DIPONEGORO MEDICAL JOURNAL
(Jurnal Kedokteran Diponegoro)
Online : http://ejournal3.undip.ac.id/index.php/medico
E-ISSN : 2540-8844
Volume 9, Nomor 2, Maret 2020

THE RELATIONSHIP BETWEEN ESR, HEMATOCRIT, PLATELETS COUNT AND OUTCOME OF CNS TUMOR PATIENTS WHO RECEIVED CHEMOTHERAPY AT RSUP DR. KARIADI SEMARANG

Hyasinta Paramita Budi[1], Maria Belladona Rahmawati[2],
Trianggoro Budisulistyo[2], Hexanto Muhartomo[2]
[1] Undergraduate Student, Faculty of Medicine, Diponegoro University
[2] Leturer, Department of Neurology, Faculty of Medicine, Diponegoro University

ABSTRACT

Background : Central nervous system tumors, both primary and secondary tumor, are malignancies which result in mental disorder, and neurological deficit. Therefore, the patients can end up being social burden for their environment. Hematological laboratory test including ESR, hematocrit, and platelets count are very practical. However, they are functional for predicting outcome. **Aim**: The current study aimed to determine the relationship between ESR, hematocrit, platelets count, and outcome of CNS tumor patients who received chemotherapy at RSUP dr. Kariadi Semarang. **Method** : This recent study was conducted at Medical Record Installation by collecting data from patient's medical record. Data taken by researcher were hematologic profile (ESR, hematocrit, and platelets count), demographic data (age, gender, type of tumor, symptomatic treatment, and comorbidity), and outcome. Data were analyzed using univariate analytical method to show data distribution, bivariate analytical method to determine the relationship with outcome, and multivariate analytical method to determine which variable had the most significant relation. **Result** : Bivariate analytical method using chi-square test showed insignificant p value for hematocrit (p=0,541 total data, p=0,960 case, p=0,518 control). Platelets count analysis didn't give significant p value either (p=0,541 total, p=0,790 case, p=0,292 control). There were no data could be obtained about ESR. **Conclusion** : The current study showed no relationship between hematocrit and outcome, neither the relationship between platelets count and outcome.

Keywords *: ESR, hematocrit, platelets count, outcome*

INTRODUCTION

Central Nervous System (CNS) tumor can be described as tumors which grow in brain tissue and spinal cord. International Classification of Disease for Oncology, Third Edition (ICD-O-3) also classified tumors of meninges tumor, pituitary gland tumor, pineal gland tumor, and neuron as CNS tumor.[1] Incidence of CNS tumor is rare among adults and children. However, statistical record says that it is growing in number every year.[2]

CNS tumors are malignancies that do not heal and the inflammatory process takes place continuously. Prolonged inflammation plays a role in the development of malignancy. Therefore, inflammatory biomarkers can be used as predictors of malignant patient outcomes. One of the inflammatory biomarkers that is often used is Erythrocyte Sedimentation Rate (ESR).[3] In several studies, it is mentioned that high ESR were associated with low patient survival. Another predictor that can be used is platelet count. In some previous studies, high platelets associated with low survival of patients with malignancies that caused thrombocytosis was a poor prognosis predictor.[4] Besides inflammation, malignancy can have another effect, anemia. Anemia in malignancy is a natural thing to happen. Anemia is made worse by chemotherapy. In malignant patients, the number of hematocrit is lower. This mechanism occurs because of the high

DIPONEGORO MEDICAL JOURNAL
(Jurnal Kedokteran Diponegoro)
Online : http://ejournal3.undip.ac.id/index.php/medico
E-ISSN : 2540-8844
Volume 9, Nomor 2, Maret 2020

activity of eryptosis that is not matched by erythropoiesis.[5]

The outcome of patients with CNS tumors with chemotherapy is currently not promising because the role of chemotherapy drugs in CNS tumors is limited by blood brain barrier (BBB) .[6] Hematologic examinations especially ESR, hematocrit, and platelets count are practical to do. However, their function as predictors of outcome makes their relationship with chemotherapy interesting to be studied which has so far been carried out as one of the treatment options in CNS tumor patients.

METHODS

An observational analytic retrospective case control study was conducted at RSUP dr. Kariadi Semarang in October 2019. Samples were chosen purposively as long as samples matched the inclusion and exclusion criteria. Samples included patients who received chemotherapy as case group and patient who did not receive chemotherapy as control group. The inclusion criteria for case group were receiving chemotherapy and having complete data in medical record. The exclusion criteria for control group was craniotomy.

Data collection was performed in Medical Record Installation of RSUP dr. Kariadi Semarang after having permission from the Main Director of RSUP dr. Kariadi Semarang. Data were collected from patient's medical record and recorded on the form prepared. Minimum number of sample in the current study was 25 samples each group. However, 26 samples were being observed each group. The recent study collected data from medical records in January 2017 until September 2019. Hematologic profile (erythrocyte sedimentation rate, hematocrit, platelets count), demographic data (age, gender, type of tumor, comorbidity, symptomatic treatment), and outcome were data which collected from medical records. The independent variables of this study were ESR, hematocrit, and platelets count while the dependent variable of this study was outcome.

Tabulating data was done after cleaning, editing, and coding process. SPSS ver 25 was used to analyze the relationship between variables. Descriptive statistical method (frequency distribution), analytical statistical method (chi-square test), and multiple logistic regressions were used.

RESULTS

This study was conducted at Medical Record Installation of RSUP dr. Kariadi Semarang and 52 medical records from January 2017 until September 2019 were studied. Characteristic of subjects was described by age, gender, type of tumor, comorbidity, symptomatic treatment, hematocrit, and platelets count. There was no retrospective data about ESR. Furthermore, ESR was not included in this study. Age was divided into two categories, ≤18 years old and >18 years old. Distribution of age could be seen in table 1.

Table 1. Distribution of age

Age	Case n (%)	Control n (%)	Total n (%)
≤18 years old	12 (23,1)	3 (5,8)	15 (28,8)
>18 years old	14 (26,9)	23 (44,2)	37 (71,2)
Total	26 (50,0)	26 (50,0)	52 (100,0)

DIPONEGORO MEDICAL JOURNAL
(Jurnal Kedokteran Diponegoro)
Online : http://ejournal3.undip.ac.id/index.php/medico
E-ISSN : 2540-8844
Volume 9, Nomor 2, Maret 2020

Gender was divided in to two categories, male and female. Distribution of gender was shown in table 2.

Table 2. Distribution of gender

Gender	Case n (%)	Control n (%)	Total n (%)
Male	14 (26,9)	14 (26,9)	28 (53,8)
Female	12 (23,1)	12 (23,1)	24 (46,2)
Total	26 (50,0)	26 (50,0)	52 (100,0)

Type of tumor was divided into two categories, primary tumor and secondary tumor. Table 3 showed the distribution of tumor type.

Table 3. Distribution of tumor type

Tumor type	Case n (%)	Control n (%)	Total n (%)
Primary	15 (28,8)	23 (44,2)	38 (73,1)
Secondary	11 (21,2)	3 (5,8)	14 (26,9)
Total	26 (50,0)	26 (50,0)	52 (100,0)

Symptomatic treatment was divided into two categories, yes or no. If the subject was given symptomatic treatment, then it was a yes. Distribution of symptomatic treatment was shown in table 4.

Table 4. Distribution of symptomatic treatment

Symptomatic treatment	Case n (%)	Control n (%)	Total n (%)
Yes	24 (46,2)	26 (50,0)	50 (96,2)
No	2 (3,8)	0 (0,0)	2 (3,8)
Total	26 (50,0)	26 (50,0)	52 (100,0)

Comorbidity existence was divided into two categories, yes and no. Distribution of comorbidity existence could be seen in table 5.

Table 5. Distribution of comorbidity existance

Comorbidity existance	Case n (%)	Control n (%)	Total n (%)
Without comorbidity	22 (42,3)	15 (28,8)	37 (71,2)
With comorbidity	4 (7,7)	11 (21,2)	15 (28,8)
Total	26 (50,0)	26 (50,0)	52 (100,0)

Hematocrit and platelets count were divided into three categories at first. However, they were then divided into two categories, normal and abnormal, to fulfill the chi-square test condition. Distributions of hematocrit and platelets count were shown in Table 6 and 7.

DIPONEGORO MEDICAL JOURNAL
(Jurnal Kedokteran Diponegoro)
Online : http://ejournal3.undip.ac.id/index.php/medico
E-ISSN : 2540-8844
Volume 9, Nomor 2, Maret 2020

Table 6. Distribution of hematocrit

Hematocrit	Case n (%)	Control n (%)	Total n (%)
Normal	9 (17,3)	7 (13,5)	16 (30,8)
Abnormal	17 (32,7)	19 (36,5)	36 (69,2)
Total	26 (50,0)	26 (50,0)	52 (100,0)

Table 7. Distribution of platelets count

Platelets count	Case n (%)	Control n (%)	Total n (%)
Normal	19 (36.5)	17 (32,7)	36 (69,2)
Abnormal	7 (13,5)	9 (17,3)	16 (30,8)
Total	26 (50,0)	26 (50,0)	52 (100,0)

The relationship between hematocrit and outcome

Table 8. The relationship between hematocrit and outcome

Group	p	OR	CI 95%
Case	0,960	1,067	0,083-13,650
Control	0,518	2,143	0,204-22,478
Total	0,541	1,690	0,083-13,650

chi-square test

Table 8 showed that there was no significant relationship between hematocrit and outcome in total group (p>0.05) with p value of 0.541, in case group with p value of 0.960, and in the control group with p value of 0.518.

The relationship between platelets count and outcome

Table 9. The relationship between platelets count and outcome

Group	p	OR	CI 95%
Case	0,790	1,417	0,108-18,595
Control	0,292	0,300	0,029-3,071
Total	0,541	0,592	0,109-3,227

chi-square test

Based on table 9, it could be seen that there was no significant relationship between platelets count and outcome in total group (p>0.05) with p value of 0.541, in case group with p value of 0.790, and in the control group with p value of 0.292.

The relationship between demographic factors and outcome

Table 10. The relationship between demographic factors and outcome

Variable	p	OR	IK 95%
Age			
< 18 years old	0,419[£]	0,430	0,098 – 1,892
≥ 18 years old			
Gender			

DIPONEGORO MEDICAL JOURNAL
(Jurnal Kedokteran Diponegoro)
Online : http://ejournal3.undip.ac.id/index.php/medico
E-ISSN : 2540-8844
Volume 9, Nomor 2, Maret 2020

Variable	p	OR	IK 95%
Male female	0,152£	0,273	0,051 – 1,465
Tumor type Primary Secondary	0,415£	0,288	0,033 – 2,548
Symptomatic treatment Yes No	1,000£	–	–
Comorbidity existence No Yes	<0,001£*	41,143	4,42 – 382,99

chi-square test; * Significant (p < 0,05); £ Fisher's exact

It is shown in the table 10 that most of demographic factors were not significant. It is only comorbidity existence which showed significant relationship with p value of <0.001 (<0.05). Demographic factors carried out bivariate test with p value <0.25, gender and comorbidity existence, were then performed a multivariate test with logistic regression test.

Table 11. multivariate test using logistic regression

Variable	p	OR	CI 95%
Gender	0,056	0,117	0,013 – 1,056
Comorbidity existence	0,001*	67,370	5,698 – 796,606

* Significant (p < 0,05)

Table 11 showed that comorbidity existence was dominant demographic factor compared with the other demographic factors with p value if 0.001.

DISCUSSION

Our finding showed that there was no significant relationship between hematocrit and outcome. Treatment of chemotherapy did not give any impact in the relationship. This finding was consistent with previous study showing that chemotherapy had effect on hematotoxicity which had relation with abnormal hematocrit. However, it did not have any effect on bad outcome or death.[7] Abnormal hematocrit gave significant effect on length of stay based on previous study about hematocrit. Side effect of long term chemotherapy session was chemo resistance because of many chemotherapy regiment which need oxygen to give impact on cytostatic event.[8,9] However, the length of stay was not studied in this research.

The relationship between platelets count and outcome was not found significant. It is not corresponding with previous theory which mentioned that platelets count had significant relation with outcome.[10,11] This incompatibility could be affected by many factors. Factor which most affected was time of study which could only be done when patient was being hospitalized and there was no follow up afterwards. Secondary data taken from patient medical record could be affected either, in relation with incomplete data. Previous cohort study was conducted at least 6 month to see complication of abnormal platelets count. [12]

Multivariate analytical method on demographic variables showed that comorbidity existence had become the most dominant variables among the other

DIPONEGORO MEDICAL JOURNAL
(Jurnal Kedokteran Diponegoro)
Online : http://ejournal3.undip.ac.id/index.php/medico
E-ISSN : 2540-8844
Volume 9, Nomor 2, Maret 2020

variables. Previous study had shown that comorbidity existence had a relationship with decreased survival rate. This theory was also in relation with treatment tolerance of patient when undergone their treatment session.[13] Comorbidity has also been studied about its relation with hospital-acquired conditions such as deep venous thrombosis, urinary tract infection, which could increase morbidity and mortality.[14] However, this recent study did not collect specific data about comorbidity.

CONCLUSIONS AND SUGGESTIONS

Conclusions

There was no significant relationship between hematocrit and outcome. There was no significant relationship between hematocrit and outcome. ESR could not be studied because there were no retrospective data in medical record.

Suggestions

Based on the research conclusions, the authors suggest several things, including:

1. Additional cohort study might be required to get more appropriate results
2. It would be necessary to conduct focused study for each variables, such as comorbidity, symptomatic treatment, and tumor type, to get more appropriate results

REFERENCES

1. Lee C H, Jung K W, Yoo H, Park S, Lee SH. Epidemiology of primary brain and central nervous system tumors in Korea. Journal of Korean Neurosurgical Society. 2010 [cited 2019 November 14];48(2):145-152.
2. Ostrom QT, Gittleman H, Liao P, Rouse C, Chen Y, Dowling J, et al. CBTRUS Statistical Report: Primary Brain and Central Nervous System Tumors Diagnosed in the United States in 2007-2011. Neuro-Oncology. 2014 [cited 2019 November 14];16(suppl 4):iv1-iv63.
3. Strojnik T, Šmigoc T, Lah TT. Prognostic Value of Erythrocyte Sedimentation Rate and C-Reactive Protein in the Blood of Patients with Glioma. ANTICANCER RESEARCH. 2014 [cited 2019 November 14]:9.
4. Bambace NM, Holmes CE. The platelet contribution to cancer progression. J Thromb Haemost. 2011 [cited 2019 November 14];9(2):237-249.
5. Lang E, Lang F. Mechanisms and pathophysiological significance of eryptosis, the suicidal erythrocyte death. Semin Cell Dev Biol. 2015 [cited 2019 November 14];39:35-42.
6. Walker D, Bendel A, Stiller C, Indelicato D, Smith S, Murray M, et al. Central Nervous System Tumors. In: Bleyer A, Barr R, Ries L, Whelan J, Ferrari A, eds. Cancer in Adolescents and Young Adults. Cham: Springer International Publishing; 2017 [cited 2019 November 14]:335-381.
7. Jeremic B, Grujicic D, Jevremovic S, Stanissavljevic B, Milojevic, L, Djuric L, et al. Carboplatin and etoposide chemotherapy regimen for recurrent malignant glioma: a phase II study. J Clin Oncol. 1992 [cited 2019 November 15];10(7):1074-1077.
8. Senders JT, Muskens IS, Cote DJ, Galdhaber N, Dawood H, Gormley W, et al. Thirty-day outcomes after craniotomy for primary malignant brain tumors: a national surgical quality improvement program analysis. Neurosurgery. 2018 [cited 2019 November 15];83(6):1249-1259.
9. Alan N, Seicean A, Seicean S, Neuhauser D, Weil RJ. Impact of preoperative anemia on outcomes in patients undergoing elective cranial surgery. Journal of neurosurgery. 2014

DIPONEGORO MEDICAL JOURNAL
(Jurnal Kedokteran Diponegoro)
Online : http://ejournal3.undip.ac.id/index.php/medico
E-ISSN : 2540-8844
Volume 9, Nomor 2, Maret 2020

[cited 2019 November 15];120(3):764-772.
10. Packer RJ, Sutton LN, Elterman R, lange B, Goldwein J, Nicholson, HS, et al. Outcome for children with medulloblastoma treated with radiation and cisplatin, CCNU, and vincristine chemotherapy. Journal of neurosurgery. 1994 [cited 2019 November 15];81(5):690-698.
11. Kadota RP, Stewart CF, Horn M, Kuttesch J F, Burger P, Kepner J, et al. Topotecan for the treatment of recurrent or progressive central nervous system tumors–a pediatric oncology group phase II study. Journal of neuro-oncology. 1999 [cited 2019 November 16];43(1):43-47.
12. Ay C, Dunkler D, Marosi C, Chiriac A, Vormittag, R, Simanek R, et al. Prediction of venous thromboembolism in cancer patients. Blood. 2010 [cited 2019 November 16];116(24):5377-5382.
13. Ening G, Osterheld F, Capper D, Schmieder K, Brenke C. Charlson comorbidity index: an additional prognostic parameter for preoperative glioblastoma patient stratification. Journal of cancer research and clinical oncology. 2015 [cited 2019 November 16];141(6):1131-1137.
14. Lakomkin N, Hadjipanayis CG. Hospital-acquired conditions: predictors and implications for outcomes following spine tumor resection. Journal of Neurosurgery: Spine. 2017 [cited 2019 November 16];27(6):717-722.