

## The Role of Mineral Serum Level in Risk Factor of Stroke. Babol, North of Iran

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### Abstract

**Background:** The relationship between stroke and mineral status is inconsistent. With regard to doubt in the role of mineral, this study was conducted.

**Material and Method:** This cross-sectional study on 216 stroke patients who referred to the Ayatollah Rouhani Hospital of Babol over one-year period were conducted. Serum level of calcium (Ca), magnesium (Mg), Vitamin D (VD) were measured. Chi-square or Fisher exact test in spss 23 used.

**Result:** Difference of hemorrhagic subtype was statistically significant in hypertensive patients (20(87%) ICH vs. 1(12.5%) SAH,  $p = 0.001$ ). In thrombotic patients, 98 cases (89%) low VD vs. 12 cases (10.9%) normal VD, ( $p = 0.001$ ) were seen. Also, low VD was more seen significantly in DM patients 72(90%) in compare to non-DM patients 96(72.7%), ( $p = 0.003$ ).

Of 120 cases (56.3%) who had HTN, 103 cases (85.8%) low VD vs. 17 cases (14.2%) normal VD, ( $p = 0.01$ ), 68 cases (57.1%) hypo calcemic vs. 45 cases (37.8%) normal Ca serum level, ( $p < 0.0001$ ) and 57 cases (49.1%) hypomagnesemia vs. 59 cases (50.9%) normal magnesium ( $p = 0.04$ ) were seen.

Difference in sex was statistically significant with hypomagnesemia (49 cases (53.8%) male vs. 38 cases (33.9%) female,  $p = 0.007$ ). Hypomagnesemia were seen in 87 cases (40.8%) that 49 cases of this were hypo-calcemic (56.3%), ( $p = 0.03$ ). Differences in magnesium with VD was statistically significant (170 cases (79.4%) low VD vs. 44 cases (20.6%) normal,  $p = 0.007$ ).

**Conclusion:** Low VD in thrombotic and diabetic patients, low Ca and VD in hypertensive patients and hypocalcemia were more seen in hypermagnesemic patients. Preventive policies such as screening of mineral serum level are suggested.

### Keywords

Stroke, Vitamin D, Calcium, Magnesium

### Abbreviation

**ICH:** Intracerebral Hemorrhage; **SAH:** Subarachnoid Hemorrhage; **HTN:** Hypertension; **IHD:** Ischemic Heart Disease; **DM:** Diabetes Mellitus; **HLP:** Hyperlipidemia; **Mg:** Magnesium; **VD:** Vitamin D; **SBP:** Systolic Blood Pressure; **DBP:** Diastolic Blood Pressure; **FBS:** Fasting Blood Sugar

### Background

Stroke in addition to being the second most important causes of death and

major cause of motor disability [1]. Stroke, the sudden loss of neurons in the brain because of decreasing cerebral blood flow due to blockage or rupture of one of the cerebral vessels, is also a leading cause of cognitive impairment, depressive disorders and seizures in elderly [2]. In the low and middle income countries, 70% of all strokes and 87% of stroke-related deaths occur [3]. Data on the epidemiology of stroke, patterns and risk factors in Iran are brief and scattered [4]. The incidence of stroke in Iran is 43 per 100,000 populations [5]. As the classic risk factors of stroke have been identified and preventive measures have been taken to eliminate them, the incidence of stroke has decreased in recent years. Investigating other possible risk factors of stroke is highly important and need to research in this field [6].

Based on available data some minerals are associated with the stroke, as a diet rich in Ca and Mg may reduce the risk of stroke [7]. Because minerals are essential elements for the human body, epidemiologic studies have investigated the relationship between ischemic stroke and dietary mineral consumption, but the results are inconsistent [8]. As a result of the homeostasis process, the levels of all of these minerals are constantly maintained appropriately to prevent an excess (toxicity) or shortage (deficiency) of the nutrients. The increasing or lowering levels of essential minerals can be associated with variety of illnesses [8, 9].

Serum Ca level as an essential bulk metal in a wide range of biological processes for cellular signaling, is tightly regulated through a series of ion channels and pumps [10]. Mg is an intracellular action essential for many enzymatic processes and cellular functions. It acts as an endogenous Ca channel antagonist at neuronal synapses. Mg has an inhibitory effect at neuronal synapses [11, 12].

In addition, the VD may play a protective role during cerebral ischemia, although it associates with a wide range of illness states and physiological derangements [13] that can lead to worsen outcomes after stroke [10, 14, 15].

This association was independent of several important confounders and only partly explained by conventional risk factors and cardiovascular disease as potential causal intermediates [15]. Although we know that minerals are essential elements for human body and some researchers have investigated the association between stroke and minerals, the results are inconsistent. With regard to doubt in role of mineral in subtype and risk factors of stroke and limited study about this issue, this study was conducted in Babol, North of Iran.

## Material and Methods

This descriptive-analytic study on patients referred to the Ayatollah Rouhani Hospital of Babol (the second most populated city in the north of Iran) with a diagnosis of stroke in period of one year was conducted. This Hospital is major center for stroke patients in the Mazandaran province, north of Iran and referral center for patients from hospitals and medical centers in the region with a population of about 550,000 inhabitants that had stroke care unit (SCU) regarding the sample size formula and its incidence in the region will be

approximately 120 cases [16].

### Study population

Stroke defined as rapidly developing focal symptoms and signs of cerebral function that correlate with the area of the brain supplied by the affected blood vessel. Diagnosis of stroke and its types was based on common standards in epidemiological studies done on this group of diseases [17]. Stroke was diagnosed by a neurologist, based on the patient's history, neurological examination and neuroimaging studies which were performed for all stroke patients. Stroke in this study was divided into ischemic and hemorrhagic types. The ischemic type was divided into thrombotic and embolic. Hemorrhagic stroke was divided into Subarachnoid hemorrhage (SAH) and Intracerebral hemorrhage (ICH). Although the most stroke cases were ischemic types, ICH was defined as a stroke for which CT or MRI demonstrated blood within the brain parenchyma, with or without extension into the ventricles or subarachnoid space. SAH was defined as an abrupt onset of a headache or loss of consciousness with or without focal neurologic signs. In addition, CT scans demonstrated subarachnoid blood. Lumbar punctures were performed in CT-negative patients with an appropriate history [18].

### Inclusion criteria

The criteria for entering this study were any patients with the diagnosis of the first stroke who were hospitalized in Ayatollah Rouhani Hospital that were written informed consent.

### Exclusion criteria

Exclusion criteria for stroke cases were transient ischemic accident (TIA) hemiparesis or any focal neurological findings due to head trauma, brain mass lesions such as brain tumor or brain abscess, hemiplegic migraine attack and postictal of seizures. Cases with metabolic and systemic disorders that lead to hemiparesis, cases with history of bone disease or fracture, renal or liver disease, cases under corticosteroid therapy or supplement excluded from this study.

## Severity and Disability Definition

Severity of stroke was determined on the basis of NIH Stroke Scale (NIHSS) criteria, scores  $\leq 8$  mild stroke; scores 9 – 15 moderate stroke; and scores  $\geq 16$  severe stroke [18].

The degree of disability of patients was determined according to the Modified Ranking Scale (mRS) criteria [19].

- 0) - No symptoms.
- 1) - No significant disability. Able to carry out all usual activities, despite some symptoms.
- 2) - Slight disability. Able to look after own affairs without assistance, but unable to carry out all previous activities.
- 3) - Moderate disability. Requires some help, but able to walk unassisted.

4) - Moderately severe disability. Unable to attend to own bodily needs without assistance, and unable to walk unassisted.

5) - Severe disability. Requires constant nursing care and attention, bedridden, incontinent.

6) - Dead.

### Clinical variables

Demographic characteristics of patients, types of stroke, severity of stroke in the admission time, the degree of disability of patients at discharge time, risk factors such as HTN, IHD, DM, HLP, smoking and village or city residency were recorded.

HTN was defined if SBP was more than 140 mmHg or more than 90 mmHg for DBP. The DM was defined as FBS more than 126 mg/dl. The HLP was defined for patients who had Low HDL (less than 40 mg/dl in men or 50 mg/dl in women) or high LDL (more than 130 mg/dl). The high triglyceride (TG) was identified based on triglycerides more than 150 mg/d [20]. The background information, history of cardiac medications, ECG findings and history of IHD were obtained. Smoking in this study defined as smoking at least five cigarettes per day at least for last year. Village or city residency of the patients was based on their identity card information (birth certificate), living in areas of at least 5 km from the city is considered as a village.

### Sample collection and laboratory test

The maximum interval between the onset of the stroke and the time of admission for these patients was up to 12 hours. In each patient, at the emergency department immediately after diagnosis of stroke, venous blood samples were collected under standardized conditions. Serum level of Ca and Mg and VD and routine laboratory tests was performed, simultaneously at the laboratory of Ayatollah Rouhani Hospital.

**Mg:** The Mg level was measured by Pars Azmoon kit according to the protocol. The colorimetric technique was used to determine the concentration of Mg at 450 nanometers. Normal serum concentrations of Mg<sup>2+</sup> was considered 1.5 to 2.5 mEq/L (1.8 to 3.0 mg/dl) [21].

**Ca:** The Ca level was measured by Hitachi e902 by Pars Azmoon kit. A normal serum concentration of Ca<sup>2+</sup> was considered 8.2 to 10.5 mEq/L.

**Vit D:** The serum level of VD was determined using the radioimmunoassay method. Serum calcium levels measured according to the standard method of the clinical laboratory of this hospital. Serum level of VD categorized in four groups and under 30 ng/ml considered as low serum level.

- a. Deficient group (under 20 ng/ml)
- b. Insufficient group (20-30 ng/ml)
- c. Normal Range (30-100 ng/ml)
- d. High (upper than 100 ng/ml) [22].

All samples analyzed with commercially available kits of the same lot number according to the manufacturer's protocol, and blind to any clinical information at the laboratory of Ayatollah Rouhani Hospital. A checklist was used to identify

demographic characteristics of patient's types of stroke, severity of stroke in the admission time, the degree of disability of patients at discharge time, stroke risk factors and serum level of electrolytes.

### Ethics

The study was approved by the ethics committee of Babol University of Medical Sciences (BUMS: 3407-9542120). From each participant or the next of kin before any interview or neurologic examination informed consent was obtained.

### Statistical analysis

The chi-square or Fisher exact test with calculation of odds ratio and 95% confidence interval in SPSS v23 were applied for statistical analysis between the demographics and clinical variables with mineral serum level. Also, p-values < 0.05 were considered as significant.

### Finding

Of 216 stroke patients that entered in this study, 120 cases (55.6%) were female and 155 cases (71.8%) were elderly. The mean age of stroke survivors was 67.38 ± 13.66 years. Also, the distribution of stroke type was 185 cases (85.6%) ischemic vs. 32 cases (14.4%) hemorrhagic. The most underlying disease, 120 cases (55.6%) was HTN. The stroke severity was determined in admission which 121 cases (56%) mild, 89 cases (41.2%) moderate and 6 cases (2.8%) were severe. In addition, in discharge of the stroke survivor 139 cases (64.4%) mild, 49 cases (22.7%) moderate and 28 patients (12.9%) were severe or death. Also, difference of hemorrhagic stroke subtype was statistically significant in hypertensive patients (20(87%) ICH vs. 1(12.5%) SAH, p = 0.001) (Table 1).

Most of the stroke survivor 171 cases (79.2%) had low VD. In thrombotic stroke patients, 98 cases (89%) low VD vs. 12 cases (10.9%) normal VD, (p = 0.001) was seen. Also, low VD was more seen significantly in DM patients 72(90%) in compare to non-DM patients 96(72.7%), (p = 0.003) (Table 2).

Of 120 cases (56.3%) who had HTN, 103 cases (85.8%) low VD vs. 17 cases (14.2%) normal VD, (p = 0.01), 68 cases (57.1%) hypo calcemic vs. 45 cases (37.8%) normal Ca serum level, (p < 0.0001) (Table 3) and 57 cases (49.1%) hypomagnesemia vs. 59 cases (50.9%) normal Mg (p = 0.04) were seen.

Difference in sex was statistically significant with hypomagnesemia (49 cases (53.8%) male vs. 38 cases (33.9%) female, (p = 0.007) (Table 4). Hypomagnesemia were seen in 87 cases (40.8%) that 49 cases of this were hypo-calcemic (56.3%), (p = 0.03) and with increasing serum level of Ca the hypomagnesemia was decreased (Table 3). Differences in Mg with VD was statistically significant (170 cases (79.4%) low VD vs. 44 cases (20.6%) normal, p = 0.007) (Table 2).

### Discussion

Differences in ischemic subtype of stroke with VD serum level was statistically significant and low level of VD was more seen in thrombotic stroke patients and DM patients.

**Table 1:** Background disease and characteristic of stroke patients and correlation with type of stroke.

Variable	Category	N (%)	Ischemic			Hemorrhagic		
			p-value	Thrombotic	Embolic	p-value	SAH	ICH
Stroke	Ischemic	185(85.6)	-	110(59.5)	75(40.5)	-	-	-
	Hemorrhagic	32(14.4)		-	-		8(25.8)	23(74.2)
Sex	Male	96(44.4)	0.64	44(40)	33(44)	0.67*	4(50)	15(65.2)
	Female	120(55.6)		66(60)	42(56)		4(50)	8(34.8)
Residential status	Rural	125(57.9)	0.17	69(62.7)	39(52)	0.41	9(39.1)	14(60.9)
	Urban	91(42.1)		41(37.3)	36(48)		5(62.5)	9(39.1)
Admit score	Mild	121(56)	0.13	62(56.4)	48(64)	0.02	7(87.5)	4(17.4)
	Moderate	89(41.2)		43(39.1)	27(36)		1(12.5)	18(78.3)
	Severe	6(2.8)		5(4.5)	0(0)		0(0)	1(4.3)
Discharge scale	Mild	139(64.4)	0.004	63(57.3)	58(77.3)	0.4	6(75)	12(52.2)
	Moderate	49(22.7)		30(27.3)	16(21.3)		0(0)	3(13)
	Severe	15(6.9)		13(11.8)	0(0)		1(12.5)	1(4.3)
	Death	13(6)		4(3.6)	1(1.3)		1(12.5)	7(30.4)
HTN	Yes	120(56.3)	0.09	65(59.6)	34(46.6)	0.001	1(12.5)	20(87)
	No	93(43.7)		44(40.4)	39(53.4)		7(87.5)	3(13)
IHD	Yes	91(44.6)	0.08	44(41.9)	39(55.7)	0.38	7(87.5)	7(33.3)
	No	113(55.4)		61(58.1)	31(44.3)		1(12.5)	14(66.7)
DM	Yes	80(37.7)	0.04	47(43.5)	21(28.4)	0.09	1(12.5)	11(50)
	No	132(62.3)		61(56.5)	53(71.6)		7(87.5)	11(50)
HLP	Yes	84(40.8)	0.9	45(42.9)	32(43.2)	0.63	1(14.3)	6(30)
	No	122(59.2)		60(57.1)	42(56.8)		6(85.7)	14(70)
Smoking	Yes	59(29.4)	0.22	25(23.8)	23(33.3)	0.9	2(33.3)	9(42.9)
	No	142(70.6)		80(76.2)	46(66.7)		4(66.7)	12(57.1)
MG***	Low	87(40.7)	0.18	43(39.1)	21(28)	0.7	7(87.5)	16(76.2)
	Normal	116(54.2)		60(54.5)	51(68)		1(12.5)	4(19)
	High	11(5.1)		7(6.4)	3(4)		0(0)	1(4.8)
Vit D	Low	171(79.2)	0.001	98(89.1)	46(61.3)	> 0.05	7(87.5)	20(87)
	Normal	45(20.8)		12(10.9)	29(38.7)		1(12.5)	3(13)
	High	0(0)		0(0)	0(0)		0(0)	0(0)
Ca	Low	96(44.7)	0.29	48(43.6)	24(32.4)	> 0.05	2(25)	6(75)
	Normal	109(50.7)		56(50.9)	46(62.2)		5(21.7)	5(21.7)
	High	10(4.7)		6(5.5)	4(5.4)		0(0)	0(0)

\*\* chi-square or Fisher exact test were used between demographic and clinical variable with stroke subtype.

\*\*\* Normal serum concentrations of Mg<sup>2+</sup> was considered 1.5 to 2.5 mEq/L (1.8 to 3.0 mg/dl). Normal Range of VD (30-100 ng/ml), low serum level (under 30 ng/ml) and high serum level (upper than 100ng/ml) were considered. A normal serum concentration of Ca<sup>2+</sup> was considered 8.2 to 10.5 mEq/L.

In Dorresteijn et al. study, lower VD status was associated with an increased risk of stroke by synthesizing the data of nineteen relevant studies. This association remained in the ischemic stroke group, while the relationship between VD status and hemorrhagic stroke was insignificant [23].

Chaudhuri et al. found that VD deficiency had an independent association with ischemic stroke and significant association with cardio embolic stroke [24]. Also, Aihara et al.

demonstrated vascular effects of VD with inhibition of thrombosis and reduction in arterial calcification [25]. This anti-inflammatory effect may have a protective role as there is increasing evidence that systemic inflammation leads to atherosclerosis [26]. That was contrast with Afzal et al. study [27].

It seems that base on pathophysiology of ischemic stroke, due to inflammatory process in the atherosclerotic vessels and

**Table 2:** Difference in serum level of vitamin D with demographic variable, underlying disease and type of stroke.

Variable	Category	Vitamin D		Total	p-value
		Low	Normal		
Sex	Female	98(81.7)	22(18.3)	120(55.6)	0.31
	Male	73(76)	23(24)	96(44.4)	
Ischemic	Embolic	46(38.7)	29(61.3)	75(40.5)	0.001
	Thrombotic	98(89)	12(10.9)	110(59.5)	
Hemorrhagic	SAH	7(87.5)	1(12.5)	8(25.8)	> 0.05
	ICH	20(87.0)	3(13)	23(74.2)	
Residential status	Rural	100(80)	25(20)	125(57.9)	0.73
	Urban	71(78)	20(22)	91(42.1)	
HTN	No	66(71)	27(29)	93(43.7)	0.01
	Yes	103(85.8)	17(14.2)	120(56.3)	
IHD	No	92(81.4)	21(18.6)	113(55.4)	0.38
	Yes	69(75.8)	22(24.2)	91(44.6)	
DM	No	96(72.7)	36(27.3)	132(62.3)	0.4
	Yes	72(90)	8(10)	80(37.7)	
HLP	No	93(76.2)	29(23.8)	122(59.2)	0.4
	Yes	68(81)	16(19)	84(40.8)	
Smoking	No	117(82.4)	25(17.6)	142(70.6)	0.33
	Yes	45(76.3)	14(23.7)	59(29.4)	
MG	Low	78(89.7)	9(10.3)	87(40.7)	0.007
	Normal	85(73.3)	31(26.7)	116(54.2)	
	High	7(63.6)	4(36.4)	11(5.1)	

\*\* Normal Range of VD (30-100 ng/ml), low serum level (under 30 ng/ml) and high serum level (upper than 100 ng/ml) were considered.

the role of VD in the inflammatory response maybe consider. However, if this relationship is confirmed in other studies, it may be reducing the incidence of thrombotic ischemic stroke with modifying the serum level of VD.

In hypertensive patient's difference in Ca, VD and hemorrhagic subtype were statistically significant. In ICH patients 87% had HTN, although in SAH patients 87% had not HTN.

In this regard, Gonullu et al. Study, demonstrated that stroke and its subgroups associated with some risk factors such as HTN, DM, and also IHD, HLP [28]. Ahangar et al. reported that hypertension had significantly associated with hemorrhagic stroke [29].

In hypertensive patients, frequency of patients with abnormal serum levels of Ca and low VD were higher in comparing to normal blood pressure patients.

Larsson et al. found direct association between Ca intake and the risk of intracerebral hemorrhage [30]. Liang et al, found inverse associations between ischemic stroke risk and dietary intake of Ca which had demonstrated beneficial effects [31].

**Table 3:** Difference in serum level of calcium with demographic variable, underlying disease and type of stroke.

Variable	Category	Calcium			Total	p-value
		Hyper-calcemia	Normal	Hypo-calcemia		
Sex	Female	7(5.9)	60(50.4)	52(43.7)	119(55.3)	0.6
	Male	3(3.1)	49(51)	44(45.8)	96(44.7)	
Ischemic	Embolic	4(5.4)	46(62.2)	24(32.4)	74(40.2)	0.2
	Thrombotic	6(5.5)	56(50.9)	48(43.6)	110(59.8)	
Hemorrhagic	SAH	0(0)	2(25)	6(75)	8(25.8)	> 0.05
	ICH	0(0)	5(21.7)	18(78.3)	23(74.2)	
Residential status	Rural	7(5.6)	64(51.2)	54(43.2)	125(58.1)	0.69
	Urban	3(3.3)	45(50.0)	42(46.7)	90(41.9)	
HTN	No	4(4.3)	62(66.7)	27(29)	93(43.9)	< 0.0001
	Yes	6(5)	45(37.8)	68(57.1)	119(56.1)	
IHD	No	4(3.5)	56(49.6)	53(46.9)	113(55.7)	0.48
	Yes	6(5)	47(47.5)	37(47.5)	90(44.3)	
DM	No	5(3.8)	69(52.7)	57(43.5)	131(62.1)	0.74
	Yes	4(5)	38(47.5)	38(47.5)	80(37.9)	
HLP	No	4(3.3)	60(49.6)	57(47.1)	121(59)	0.6
	Yes	4(4.8)	46(54.8)	34(40.5)	84(41)	
Smoking	No	7(5)	73(51.8)	61(43.3)	141(70.5)	0.26
	Yes	1(1.7)	26(44.1)	32(54.2)	59(29.5)	
MG	Low	4(4.6)	34(39.1)	49(56.3)	87(40.8)	0.03
	Normal	6(5.2)	65(56)	45(38.8)	116(54.5)	
	High	0(0)	8(80)	2(20)	10(4.7)	

\*\* A normal serum concentration of ca<sup>2+</sup> was considered 8.2 to 10.5 mEq/L.

In DM patients 90% of these patients had lower level of VD and 60% cases were thrombotic. Williams et al. study, showed diabetes was associated with an increased risk of ischemic stroke, changing clinical pictures and worsens the prognosis [32]. In Tzimalos study, have shown that hyperglycemia worsens the prognosis of ischemic stroke [33]. In Fuentes study, in ischemic stroke patients, persistent hyperglycemia (above 155 mg/dl) is found that associated with the poorer outcome [34]. Poorly controlled hyperglycemia reduces cerebral blood flow and oxygenation of tissues, and increases intracranial pressure, cerebral edema and neuronal death [35].

Differences in Mg with Ca and VD was statistically significant which 45% had hypocalcemia and 80% had low level of VD. Hypomagnesemia were seen in 87 cases (40.8%) that 49 cases of this were hypocalcemic (56.3%) and with increasing serum level of Ca the hypomagnesemia was decreased.

In Lingham et al. study, showed a significant inverse association between Mg intake and risk of stroke. Daily intake mg was associated with reduction in the risk of total stroke, as well as Mg intake was inversely associated with risk of ischemic stroke [11].

**Table 4:** Difference in serum level of Magnesium with demographic variable, underlying disease and type of stroke.

Variable	Category	Magnesium			Total	p-value
		High	Normal	Low		
Sex	Female	0(0)	74(66.1)	38(33.9)	112(55.2)	0.007
	Male	0(0)	42(46.2)	49(53.8)	91(44.8)	
Ischemic	Embolic	3(4)	51(68)	21(28)	75(40.5)	0.18
	Thro-botic	7(6.4)	60(54.5)	43(39.1)	110(59.5)	
Hemorrhagic	SAH	0(0)	1(12.5)	7(87.5)	8(27.6)	0.7
	ICH	1(4.8)	4(19)	16(72.6)	21(72.4)	
Residential status	Rural	0(0)	62(53)	55(47)	117(57.6)	0.19
	Urban	0(0)	54(62.8)	32(37.2)	86(42.4)	
HTN	No	0(0)	55(65.5)	29(34.5)	84(42)	0.04
	Yes	0(0)	59(50.9)	57(49.1)	116(58)	
IHD	No	0(0)	63(59.4)	43(40.6)	106(55.2)	0.66
	Yes	0(0)	48(55.8)	38(44.2)	86(44.8)	
DM	No	0(0)	78(62.4)	47(37.6)	125(62.5)	0.05
	Yes	0(0)	36(48)	39(52)	75(37.5)	
HLP	No	0(0)	58(51.3)	55(48.7)	113(58.2)	0.01
	Yes	0(0)	56(69.1)	25(30.9)	81(41.8)	
Smoking	No	0(0)	81(60.9)	52(39.1)	133(70)	0.11
	Yes	0(0)	27(47.4)	30(52.6)	57(30)	

\*\* Normal serum concentrations of Mg<sup>2+</sup> was considered 1.5 to 2.5 mEq/L (1.8 to 3.0 mg/dl).

This study has several limitations include of not controlling group and we could not investigate the nutrition status before the stroke because of lack of information and other effective parameter such as electrolyte imbalance (sodium, potassium). Short period of follow-up and small population.

This study has several strengths; surveying the serum level of these elements with the type of stroke and the risk factors for stroke in our area (as far as we know) has not been done and few paper that was published in this issue.

## Conclusion

Low serum level of VD was seen in thrombotic ischemic and DM patients. Hypertensive patients had more low serum levels of Ca and VD. Most of hypermagnesemic patients had hypocalcemia. HTN was more seen in ICH patients. Preventive policies such as screening of mineral serum level and correction of this under the supervision of the physician are suggested.

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## Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

## Authors' Contributions

Alijan A. Ahangar and Payam Saadat participated in neurologic examination and diagnosis of stroke patients approved the final version and supervised the study. Soraya Khafri designed the study, prepared the manuscript, analysis and writing of manuscript. Shayan Alijanpour participated in data analysis and writing of manuscript.

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## References

- Johnson W, Onuma O, Owolabi M, Sachdev S. 2016. Stroke: a global response is needed. *Bull World Health Organ* 94(9): 634-634A. <https://doi.org/10.2471/BLT.16.181636>
- Owolabi MO, Arulogun O, Melikam S, Adeoye AM, Akarolo-Anthony S, et al. 2015. The burden of stroke in Africa: a glance at the present and a glimpse into the future. *Cardiovasc J Afr* 26(2 Suppl 1): S27-S38. <https://doi.org/10.5830/CVJA-2015-038>
- Feigin VL, Forouzanfar MH, Krishnamurthi R, Mensah GA, Connor M, et al. 2014. Global and regional burden of stroke during 1990-2010: findings from the Global Burden of Disease Study 2010. *Lancet* 383(9913): 245-255. [https://doi.org/10.1016/S0140-6736\(13\)61953-4](https://doi.org/10.1016/S0140-6736(13)61953-4)
- Ahangar AA, Saravi M, Alijanpour S, Boora MM, Hoseinalipour S, et al. 2016. Comparison of risk factors of stroke and myocardial infarction in patients 15 to 45 years in affiliated hospitals of Babol University of Medical Sciences. *Zahedan J Res Med Sci* 18(12): e5332. <http://doi.org/10.17795/zjms-5332>
- Hosseini AA, Sobhani-Rad D, Ghandehari K, Benamer HT. 2010. Frequency and clinical patterns of stroke in Iran-Systematic and critical review. *BMC neurol* 10(1): 72. <https://doi.org/10.1186/1471-2377-10-72>
- Saadat P, Ahangar AA, Babaei M, Kalantar M, Bayani MA, et al. 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. <https://doi.org/10.1155/2018/6580178>
- Jayedi A, Ghomashi F, Zargar MS, Shab-Bidar S. 2018. Dietary sodium, sodium-to-potassium ratio, and risk of stroke: a systematic review and nonlinear dose-response meta-analysis. *Clin Nutr* (In Press). <https://doi.org/10.1016/j.clnu.2018.05.017>
- Mohammadifard N, Gotay C, Humphries KH, Ignaszewski A, Esmailzadeh A, et al. 2018. Electrolyte minerals intake and cardiovascular health. *Crit Rev Food Sci Nutr* 1-11. <https://doi.org/10.1080/10408398.2018.1453474>
- Can A, Rudy RF, Castro VM, Dligach D, Finan S, et al. 2018. Low serum calcium and magnesium levels and rupture of intracranial aneurysms. *Stroke* 49(7): 1747-1750. <https://doi.org/10.1161/STROKEAHA.118.020963>
- Harrington JM, Young DJ, Essader AS, Sumner SJ, Levine KE. 2014. Analysis of human serum and whole blood for mineral content by ICP-

- MS and ICP-OES: development of a mineralomics method. *Biol Trace Elem Res* 160(1): 132-142. <https://doi.org/10.1007/s12011-014-0033-5>
11. Lingam I, Robertson NJ. 2018. Magnesium as a neuroprotective agent: a review of its use in the fetus, term infant with neonatal encephalopathy, and the adult stroke patient. *Dev Neurosci* 40(1): 1-12. <https://doi.org/10.1159/000484891>
  12. Evans MA, Kim HA, Ling YH, Uong S, Vinh A, et al. 2018. Vitamin D<sub>3</sub> supplementation reduces subsequent brain injury and inflammation associated with ischemic stroke. *Neuromolecular Med* 20(1): 147-159. <https://doi.org/10.1007/s12017-018-8484-z>
  13. Beveridge LA, Khan F, Struthers AD, Armitage J, Barchetta I, et al. 2018. Effect of vitamin D supplementation on markers of vascular function: a systematic review and individual participant meta-analysis. *J Am Heart Assoc* 7(11): e008273. <https://doi.org/10.1161/JAHA.117.008273>
  14. Bendik I, Friedel A, Roos FF, Weber P, Eggersdorfer M. 2014. Vitamin D: a critical and essential micronutrient for human health. *Front Physiol* 5: 248. <https://doi.org/10.3389/fphys.2014.00248>
  15. Busch M, Scheidt-Nave C, Thieme U, Burghaus I, Trampisch H, et al. 2011. O3-3.3 Association of low vitamin D levels with increased risk of stroke in older adults. *Journal of Epidemiology & Community Health* 65(Suppl 1): A34.
  16. Ahangar AA, Saadat P, Heidari B, Taheri ST, Alijanpour S. 2018. Sex difference in types and distribution of risk factors in ischemic and hemorrhagic stroke. *Int J Stroke* 13(1): 83-86. <https://doi.org/10.1177/1747493017724626>
  17. Ropper A, Martin A, Joshua P, Klein P. 2014. Cerebrovascular diseases. In: Ropper A, Martin A, Joshua P, Klein P (eds) *Adams and Victor's Principles of Neurology*. McGraw-Hill Education, NY, USA, pp 778-781.
  18. Ahangar AA, Saadat P, Niroomand S, Alijanpour S, Sohrabnezhad R, et al. 2010. Increased zinc serum level: new clues in Babol stroke patients, Northern Iran. *Stroke Res Treat* 2018: 7681682. <https://doi.org/10.1155/2018/7681682>
  19. Bruno A, Shah N, Lin C, Close B, Hess DC, et al. 2010. Improving modified Rankin Scale assessment with a simplified questionnaire. *Stroke* 41(5): 1048-1050. <https://doi.org/10.1161/STROKEAHA.109.571562>
  20. Hauser S, Josephson S. 2013. *Harrison's neurology in clinical medicine*. McGraw-Hill Education, NY, USA.
  21. Euser AG, Cipolla MJ. 2009. Magnesium sulfate for the treatment of eclampsia: a brief review. *Stroke* 40(4): 1169-1175. <https://doi.org/10.1161/STROKEAHA.108.527788>
  22. Sperling MA. 2014. *Pediatric Endocrinology*. Saunders, PA, USA.
  23. Dorresteijn LD, Kappelle AC, Boogerd W, Klokman WJ, Balm AJ, et al. 2002. Increased risk of ischemic stroke after radiotherapy on the neck in patients younger than 60 years. *J Clin Oncol* 20(1): 282-288. <https://doi.org/10.1200/JCO.2002.20.1.282>
  24. Chaudhuri JR, Mridula KR, Suvarna Alladi AA, Umamahesh M, Balaraju B, et al. 2014. Serum 25-hydroxyvitamin D deficiency in ischemic stroke and subtypes in Indian patients. *J Stroke* 16(1): 44-50. <https://doi.org/10.5853/jos.2014.16.1.44>
  25. Aihara K, Azuma H, Akaike M, Ikeda Y, Yamashita M, et al. 2004. Disruption of nuclear vitamin D receptor gene causes enhanced thrombogenicity in mice. *J Biol Chem* 279(34): 35798-35802. <https://doi.org/10.1074/jbc.M404865200>
  26. Jouni ZE, Winzerling JJ, McNamara DJ. 1995. 1,25-Dihydroxyvitamin D<sub>3</sub>-induced HL-60 macrophages: regulation of cholesterol and LDL metabolism. *Atherosclerosis* 117(1): 125-138. [https://doi.org/10.1016/0021-9150\(95\)05569-1](https://doi.org/10.1016/0021-9150(95)05569-1)
  27. Afzal S, Nordestgaard BG. 2017. Vitamin D, hypertension, and ischemic stroke in 116 655 individuals from the general population: a genetic study. *Hypertension* 70(3): 499-507. <https://doi.org/10.1161/HYPERTENSIONAHA.117.09411>
  28. Gönüllü H, Karadaş S, Milanlioglu A, Gönüllü E, Celal K, et al. 2013. Levels of serum trace elements in ischemic stroke patients. *J Exp Clin Med* 30(4): 301-304. <http://doi.org/10.5835/jecm.omu.30.04.004>
  29. Ahangar AA, Saadat P, Alijanpour S, Taheri ST. 2018. Clinical patterns and early prognosis of stroke in Babol, Northern Iran. *American Journal of Biomedical Science and Engineering* 4(3): 30-35.
  30. Larsson SC, Virtamo J, Wolk A. 2011. Potassium, calcium, and magnesium intakes and risk of stroke in women. *Am J Epidemiol* 174(1): 35-43. <https://doi.org/10.1093/aje/kwr051>
  31. Liang W, Lee AH, Binns CW. 2011. Peer reviewed: dietary intake of minerals and the risk of ischemic stroke in Guangdong Province, China, 2007-2008. *Prev Chronic Dis* 8(2): A38.
  32. Williams LS, Rotich J, Qi R, Fineberg N, Espay A, et al. 2002. Effects of admission hyperglycemia on mortality and costs in acute ischemic stroke. *Neurology* 59(1): 67-71. <https://doi.org/10.1212/WNL.59.1.67>
  33. Tziomalos K, Spanou M, Bouziana SD, Papadopoulou M, Giampatzis V, et al. 2014. Type 2 diabetes is associated with a worse functional outcome of ischemic stroke. *World J Diabetes* 5(6): 939-944. <https://doi.org/10.4239/wjd.v5.i6.939>
  34. Fuentes B, Ortega-Casarrubios MA, SanJosé B, Castillo J, Leira R, et al. 2010. Persistent hyperglycemia > 155 mg/dL in acute ischemic stroke patients: how well are we correcting it? Implications for outcome. *Stroke* 41(10): 2362-2365. <https://doi.org/10.1161/STROKEAHA.110.591529>
  35. Snarska KK, Bachórzewska-Gajewska H, Kapica-Topczewska K, Drozdowski W, Chorąży M, et al. 2017. Hyperglycemia and diabetes have different impacts on outcome of ischemic and hemorrhagic stroke. *Arch Med Sci* 13(1): 100-108. <https://doi.org/10.5114/aoms.2016.61009>