrease the sensitivity of the efficacy of the treatment, extend the time of hospitalization, and can refer to suicidal ideas or actions (Widiyono, 2017).

In another study, Noah *et. al.* (2016), who examined 154 patients who experienced pain and depression, found that the pain score improved as the symptoms of depression also improved (Noah *et. al*. 2016).

V. CONCLUSION

1. There is a strong correlation between the level of depression (patient health questionnaire-9) and the degree of pain (visual analog scale) in cancer patients.
2. The level of depression assessed by PHQ-9 in the overall samples had the most PHQ-9 values with moderate depression
3. The level of pain assessed by VAS in the overall samples had the most moderate degree of pain

REFERENCES

[1]. American Psychiatric Association, 2017, *Depression*, Tersedia di: [Diakses: 24 November2018] https://www.psychiatry.org/patientsfamilies/depression/what is-depression.
[2]. Abraham SE, Schlicht CR. Chronic Pain Management. In : Barash PG, Cullen BF, Stoleting RK, editors. Clinical Anesthesia, 4th edition. Philadelphia : Lippincott Williams and Wilkins.2001;1453-62
[3]. Akmal, Mutaroh, dkk,. 2010. Ensiklopedi Kesehatan untuk Umum,. Jogjakarta: Ar-Ruzz Media
[4]. Andersen G, Sjogren P. [Epidemiology of cancer pain]. Ugeskr Laeger 1998;160(18):2681–2684.
[5]. Argoff C, Mc Cleane G. Pain Management Secret. 3rd ed. Philadelphia. Elsiver. 2009
[6]. Bair MJ, Robinson RL, Eckert GJ, Stang PE, Croghan TW, Kroenke K. Impact of pain on depression treatment response in primary care. Psychosom Med 2004;66(1):17–22
[7]. Bonica JJ, Loeser JD. History of pain concepts and therapies. In : Loeser JD, editor. The Management of Pain, 3rd edition. Lippincot William Wilkins.1990;2-15
[8]. Boulanger, K.T. 2012. Factors related to satisfaction, pain and affect outcomes in Massage Therapy clients. Philosophy Degree in Community and Behavioral Health in The Graduate College of The University of Iowa
[9]. Carli F, Baldini G. Chapter 48 : Perioperative Pain Management and Enhanced Outcomes .Morgan Clinical Anesthesiology. 5th edition. New York : Mc Graw Hill Lange Medical Books ; 2013.; p.10871105.

[10]. Caraceni A, Portenoy R. An international survey of cancer pain characteristics and syndromes. IASP task force on cancer pain. International Association for the Study of Pain. Pain 1999;82(3):263–274
[11]. Cohen, S.P and Raja, S.N., 2016, 'pain', *Goldman-Cecil Medicine*, Edisi 25, Chapter 29, hal. 133-143.
[12]. Chinese cancer patients. Support Care Cancer 2014;22(2):453–9.
[13]. Dahlan, M.S., 2017, *Multiaksial Statistik Diagnosis dan Multiaksial Substansi Diagnosis Pintu Gerbang Epidemiologi, Biostatistik, dan Metode Penelitian,* 2 ed, Epidemiologi Indonesia.
[14]. Diananda, R., 2009. Kanker Serviks: Sebuah Peringatan Buat Wanita. In: Diananda, R. Mengenal Seluk-Beluk Kanker. Yogyakarta: Katahari, 43-60.
[15]. Elia N, Martin R, Trame`r. Ketamine and Postoperative Pain – A Quantitative Systematic Review of Randomised Trials. IASP.2005;13.61-70
[16]. First MB. Psychiatric classification. In: Tasman A, Kay J, Lieberman JA, First MB, Maj M. editors. Psychiatry. Vol. 1. 3rd ed. West Sussex: John Wiley & Sons Ltd; 2008. p. 666-78
[17]. Fishbain, DA., 2013, 'Psychiatric Pain-Associated Co-morbidities', *Wall and Melzack's Textbook of Pain*, Edisi 6, Chapter 19, hal. 273-282.
[18]. Gagliese,L., Gauthier, L.R., Rodin, G., 2007, *Cancer pain and depression: A systematic review of age-related patterns*, Tersedia di :https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2670711/.
[19]. Giesecke T, Gracely RH, Williams DA, Geisser ME, Petzke FW, Clauw DJ. The relationship between depression, clinical pain, and experimental pain in a chronic pain cohort. Arthritis Rheum 2005;52(5): 1577–1584
[20]. Gebauer, S., 2018, *Basic of Anasthesia: Palliative Care*, Edisi 7, Chapter 49, hal. 829-844.
[21]. Grossman, S.A and Nesbit, S., 2013, 'Cancer-Related Pain', *Abeloff's Clinical Oncology,* Edisi 5, Chapter 40, hal. 608-619.
[22]. Hinz, A., Mehnert, A., Kocalevent, R.D., Brahler, E., Forkmann, T., Singer, S., dan Schulte, T., 2016, *Assessment of depression severity with the PHQ-9 in cancer patients and in general population*
[23]. Hong JS, Tian J. Prevalence of anxiety and depression and their risk factors in
[24]. International Association for the Study of Pain, 2018, *Cancer Pain,*
[25]. Jane C, Ballantyne. Acute Pain Management. In: Longnecker D, Brwon D, Newman M, Zapol W. Anesthesiology. USA. The McGraw-Hill Companies. 2008: 1743-63
[26]. Kaplan, H.I. & Sadock, B.J., 2015. *Ilmu Kedokteran Jiwa Darurat.* Jakarta: Widya Medika.
[27]. Kementerian Kesehatan Republik Indonesia, 2015, *kanker,* [Diakses: 24 November 2018], tersedia di:
[28]. Klimek, L., Bergmann, K.C., Biedermann, T., Bousquet, J., Hellings, P., Jung, K., Merk, H., Olze, H., Schlenter, W., Stock, P., Ring, J., Wagenmann, M., Wehrmann, W., Mösges, R., Pfaar, O., 2017, Visual analogue scales (VAS): Measuring instruments for the documentation of symptoms and therapy monitoring in cases of allergic rhinitis in everyday health care', *Visual Analogue Scale (VAS)*, vol. 26, no. 1, hal. 16-24.
[29]. Kroenke, K., Spitzer, R.L., Williams, J.B.W., Löwe, B., 2010. The Patient Health Questionnaire Somatic, Anxiety, and Depressive Symptom Scales: a systematic review. Gen. Hosp. Psychiatry 32, 345–359.
[30]. Kumar, H.K. & Elavarasi, P., 2016, '*Defenition of Pain and Classification of Pain Disorder' Journal of Advance Clinical & Research Insight*, vol. 3, hal. 87-90.
[31]. Kurt, K., Dale, T., Jingwei, W., Julie, K.L., Janet, S.C., dan Wanzhu, T., 2010, ' The Association of Depression and Pain with Health-Related Quality of Life, Disability, and Health Care Use in Cancer Patients', *Journal of Pain and Symptom Management*, vol. 40, no. 3, hal. 327-341.
[32]. Kuzeyli Yildirim Y, Uyar M, Fadillioğlu C. Cancer pain and its influence on quality of life. Agri 2005;17(4):17–22.
[33]. Kroenke, K., Spitzer, R.L, Williams, J.B., 2001. The PHQ-9: validity of a brief depression severity measure. J Gen Intern Med 16. p:606–613
[34]. Larkin R. Acute pain management ; scientific evidence. National Health and Medical Research Council. Commonwealth of Australia, 1999
[35]. Lloyd-Williams M, Dennis M, Taylor F. A prospective study to determine the association between physical symptoms and depression in patients with advanced cancer. Palliat Med 2004;18(6):558–563.
[36]. Maharani S, 2009. Kanker: Mengenal 13 Jenis Kanker dan Pengobatannya. Yogyakarta: Katahati.
[37]. Meyer RA, Ringkamp M, Campbell JN. Peripheral neural mechanism of nociception. In : McMahon SB, Koltzenburg M, editors. Textbook of Pain, 5th ed. China : Churchill Livingstone.2006;8-19
[38]. National Institute of Mental Health, 2011, *Depression*
[39]. Ozkan S. Psychiatric aspects of pain in cancer patients. Asian Pac J Cancer Prev 2010;11 Suppl 1:113–6.
[40]. Oxenham, D., 2014, *Davidson's Principles and Practice of Medicine*, Edisi 22, Chapter 12, hal. 283-292.
[41]. Rayner, L., Hatopf, M., Petkova, H., Matchama, F., Simpson, A., McCrackenc, L.M., 2016, 'Depression in patients with chronic pain attending treatment centre: Prevalence and impact on health care costs' ,*Wall & Melzack's Textbook of Pain*, vol. 1, no. 7,

hal. 1472-1479.
[42]. Rosalia, L.P., 2016, Prevalensi Nyeri Kanker dan Karakteristik Pasien Nyeri Kanker di RSUP, dr Sardjito Yogyakarta, Tesis, Program Studi Pendidikan Dokter Spesialis Ilmu Penyakit Dalam Fakultas Kedokteran Universitas Gadjah Mada, Yogyakarta
[43]. Rosenquit RW, Vrooman BM, Chapter 47 : Chronic Pain Management. Morgan Clinical Anesthesiology. 5th edition. New York : Mc Graw Hill Lange Medical Books ; 2013.; p.1023-85
[44]. Sastroasmoro, S. & Ismael, S., 2016, Dasar-dasar Metodologi Penelitian Klinis, Sagung Seto, Jakarta.
[45]. Sadock, J.b. & Sadock, A.V., 2014. *Kaplan and Sadock's Concise Textbook of Clinical Psychiatri,* USA: Lippincott Williams & Wilkins. Terjemahan Prfitasari dan Nisa, T.M. *Kaplan & Sadock Buku Ajar Psikiatri Klinis.* Ed 2. Jakarta: Penerbit Buku Kedokteran EGC.
[46]. Schonberger, R.B., Feinleib, J., Holt, N., Dai, F., Brandt, C., Burg, M.M., 2014. Preoperative depression symptom severity and its impact on adherence to preoperative beta-blocker therapy. J. Cardiothorac. Vasc. Anesth. 28, 1467–73.
[47]. Siregar AF. Perbandingan Hemodinamik pada Tindakan Laringoskopi dan Intubasi pada Premedikasi Fentanil 2uq/kgbb Intravena+Deksketoprofen 50 mg Intravena dengan Fentanil 4 uq/kgbb Intravena. Departemen Anestesiologi dan Terapi Intensif FK USU.2010.1-48
[48]. Smith KA, Ploghaus A, Cowen PJ et al. Cerebellar responses during anticipation of noxious stimuli in subjects recovered from depression. Functional magnetic resonance imaging study. Br J Psychiatry 2002; 181:411–415.
[49]. Spiegel D, Sands S, Koopman C. Pain and depression in patients with cancer. Cancer 1994;74(9):2570–8
[50]. Sunaryati, S.S. 2011. 14 Penyakit Paling Sering Menyerang dan Mematikan. Jogjakarta: Flash Books
[51]. Strong, J. et al (2002) Pain assessment and measurement. In: Strong, J. et al ed. Pain, A Textbook for Therapists.Churchill Livingstone. Edinburgh pp123-147
[52]. Tavoli A, Mohagheghi MA, Montazeri A, Roshan R, Tavoli Z, Omidvari S. Anxiety and depression in patients with gastrointestinal cancer: does knowledge of cancer diag-nosis matter? BMC Gastroenterol 2007;7:28.
[53]. Tuck, A.N., Scribani, M.B., Grainger, S.D., Johns, C.A., Knight, R.Q., 2018. The 9-Item Patient Health Questionnaire (PHQ-9): an aid to assessment of patient-reported functional outcomes after spinal surgery. Spine J. 18, 1398–1405.
[54]. Walker, B.J., Polaner, D.M., dan Berde, C.B., 2018, 'Acute Pain', *A Practice of Anesthesia for Infants and Children*, edisi 15, hal. 1023-1062.
[55]. Widiyono, S, Tingkat Depresi pada Pasien Kanker di RSUP Dr. Sardjito, Yogyakarta, dan RSUD Prof. Dr. Margono Soekarjo, Purwokerto: Pilot Study, 2017: Indonesian Journal of Cancer Vol. 11, No. 4, hal 171-177
[56]. Woolf CJ. Pain moving from symptom control toward mechanism-spesific pharmacologic management. Annals of Internal Medicine. 2004:140;441-51
[57]. World Health Organization, 2017, *Depression*, [Diakses: 10 Mei 2018], Tersedia di: http://www.who.int/mental_health/management/depression/en/.
[58]. World Health Organization, 2018, *Cancer*, [Diakses: 28 April 2018], Tersedia di: http://www.who.int/news-room/fact-sheets/detail/cancer.
[59]. Young, K., 2017, 'Assessment of Acute Pain in Children', *Clinical Pediatric Emergency Medicine*, vol. 18, no. 4, hal. 235-241.