

Original Article

Study of the Association Between Cerebral Venous Thrombosis and Inflammatory Biomarkers

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Received: 09 July 2023

Revised: 16 August 2023

Accepted: 02 September 2023

Published: 16 September 2023

Abstract - CVT is a relatively rare but serious type of stroke that affects young ages. Evidence is currently mounting on the role of inflammation in CVT. The research aims to study the relationship between inflammatory markers and CVT at the onset of thrombosis to determine the possibility of using these markers as a laboratory tool for the correct approach to diagnosis. **Methods:** A prospective cohort study was conducted between January 2021 and January 2023, in which the sample size consisted of 28 patients having CVT and 28 controls not suffering from CVT, with a statistical power of 95%. Intravenous samples were taken to conduct the following laboratory analyzes (Neutrophils – Lymphocytes – Platelets – CRP – ESR – NLR - PLR). Previous laboratory analyzes were compared between cases and controls and then analyzed statistically. **Results:** When comparing the ages of patients between the cases and controls, we did not find a statistically significant difference between the two groups, and the P-value was 0.980, as we found in our study a statistically significant difference between the two groups in terms of the values of the following laboratory analyzes (Neutrophils- Lymphocytes- Platelets -CRP - ESR – NLR- PLR), as the P-value reached the following 0.034 0.000-0.003-0.000-0.000-0.003-0.000, respectively. **Conclusion:** Our study confirmed the role of inflammation in the occurrence of cerebral venous sinus thrombosis and found that NLR, PLR, CRP and ESR can be used in clinical practice as a laboratory tools for predicting the diagnosis regardless of the etiology because they are inexpensive and widely available parameters.

Keywords - Cerebral venous sinus thrombosis CRP, ESR, Inflammatory Markers, NLR, PLR.

1. Introduction

Since Ripps discovered cerebral venous thrombosis in 1825 during his autopsy of a man who was suffering from severe headaches, delirium and epilepsy, and up to our days, our knowledge of thrombosis of the cerebral sinuses and veins has changed radically thanks to the great progress that has occurred in all fields; Especially in the field of neuroradiological diagnosis, because due to the presence of magnetic resonance and its widespread use with a high clinical orientation, the rate of recurrence of cerebral venous sinus thrombosis has become higher than before, in addition to the fact that clinical manifestations have become more diverse than what was previously known. [1-3]

Thrombosis in the cerebral sinuses and veins is much less common than arterial ischemic events, as cerebral venous sinus thrombosis affects about 5,000 people annually in the United States, with an estimated incidence of 0.22 to 1.57 per 100,000, constituting about 0.5% of all strokes. [4-6] .

Cerebral venous sinus thrombosis affects young people and young adults, so it must be kept in mind when reviewing a young patient with symptoms of a cerebral vascular accident

without a risk factor for arterial injury, as its incidence increases during pregnancy and childbirth, and in the case of oral contraceptive use, and this explains its prevalence in females more than males [7,8].

Cerebral venous thrombosis did not receive attention in clinical research, as did arterial accidents, as the lack of cases limited the possibility of epidemiological studies and clinical trials. [9]

The diversity of the clinical picture of cerebral venous thrombosis, the absence of specific clinical symptoms and signs, and the course of the disease in multiple clinical forms, acute, subacute, and chronic, make the diagnosis of cerebral venous thrombosis difficult, as the diagnosis requires an average of seven days since the onset of symptoms in the best international centers. [10, 11]

Hence, we hope that this study will contribute to shedding light on the case of cerebral venous thrombosis in our country in order to establish an appropriate diagnosis and treatment and reduce mortality and sequelae, as the progress made in the treatment of cerebral venous sinus thrombosis prompted to focus on the relationship between inflammatory symptoms and venous sinus thrombosis that It is still controversial, as



there is not much information available about its usefulness as biomarkers at the beginning of the disease and its role in helping the clinical approach to diagnosis, and based on the above, the study of this relationship was very important in heading towards cerebral venous sinus thrombosis and its early diagnosis and thus early treatment and improvement, in addition to reducing the resulting disability and its possible complications in patients.

2. Patients & Methods

A prospective cohort study was conducted between January 2021 and January 2023, in which the sample size consisted of 28 patients admitted to the neurological department at Tishreen University Hospital in Lattakia for having cerebral venous sinus thrombosis diagnosed by MRU &, whose age exceeded 18 years old and the same as the controls attending the neurological diseases clinic and not suffering from venous sinus thrombosis, with a statistical power of 95%. Intravenous samples were taken for cases and controls to conduct the following laboratory analyzes (Neutrophils – Lymphocytes – Platelets – CRP – ESR – Neutrophil/Lymphocytes - Platelets/Lymphocytes). Previous laboratory analyzes were compared between cases and controls, and then the data were analyzed statistically.

Patients with Tumors, cachexia, previous blood disorders, severe infections during the previous week and patients taking anticonvulsants known to affect blood counts, taking corticosteroids showed congenital transverse sinus thrombosis on resonance imaging (according to a negative Ddimer + radiograph) were excluded from the study.

3. Statistical Study

Study design: prospective cohort study.
 Qualitative variables were expressed in percentages and confidence intervals.
 Quantitative variables were expressed as the mean ± standard deviation.
 One Way Anova test to study the differences of means between several independent groups.
 Chi-square test to study the relationship between qualitative variables.
 The results were considered statistically significant with a p-value of < 5%.
 IBM SPSS statistics (version20) is adopted for calculating statistical coefficients and analyzing results.

4. Results

At the time of conducting this research, which extends from January 2021 to January 2023, 28 cases of thrombosis of the sinuses and cerebral veins diagnosed in Tishreen University Hospital were followed up, as we relied on the diagnosis on the brain resonator and the resonator of the venous sinuses. In only two cases, we resorted to arteriography to confirm the diagnosis and 28 of the controls

attended the neurological disease clinic and did not suffer from venous sinus thrombosis.

The arithmetic mean of the ages of patients in the control group was 41.00 years with a standard deviation of 16.44 years, while the arithmetic mean of the ages of patients in the cases group was 40.71 years with a standard deviation of 16.92 years. When comparing the ages of patients between the two groups of cases and controls, we did not find a statistically significant difference between the two groups.

The P-value was value of 0.980, as we found in our study a statistically significant difference between the two groups of cases and controls in terms of the values of the following laboratory analyzes (Neutrophils- Lymphocytes- Platelets - CRP - ESR - (Neutrophils/Lymphocytes - Platelets/Lymphocytes), as the P-value reached the following 0.034 0.000-0.003-0.000-0.003-0.000, respectively.

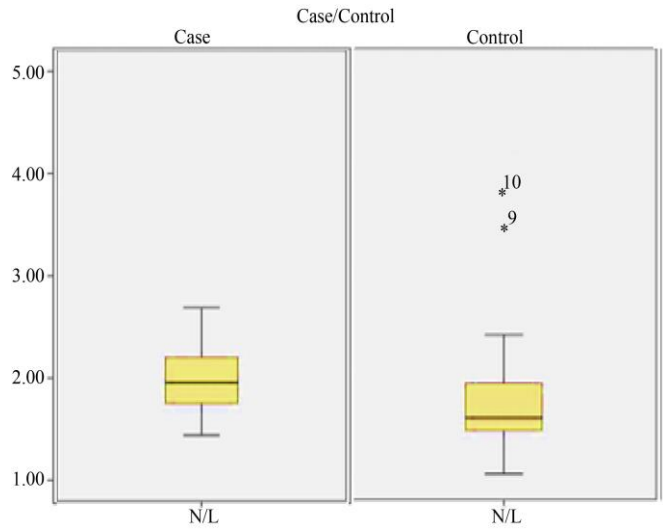


Fig. 1 NLR

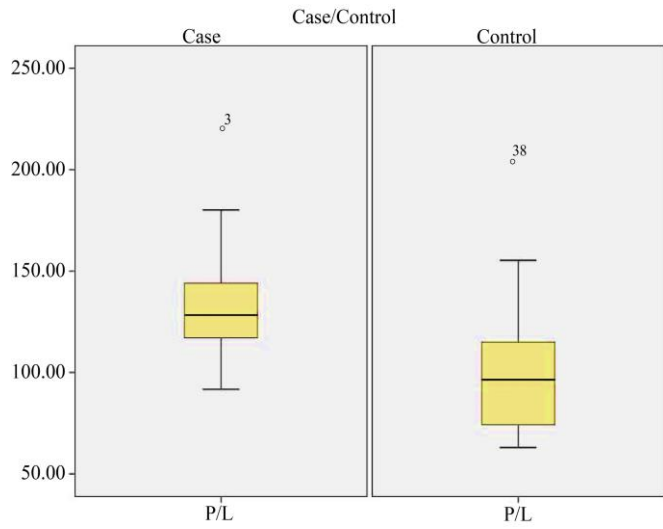


Fig. 2 PLR

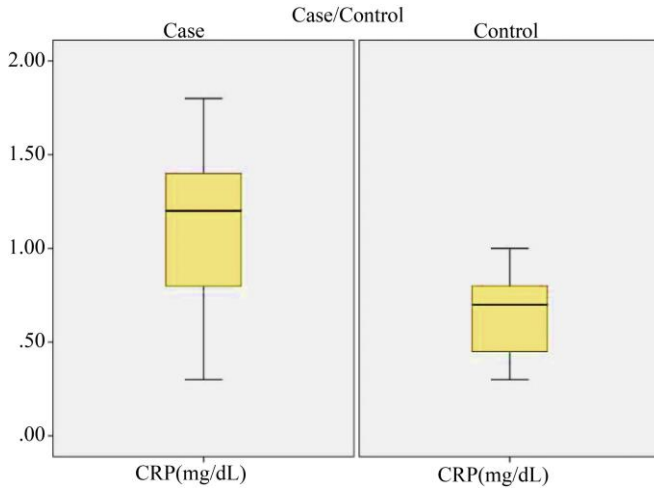


Fig. 3 CRP
Case/Control

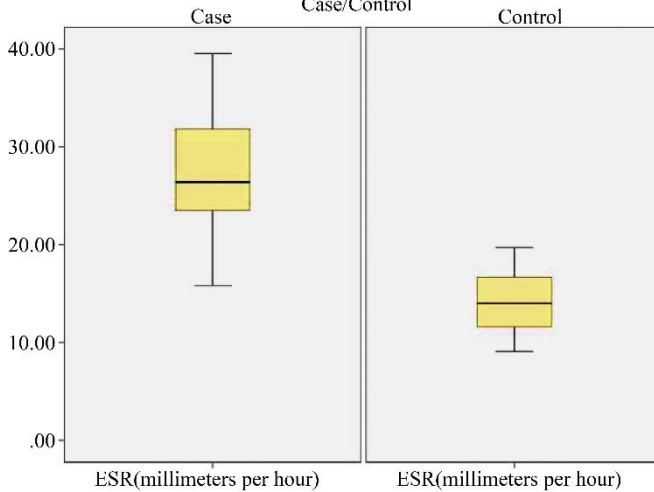


Fig. 4 ESR
Case/Control

4. Discussion

The results of our study showed that inflammation may be connected to the pathogenesis of CVT.

The most common symptom is headache in 90% of cases, as the headache was severe and continuous in almost all cases, not improving on analgesics, awakens the patient from sleep in many cases, and is accompanied by vomiting, while the most common sign was pilledema in 50% of cases.

We did not find a statistically significant difference between the patients of the two groups of cases and controls in terms of age, and this led to isolating any effect of age on the presence or absence of statistically significant differences in the variables that we studied between the two groups of cases and controls.

The NLR and PLR are simply calculated biomarkers from the lymphocyte, neutrophil and platelet counts in the venous blood samples. They have been investigated in several studies,

and elevated levels were shown to be important biomarkers in coronary artery diseases.

By comparing the studied variables between the two groups of cases and controls, we found a statistically significant difference between the two groups of cases and controls: as the neutrophil count increased, the lymphocyte count decreased, the neutrophil/lymphocyte ratio increased, the platelet count increased, the platelet/lymphocyte ratio increased, the erythrocyte sedimentation rate (ESR) increased, and C-reactive protein value increased when comparing cases with controls.

The foregoing confirms the relationship between inflammatory markers and sinus thrombosis, which is still controversial among the various studies conducted recently, and this is what suggests the use of NLR, PLR, CRP and ESR in clinical practice as a laboratory tool for the correct orientation of the diagnosis regardless of the causes because they are inexpensive and readily available parameters. The wide scope prompts more research to confirm the role of inflammatory markers definitively in the early diagnosis of cerebral venous sinus thrombosis, and thus its early treatment and improvement of its prognosis, in addition to reducing the disability resulting from it and its possible complications in patients.

Consistent with most of the previous studies, we found higher levels of NLR and PLR levels in CVT patients compared with the healthy controls.

By reviewing the medical literature, Xifang Zhang et al. concluded that NLR, PLR, SII, and MHR can assist in diagnosing CVT, confirming that inflammation plays an important role in CVT [4]. Our study also confirmed the role of the inflammatory event in the occurrence of cerebral venous sinus thrombosis (CVT).

Tekesin and Tunç suggested that NLR, PLR, CRP and ESR could be used in clinical practice to predict the incidence of CVT in suspected patients because they are inexpensive and widely available parameters; however, more large-scale studies are needed to confirm this relationship [5].

Liyan Wang suggested that inflammation may develop after CVT and gradually decrease during the development of thrombosis, as inflammation was significantly associated with thrombosis severity and poor short-term outcome. In clinical practice, it is a laboratory tool for the correct diagnosis orientation regardless of the causes because they are inexpensive and widely available parameters [6].

Study limitations: The sample size was limited to 28 patients admitted to the neurological department at Tishreen University Hospital in Lattakia because they had cerebral venous sinus thrombosis fixed by the cerebral sinus resonator

and the cerebral venous sinuses. Because the time of conducting the research coincided with the time of the outbreak of the new COVID-19 epidemic, and therefore we recommend conducting future studies that include larger samples of patients. Single center study: It was limited to patients attending Tishreen University Hospital in Lattakia, to the exclusion of other hospitals in the Syrian Arab Republic.

5. Conclusion

Our study confirmed the role of the inflammatory event in the occurrence of cerebral venous sinus thrombosis and found that NLR, PLR, CRP and ESR can be used in clinical

practice as a laboratory tools for the correct orientation of the diagnosis regardless of the etiology because they are inexpensive and widely available parameters.

Based on the results of our study, we recommend the following:

- Conducting laboratory analyzes of inflammatory markers (NLR, PLR, CRP and ESR) routinely in all patients suspected of having cerebral venous sinus thrombosis to guide the correct diagnosis regardless of the cause.
- Conducting further studies to confirm the results of our study while avoiding the limitations that faced our study.

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Table 1. The percentage of infection of each sinus separately in the patients of the case group

Affected sinus	Number of patients	The percentage of patients in relation to the group of cases
Longitudinal sagittal sinus	9	32.14%
Intercepted sinus	13	46.42%
Sigmoid sinus	2	7.14%
cavernous sinus	1	3.57%
Straight sinus	3	10.71%

Table 2. Symptoms and clinical signs in case group patients

Symptoms and clinical signs	Number of patients	The percentage of patients in relation to the group of cases
Headache	25	89.28%
Papilledema	14	50.00%
Diplopia	5	27.77%
Hemiparesis	6	21.42%
Seizures	9	32.14%
Consciousness disorders	8	28.57%
Aphasia	2	7.14%
Ataxia with cerebellar abnormalities	1	3.57%
Cranial nerve paralysis	1	3.57%

Table 3. Risk factors and causes of cerebral venous thrombosis in case group patients

Risk Factors	Number of patients	The percentage of patients in relation to the group of cases
Systemic vasculitis	1	3.57%
Anemia	1	3.57%
Clotting factor disorder	3	10.71%
Take oral contraceptives	4	14.28%
Generalized systemic lupus erythematosus	2	7.14%
Septic causes	1	3.57%
Polycythemia	1	3.57%
Behçet's disease	1	3.57%
Nephrotic Syndrome	1	3.57%
liver cirrhosis	1	3.57%
Antiphospholipid syndrome	1	3.57%
Tumors	2	7.14%
Idiopathic	9	32.14%

Table 4. Comparing the group of controls and cases

	The arithmetic mean and standard deviation in the control group	The arithmetic mean and standard deviation in a cases group	P-VALUE
Neutrophil count	4.28±0.48	0.77±4.69	0.034
Lymphocyte count	2.80±0.70	2.20±0.34	0.000
Neutrophil/lymphocyte ratio NLR	1.78±0.66	1.98±0.32	0.003
Platelet count	260.84±20.00	289.59±42.52	0.003
Platelet/lymphocyte ratio PLR	100.34±31.90	134.50±27.27	0.000
ESR	13.86±2.92	27.38±5.98	0.000
CRP	0.63±0.21	1.13±0.39	0.000