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THE RELATION BETWEEN THE URIC ACID LEVELS AND THE RECANALIZATION TIMES IN PATIENTS WITH CEREBRAL VENOUS THROMBOSIS

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Abstract: Recanalization times in cerebral venous thrombosis (CVT) patients are generally around six months, but do vary from patient to patient. The reasons for the variation in the recanalization times between the CVT patients are still a matter of debate. Thus, in this study, the relation between the uric acid (UA) level, which has been shown to have antioxidant properties in ischemic stroke, and the recanalization time in CVT patients was investigated. In this context, the CVT patients, who were followed up between January 2015 and May 2020, were analyzed retrospectively. Of the 78 patients, who met the eligibility criteria to be included in the research, 76.9 % were female and 23.1 % were male. It was determined that headache was the most common (73.1 %) symptom, and that the gynecological reasons were the most common (38.5 %) etiological reasons. A weakly significant negative correlation was found between the UA levels and the recanalization times in the study group (P = 0.003, r= -0.327). There was a weakly negative correlation between the UA levels and the recanalization times in female patients (P = 0.046, r= -0.259). The UA levels of male patients were also found to be negatively correlated with the recanalization times, albeit not statistically significantly. The finding that the recanalization times were shortened as UA levels were increased in female CVT patients was interpreted as that there is a gender-specific relationship between the UA levels and the recanalization times in CVT patients.

Keywords: Cerebral venous thrombosis, Uric acid, Recanalization, Gender, Prognosis

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1. Introduction

Cerebral venous thrombosis (CVT) is one of the rare causes of stroke, accounting for 0.5% to 1% of all strokes (Saposnik et al., 2011). CVT has been known to be typically more difficult to diagnose as compared to the diagnoses of ischemic and hemorrhagic strokes, yet its diagnosis has become relatively easier thanks to the widespread use of magnetic resonance imaging (MRI) and increased clinical awareness. Its prevalence in women is three times more than in men (Ferro et al., 2004; Coutinho et al., 2009). The reason for this disparity has been attributed to the increased risk of CVT with pregnancy, puerperal and oral contraceptive use (Stam, 2005). CVT is most commonly seen in individuals of younger ages, as opposed to arterial stroke, which is most commonly seen in individuals over the age of 65. Only 8% of the patients with CVT were reported to be over 65 years of age (Ferro et al., 2005). Low molecular weight heparin (LMWH) treatment has been reported as an effective and safe method for the treatment of CVT. Venous infarction, hemorrhagic venous infarction or isolated subarachnoid hemorrhage do not act as a contraindication in respect of the use of anticoagulant therapy in patients with CVT. The recanalization times in CVT patients commonly range between 3 to 6 months, which sometimes extend to 12 months, but very rarely extend to longer than 12 months. High recanalization rates have been reported in many studies previously conducted (Baumgartner et al., 2003; Stolz et al., 2004; Sidhom et al., 2014; Herweh et al., 2016;).

Uric acid (UA) is an important blood antioxidant in humans. The plasma concentration of UA is ten times higher than other antioxidants. UA is responsible for two-thirds of all free radical scavenging capacity (Becker, 1993). In an experimental study, it was shown that UA treatment significantly suppressed oxidative stress, alleviated neuronal damage and reduced infarct volume in rats with transient focal cerebral ischemia/reperfusion (Ya et al., 2018). It was also demonstrated in several studies that UA has a neuroprotective effect when administered exogenously (Onetti et al., 2015; Justicia et al., 2017). Despite the controversy over the factors associated with CVT, there is only a handful of studies available in the literature that addressed the relation between CVT and the antioxidant system. In one of these few studies, it was shown that there was a decrease in

the antioxidant system level in the acute period of CVT (Tiwari et al., 2016).

In view of the foregoing, it is aimed in this study to investigate the relation between the UA levels and the recanalization times in CVT patients.

2. Material and Method

The files of 101 patients over the age of 18 who were diagnosed with CVT by means of magnetic resonance imaging (MRI) and magnetic resonance venography (MRV) between January 2015 and May 2020, were reviewed retrospectively. The patients that were followed up for at least three months and whose follow-up MRVs were taken every three months for the first year were included in the study. Accordingly, 12 CVT patients, whose follow-up MRI and MRV were not available, and 11 patients, whose imaging data did not indicate recanalization, were excluded from the study. Consequentially, the study group consisted of 78 CVT patients. Demographic characteristics, neurological and radiological findings, etiological risk factors and treatment details of these patients were recorded. Etiological risk factors that may be associated with CVT; namely infections (systemic or focal infections; otitis media, mastoiditis, sinusitis, etc.), gynecological causes (pregnancy, puerperium, use of oral contraceptives), malignancies, hematological causes (thrombocytosis, anemia, etc.), rheumatological or connective tissue diseases, causes of thrombophilia (antithrombin III, protein C-S deficiency, hyperhomocysteinemia, factor V Leiden mutation, prothrombin II mutation) were recorded. The patency of the veins in the patients included in the study was categorized as either partial or complete recanalization. Normal blood flow in previously occluded cerebral veins was defined as complete recanalization, whereas presence of residual thrombus and of blood flow disruption was defined as partial recanalization. The follow-up MRVs, which were taken every 3 months for a year, of the patients who were followed up with partial recanalization were examined in terms of complete recanalization during the said term, and the recanalization times were recorded as the time to the observation of the first partial recanalization for the patients who did not develop complete recanalization. MRIs were not repeated in patients who developed complete recanalization in the first 3 months. Neurological outcomes of the patients were categorized using the Modified Rankin Scale (mRS) as either good (mRS: 0-1) or poor (mRS: 2-6) based on the clinical status of the patients at the time of first admission and six months later. The serum UA levels measured in the blood samples taken from the patients within the first 24 hours after admission were recorded. Patients with hepatic and renal dysfunction and those with a history of heart attack were not included in the study.

The research data were analyzed using the SPSS 20 (IBM Statistical Package for Social Sciences version 20) software package. Kolmogorov-Smirnov test was used to check whether the research data conformed to the normal distribution or not. Categorical data were expressed in terms of n (%) values, whereas the numerical data were expressed in terms of median (minimum-maximum) values as they did not conform to normal distribution. Mann-Whitney U test and Kruskal Wallis tests were used in the analysis of numerical data that did not conform to normal distribution. Chi-square test was used to analyze the categorical data. Yates correction and Fisher's exact tests were applied taking the expected values in the chi-square test into consideration. Spearman's correlation analysis was used to assess the relationship between any two non-normally distributed numerical data. Probability (p) values of <0.05 were considered to indicate statistical significance.

3. Results

The median age of the patients was 33 years (min. 18 and max. 76 years). Of the 78 CVT patients included in the study, 60 (76.9%) were female and 18 (23.1%) were male. There was a significant difference between genders in terms of age distribution ($P < 0.001$). It was determined that headache was the most common (73.1%) symptom, and that the gynecological reasons were the most common (38.5%) etiological reasons. Multiple venous involvement was present in 65.4% (n=51) of the patients and the most frequently involved vein/sinus was transverse sinus (89.7%). The most common (21.8%) accompanying MRI finding was hemorrhagic infarction, and the most frequently (20.5%) affected area was the temporal lobe. It was determined that LMWH treatment was used in 83.3% (n=65) of the patients and that warfarin sodium treatment was used in 16.7% (n=13) of the patients. The incidence of epileptic seizures was 20.5% (n=16). Parenchymal lesions were observed in 14.1% (n=11) of the patients with epileptic seizures. No parenchymal lesions were observed in 6.4% (n=5) of the patients with epileptic seizures. There was a statistically significant correlation between status of having parenchymal lesion and epileptic seizure ($P = 0.025$). The most commonly affected vein/sinus in patients with epileptic seizures was transverse sinus. It was determined that superior sagittal sinus and transverse sinus were affected in 6 patients, that transverse sinus was affected in 6 patients, that superior sagittal sinus was affected in 3 patients, and that deep veins were affected in 1 patient. Clinical and demographic data and the radiological findings pertaining to the patients included in the study are shown in Table 1 and Table 2, respectively. Of the 7 CVT patients with vasculitis due to etiological reasons, 4 patients had Behçet's Disease, 1 patient had systemic lupus erythematosus, 1 patient had systemic lupus erythematosus and Sjögren's syndrome, and another 1 patient had Wegener's granulomatosis. The most common causes of infection were focal infections (65%) such as mastoiditis and otitis.

Table 1. Clinical and demographic data of patients

	n
Age (year), median (min-max)	33 (18-76)
Sex (%)	
Female	60 (76.9)
Male	18 (23.1)
Etiology (%)	
Gynecological reasons (Pregnancy, postpartum, OCS)	30 (38.5)
Thrombophilia	
Vasculitis	9 (11.5)
Infection	7 (9)
Anemia	19 (24.4)
Multiple causes	3 (3.8)
Idiopathic	5 (6.4)
Uric acid (mg/dL), Median (min-max)	4 (1-11.8)
Recanalization time (months), Median (min- max)	6 (3-24)
Recanalization (%)	
Partial	17 (21.8)
Full	61 (78.2)
High homocysteine (%)	13 (16.7)
Drug used (%)	
LMWH	65 (83.3)
Warfarin sodium	13 (16.7)
Symptoms (%)	
Headache	57 (73.1)
Unconsciousness	3 (3.8)
Aphasia	5 (6.4)
Motor deficit	13 (16.7)
Epileptic seizure (%)	16 (20.5)
mRS hospitalization (%)	
Good result (0-1)	36 (46.2)
Poor result (2-6)	42 (53.8)
mRS after discharge 6.month (%)	
Good result (0-1)	75 (96.2)
Poor result (2-6)	3 (3.8)

Table 2. Radiological findings of the patients

	n (%)
MRI finding	
No parenchymal lesion	42 (53.8)
Infarct	15 (19.2)
Hemorrhage	4 (5.1)
Hemorrhagic infarct	17 (21.8)
MRI lesion localization	
Temporal	16 (20.5)
Frontal	7 (9)
Parietal	11 (14.1)
Occipital	2 (2.6)
Involved vein/sinus	
Superior sagittal sinus	32 (41)
Left transverse	39 (50)
Left sigmoid sinus	26 (33.3)
Right transverse	31 (39.7)
Right sigmoid sinus	19 (24.4)
Jugular vein	20 (25.6)
Deep veins	6 (7.7)
Multiple venous involvement	51 (65.4)

Two of the 5 patients with multiple risk factors in etiology had a gynecological cause and Behçet's disease, 2 had a gynecological cause and factor V Leiden mutation, and 1 had a malignancy (breast cancer) and anemia.

UA levels were statistically significantly higher in males than in females (P = 0.001). There was no significant relationship between age and UA level both in male and female patient groups (P = 0.515, r=0.086; and P = 0.864, r=-0.044, respectively). Median UA level was 4 (min.1 and max. 11.8) mg/dL and the range taken as reference was 2.6 mg/dL to 6 mg/dL. It was determined that 11.5% of the patients had hyperuricemia. The median recanalization time was 6 months (min. 3 months and max. 24 months). The patient with the longest

recanalization time (24 months) was the patient with Wegener's granulomatosis. Complete recanalization was observed in 78.2% (n=61) of the patients, whereas partial recanalization was observed in 21.8% (n=17) of the patients. It was determined that 20.5% (n=16), 61.5% (n=48), 12.8% (n=10), 3.8% (n=3) and 1.3% (n=1) of the patients had either complete or partial recanalization at 3, 6, 9, 12 and 24 months, respectively.

There was no significant difference in terms of recanalization times between the patient groups categorized according to gender and etiology (P = 0.146 and P = 0.301, respectively). There was no significant correlation between the recanalization times and the etiology within the female patient group (P = 0.366). Additionally, no significant difference was found between the number of involved veins and the recanalization times (P = 0.795) and between the extent of recanalization and the clinical outcome (P = 0.473). A weakly significant negative correlation was found between the UA levels and the recanalization times in the study group (P = 0.003, r=-0.327) (Figure 1A). There was a weakly negative correlation between the UA levels and the recanalization times in female patients (P = 0.046, r=-0.259) (Figure 1B). The UA levels of male patients were also found to be negatively correlated with the recanalization times, albeit not statistically significantly (P = 0.278, r=-0.271) (Figure 1C). There was no significant difference between the UA levels and the recanalization times of patients with or without parenchymal lesions (P = 0.932, P = 0.804). A significant correlation was observed between the mRS score and the status of having parenchymal lesion at admission (P < 0.001), which turned into a non-significant correlation at 6-months' time (P = 0.094). There was no significant difference between the UA levels of the patients, in whom either partial or complete recanalization was observed (P = 0.799). Analysis of the mRS scores of the CVT patients at admission revealed that 46.2% (n=36) of the patients had good and 53.8% (n=42) of the patients had poor neurological outcomes, whereas the analysis of the mRS scores of the CVT patients at 6-months' time revealed that 96.2% (n=75) of the patients had good and 3.8% (n=3) of the patients had poor neurological outcomes. There was no mortality in the patient group included in this study.

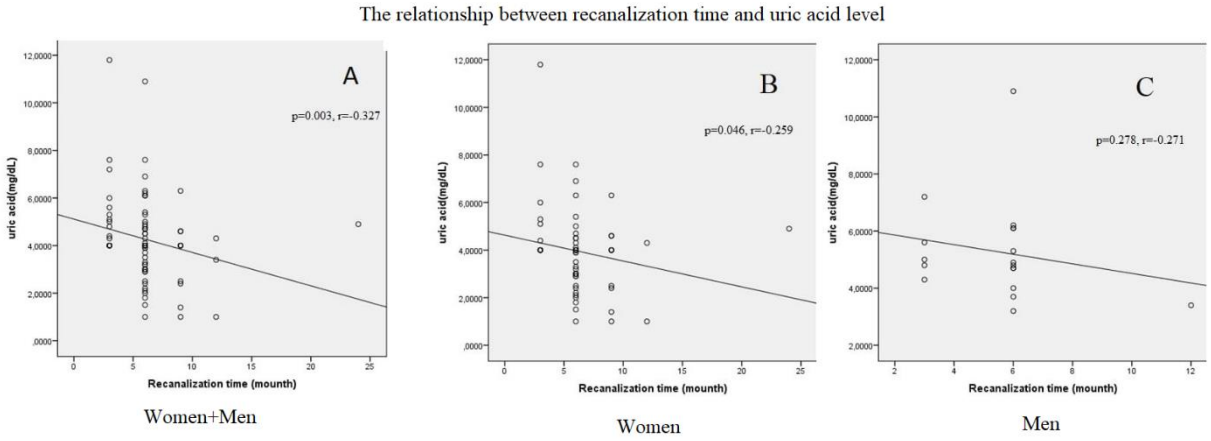

Figure 1. Correlation plot of serum uric acid level and recanalization time. The x-axis represents the recanalization time in months, and the y-axis represents the serum uric acid level in mg/dL. Each dot on the graph represents a patient. There was a significantly negative correlation between the recanalization times and the serum uric acid levels in the study group (Figure 1A). There was a significant negative correlation between the recanalization times and the uric acid levels in the female patient group (Figure 1B). There was also a negative however not a significant correlation between the recanalization times and the uric acid levels in the male patient group (Figure 1C).

4. Discussion

Similar to the demographic and clinical characteristics of the CVT patient groups investigated in the previously conducted studies available in the literature, majority of the CVT patients included in this study were female (76.9%) and gynecological reasons were the most commonly observed etiological reason (38.5%). Complete recanalization was observed in 78.2% (n=61) of the patients, whereas partial recanalization was observed in 21.8% (n=17) of the patients.

There are studies in which a better functional outcome was reported in patients with complete recanalization (Arauz et al., 2016), yet there are also other studies in which no difference was found between the scope of recanalization and the clinical outcome, similar to the finding of this study (José et al., 2004; Herweh et al., 2016). In paralel with the results of the previously conducted studies available in the literature (Putaala et al., 2010; Hiltunen et al., 2016), 96.2% of the patients included in this study were found to have clinically good outcomes with a good prognosis of CVT, at 6-months' time after being discharged.

Gazioğlu et al. (2017) reported that recanalization rates were lower in patients with thrombosis in more than one sinus. In comparison, in this study, no significant difference was found between the recanalization times in

terms of number of involved veins. A significant correlation was observed between the mRS score and the status of having parenchymal lesion at admission (P < 0.001), which turned into a non-significant correlation at 6-months' time (P = 0.094). This finding is supported by the finding of Sing et al., who reported that the presence of parenchymal lesion was not a factor in the clinical outcome (Singh et al., 2020). Etiological causes are considered among the important factors affecting the recanalization time. Accordingly, anticoagulation treatment is recommended for the treatment of CVT for a duration of 3 to 6 months, 6 to 12 months or longer depending on whether CVT is caused by a temporary risk factor, an idiopathic cause or a history of thrombophilia or recurrent thrombosis, respectively (Saposnik et al., 2011). However, no significant difference was found in this study in terms of recanalization times between the patient groups categorized according to gender and etiology (P = 0.146 and P = 0.301, respectively). Although it does not have an explicit effect on the recanalization time, it is important to find the etiologic cause in order to determine the conditions that require long-term treatment such as thrombophilia and perform the necessary treatments. The fact that recanalization takes place on or around 6 months in the vast majority of the CVT patients, that this situation persists for long periods in patients with partial recanalization, and that there is no correlation between the extent of recanalization and prognosis suggests that repeating MRIs every 3 months is unnecessary in most of the patients. On the other hand, considering that the rate of patients, in whom recanalization was observed in the first three months, was not very low (20.5% in this study), MRI can be repeated every three months for the first six-month period in these patients in order to prevent the unnecessary use of medication.

There are studies available in the literature in which UA was shown to increase inflammatory cytokines such as C-reactive protein (CRP), interleukin 6 (IL-6) and tumor necrosis factor-alpha (TNF-α) suggesting that it may be associated with vascular diseases such as coronary artery disease, ischemic stroke and hypertension (Kanellis and Kang, 2005). To give an example, Talebi et al. (2020) found that patients with high serum UA levels had an increased risk of ischemic stroke, whereas Saadat et al. (2018) did not find any significant relationship between serum UA levels and stroke risk factors such as hypertension, ischemic heart disease and hyperlipidemia. The rate of hyperuricemia reported in the literature in patients with ischemic stroke varies between 13% and 30% (Iranmanesh et al., 2012; Serdarevic et al., 2020). There are studies, in which UA levels were found to have increased in ischemic stroke patients compared to healthy control subjects (Lamani and Vishwanath, 2013; Serdarevic et al., 2020), yet there are also studies in which no significant difference was found between the patient and control groups in terms of UA levels (Varga et al., 2011). The findings on the UA levels in ischemic stroke patients as to whether it is a vascular risk factor remain to be controversial. In an experimental study, it was demonstrated that UA significantly suppressed oxidative stress, reduced neuronal damage, and decreased infarct volume in rats with ischemia/reperfusion, due to its antioxidant effect (Ya et al., 2018). In comparison, in this study, no significant difference was found between the male and female patient groups in terms of recanalization times. Yet, there was a weakly significant negative correlation between the UA levels and the recanalization times in the study group (P = 0.003, r=-0.327). In terms of gender, there was a weakly negative correlation between the UA levels and the recanalization times in female patients (P = 0.046, r=-0.259), and a negative correlation between the UA levels and the recanalization times also in male patients, which was however not statistically significant (P = 0.278, r=-0.271). The fact that UA levels were found to have increased as the recanalization times have decreased in both female and male patient groups suggests that the UA level has a positive effect on the prognosis in CVT patients. Despite the controversy over the factors associated with CVT, there is only a handful of studies available in the literature that addressed the relation between CVT and the antioxidant system, and UA levels in particular. The results of this study, one of the said few studies, support that high serum UA levels in CVT patients are associated with prognosis based on gender and are an indicator of good prognosis in female gender. These results are in line with the results of another study, one of the few such studies available in the literature (Song et al., 2018).

There were some limitations to this study. First, it was carried out as a retrospective study; secondly, number of male patients included in the study was relatively low; and thirdly, the serum UA levels of patients were not re-measured during the follow-up period.

In conclusion, the shortening of the recanalization times as the UA levels increase and the finding of a weak correlation between the said two parameters were interpreted as that high UA level has a positive effect on prognosis in CVT patients. In addition, the fact that a significant relationship was found between the UA levels and recanalization times in female patient group was interpreted as that the UA level is more effective on the prognosis of female CVT patients than the male CVT patients. In other words, the results of this study indicate that there is a gender-specific relationship between the UA levels and the recanalization times. The decrease in the antioxidant system level in the acute period in CVT and the shorter recanalization time in patients with high UA levels suggest that UA, which has antioxidant properties, can be used as an effective therapeutic agent. However, further studies with larger patient groups are needed to support the results of this study.

Author Contributions

All task made by single author and the author reviewed and approved the manuscript.

Conflict of Interest

The author declared that there is no conflict of interest.

Ethical Approval/Informed Consent

The research was conducted in line with the declaration of Helsinki and good clinical practice. The study protocol was approved by the Ataturk University, Faculty of Medicine local ethics committee (02/8/25.03.2021). Written informed consent was obtained from all individual participants and their parents before participating in the study.

References

Arauz A, Vargas-González JC, Arguelles-Morales N, Barboza MA, Calleja J, Martínez-Jurado E, Merino JG. 2016. Time to recanalisation in patients with cerebral venous thrombosis under anticoagulation therapy. J Neurol, Neurosurg, Psychiat, 87(3): 247-251.

Baumgartner RW, Studer A, Arnold M, Georgiadis D. 2003. Recanalisation of cerebral venous thrombosis. J Neurol Neurosurg Psychiat, 74(4): 459-461.

Becker BF. 1993. Towards the physiological function of uric acid. Free Radic Biol Med, 14(6): 615-631.

Coutinho JM, Ferro JM, Canhao P, Barinagarrementeria F, Cantu C, Bousser MG, Stam J. 2009. Cerebral venous and sinus thrombosis in women. Stroke, 40(7): 2356-2361.

Ferro JM, Canhao P, Bousser MG, Stam J, Barinagarrementeria F, Investigators I. 2005. Cerebral vein and dural sinus thrombosis in elderly patients. Stroke, 36(9): 1927-1932.

Ferro JM, Canhão P, Stam J, Bousser MG, Barinagarrementeria F. 2004. Prognosis of cerebral vein and dural sinus thrombosis: results of the International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT). Stroke, 35(3): 664-670.

Ferro JM, Canhao P, Stam J, Bousser MG, Barinagarrementeria F, Investigators, I. 2004. Prognosis of cerebral vein and dural sinus thrombosis: results of the International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT). Stroke, 35(3): 664-670. doi:10.1161/01.STR.0000117571.76197.26

Gazioglu S, Eyuboglu I, Yildirim A, Aydin CO, Alioglu Z. 2017. Cerebral venous sinus Thrombosis: Clinical Features, Long-Term outcome and recanalization. J Clin Neurosci, 45, 248-251. doi:10.1016/j.jocn.2017.07.028

Herweh C, Griebe M, Geisbusch C, Szabo K, Neumaier-Probst E, Hennerici MG, Nagel S. 2016. Frequency and temporal profile of recanalization after cerebral vein and sinus thrombosis. Eur J Neurol, 23(4): 681-687. doi:10.1111/ene.12901

Herweh C, Griebe M, Geisbüsch C, Szabo K, Neumaier-Probst E, Hennerici M, Nagel, S. 2016. Frequency and temporal profile of recanalization after cerebral vein and sinus thrombosis. European J Neurol, 23(4): 681-687.

Hiltunen S, Putaala J, Haapaniemi E, Tatlisumak T. 2016. Long-term outcome after cerebral venous thrombosis: analysis of functional and vocational outcome, residual symptoms, and adverse events in 161 patients. J Neurol, 263(3): 477-484.

Iranmanesh F, Sheykholeslami NZ, Gadari F, Ahmady J. 2012. Acute ischemic non-embolic stroke and serum level of uric acid. Iran J Neurol, 11(1): 1-5.

Justicia C, Salas-Perdomo A, Perez-de-Puig I, Deddens LH, van Tilborg GAF, Castellvi C, Planas AM. 2017. Uric acid is protective after cerebral ischemia/reperfusion in hyperglycemic mice. Transl Stroke Res, 8(3): 294-305. doi:10.1007/s12975-016-0515-1

Kanellis J, Kang DH. 2005. Uric acid as a mediator of endothelial dysfunction, inflammation, and vascular disease. Semin Nephrol, 25(1): 39-42. doi: 10.1016/j.semnephrol.2004.09.007.

Lamani, S, Vishwanath, H. 2013. The role of serum uric acid in acute ischemic stroke. RJPBCS, 4(4): 350-357.

Onetti Y, Dantas AP, Perez B, Cugota R, Chamorro A, Planas AM, Jimenez-Altayo F. 2015. Middle cerebral artery remodeling following transient brain ischemia is linked to early postischemic hyperemia: a target of uric acid treatment. Am J Physiol Heart Circ Physiol, 308(8): 862-874. doi:10.1152/ajpheart.00001.2015

Putaala J, Hiltunen S, Salonen O, Kaste M, Tatlisumak T. 2010. Recanalization and its correlation to outcome after cerebral venous thrombosis. J Neurol Sci, 292(1-2): 11-15. doi:10.1016/j.jns.2010.02.017

Saadat P, Ahmadi Ahangar A, Babaei M, Kalantar M, Bayani MA, Barzegar H, Frajzadeh F. 2018. Relationship of serum uric acid level with demographic features, risk factors, severity, prognosis, serum levels of vitamin d, calcium, and magnesium in stroke. Stroke Res Treat, 2018, 6580178. doi:10.1155/2018/6580178

Saposnik G, Barinagarrementeria F, Brown RD, Jr Bushnell CD, Cucchiara B, Cushman M, deVeber G, Ferro JM, Tsai FY. 2011. Diagnosis and management of cerebral venous thrombosis: a statement for healthcare professionals from the American Heart Association/American Stroke Association. Stroke, 42(4): 1158-1192. doi:10.1161/STR.0b013e31820a8364

Serdarevic N, Stanciu AE, Begic L, Uncanin S. 2020. Serum uric acid concentration in patients with cerebrovascular disease (ischemic stroke and vascular dementia). Med Arch, 742: 95-99. doi:10.5455/medarh.2020.74.95-99

Sidhom Y, Mansour M, Messelmani M, Derbali H, Fekih-Mrissa N, Zaouali J, Mrissa R. 2014. Cerebral venous thrombosis: clinical features, risk factors, and long-term outcome in a Tunisian cohort. J Stroke Cerebrovasc Dis, 23(6): 1291-1295. doi:10.1016/j.jstrokecerebrovasdis.2013.10.025

Singh VK, Jain N, Kalita J, Misra UK, Kumar S. 2020. Significance of recanalization of sinuses and resolution of parenchymal lesion in cerebral venous sinus thrombosis. J Clin Neurosci, 77, 175-180. doi:10.1016/j.jocn.2020.04.112

Song B, Liu K, Gao Y, Zhao L, Fang H, Wang Y, Xu Y. 2018. Gender-specific relationship between uric acid levels and prognosis after cerebral venous thrombosis. Curr Neurovasc Res, 15(4): 292-297. doi:10.2174/1567202616666181127163321

Stam J. 2005. Thrombosis of the cerebral veins and sinuses. N Engl J Med, 352(17): 1791-1798. doi:10.1056/NEJMra042354

Stolz E, Trittmacher S, Rahimi A, Gerriets T, Rottger C, Siekmann R, Kaps M. 2004. Influence of recanalization on outcome in dural sinus thrombosis: a prospective study. Stroke, 352: 544-547. doi:10.1161/01.STR.0000112972.09096.65

Talebi A, Amirabadizadeh A, Nakhaee S, Ahmadi Z, Mousavi-Mirzaei SM. 2020. Cerebrovascular disease: how serum phosphorus, vitamin D, and uric acid levels contribute to the ischemic stroke. BMC Neurol, 20(1): 116. doi:10.1186/s12883-020-01686-4

Tiwari HS, Misra UK, Kalita J, Mishra A, Shukla S. 2016. Oxidative stress and glutamate excitotoxicity contribute to apoptosis in cerebral venous sinus thrombosis. Neurochem

Int, 100, 91-96. doi:10.1016/j.neuint.2016.09.003

Varga I, Ionescu I, Pascu I. 2011. Assessment of oxidative stress in patients with acute ischemic stroke. Bulletin of the Transilvania University of Brasov. Med Sci, 6(42): 43.

Ya BL, Liu Q, Li HF, Cheng HJ, Yu T, Chen L, Bai B. 2018. Uric acid protects against focal cerebral ischemia/reperfusion-induced oxidative stress via activating Nrf2 and regulating neurotrophic factor expression. Oxid Med Cell Longev, 2018, 6069150. doi:10.1155/2018/6069150.