International Journal of Research in Medical Sciences
Khan JA et al. Int J Res Med Sci. 2022 Nov;10(11):2586-2591
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012
DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20222863

Original Research Article

Comparison of serum electrolytes with preeclampsia severity: a cross sectional study

Javid Ahmed Khan[1]*, Aadil Ashraf[3], Waseem A. Qureshi[2], Faizana Fayaz[4]

[1]Department of Medicine, [2]Registrar Academics, Physician, Government Medical College Srinagar, Jammu and Kashmir, India
[3]Department of Gastroenterology, AIG Hospital, Hyderabad, Telangana, India
[4]Researcher, Delhi Institute of Pharmaceutical Sciences and Research, New Delhi, India

Received: 16 September 2022
Revised: 10 October 2022
Accepted: 11 October 2022

***Correspondence:**
Dr. Javid Ahmed Khan,
E-mail: khanjaved69@yahoo.com

ABSTRACT

Background: Preeclampsia is a common complication of pregnancy that put women and their fetuses at significant risk and result in life long sequelae. The pathogenesis of this important disease is complex as such the role of different serum electrolytes is being investigated as they are considered important for blood pressure regulation.
Methods: A hospital based cross-sectional study of 100 diagnosed cases of preeclampsia divided into mild and severe according to latest International Society for the Study of Hypertension in Pregnancy (ISSHP) guidelines and equal number of age, parity and gestational age matched women (n=100), that acted as control group, with singleton normal pregnancies. Data was analyzed in SPSS V:26. Statistical tests to find out mean standard deviation and One-way ANOVA test were applied to find the significance of associations.
Results: In severe preeclampsia group, the mean values of Na^+, K^+ and Cl^- were 134.50±4.24, 4.28±0.74, 106.48±3.41 meq/l respectively in comparison to control group which had 135.57±3.29, 4.12±0.53, 108.20±3.19 meq/l respectively. Results from one way ANOVA showed that there was statistically significant difference between means of the three groups for systolic blood pressure (SBP), diastolic blood pressure (DBP), potassium and chloride levels with $p<0.05$. A post hoc analysis was used to distinguish the differences in means of these parameters.
Conclusions: Estimation of readily available serum electrolytes of sodium potassium and chloride during the course of pregnancy can help to identify and treat preeclampsia and thus reduce the burden of morbidity and mortality in pregnant women.

Keywords: Chloride, Preeclampsia, Potassium, Sodium

INTRODUCTION

Preeclampsia is a one of the main maternal health issue globally that is responsible for maternal and neonatal severe morbidity and mortality and has significant contributions to prematurity of the fetus and long-term cardiovascular disease (CVD) in the mother.[1] It affects an estimated 4.6% of pregnancies globally.[2] The International Society for the Study of Hypertension in Pregnancy (ISSHP) defines preeclampsia as the presence of new-onset hypertension (SBP≥140 mmHg, DBP≥90 mmHg, or both) accompanied by proteinuria and/or evidence of maternal acute kidney injury (AKI), liver dysfunction, neurological features, hemolysis or thrombocytopenia, or fetal growth restriction. Preeclampsia may develop or be recognized for the first time intrapartum or early postpartum in some cases. One must note that proteinuria is not mandatory for a diagnosis of preeclampsia.[3] The exact pathophysiology of preeclampsia remains unknown. There are number of theories proposed to explain the pathogenesis of preeclampsia which include abnormal placentation,

immunologic factors, inflammation and genetic factors.[4] The ultimate pathways in the pathogenesis of preeclampsia are placental hypoxia and ischemia by release of vasoactive factors into the maternal circulation and endothelial cell dysfunction leading to the signs and symptoms of preeclampsia.[5,6]

The homeostasis of sodium and potassium plays a key role in endothelium-dependent vasodilatation, which is defective in primary hypertension.[7] Sodium retention decreases the synthesis of nitric oxide, an arteriolar vasodilator elaborated by endothelial cells, and increases the plasma level of asymmetric dimethyl L-arginine, an endogenous inhibitor of nitric oxide production.[8] While as increased serum potassium levels within the physiological range leads to endothelium dependent vasodilatation.[9]

Considering these factors, it was considered important to perform a study for evaluation of electrolytes in preeclampsia and compare results with normotensive pregnant group.

METHODS

Study population

A hospital based cross sectional study of 200 pregnant women divided into three groups: 60 pregnant women with mild preeclampsia, 40 women with severe preeclampsia and age, parity and gestational age matched women that acted as control group (n=100), with singleton normal pregnancies, admitted in obstetrics wards. The study was conducted from January to May 2022 at Lal Ded hospital an associated tertiary care hospital of GMC Srinagar after the ethical committee approval. All the subjects of the study were included after taking proper relevant history and informed consent.

The subjects were classified as preeclampsia if they had de novo hypertension of ≥140/90 mmHg after 20 weeks gestation accompanied by proteinuria and/or evidence of maternal acute kidney injury, liver dysfunction, neurological or cerebral features like headache, visual disturbances, hemolysis or thrombocytopenia, and/or fetal growth restriction. They were further divided into two groups with patients with SBP≥140-160 mmHg and/or DBP≥90-110 mmHg classified as mild preeclampsia while those with SBP>160 mmHg and/or DBP 110 mmHg were classified as severe preeclampsia.

Exclusion criteria

Exclusion criteria consisted of multiple pregnancy, chronic hypertension, diabetes mellitus, women with cardiovascular diseases, chronic liver disease, patients taking steroids or diuretics, gestational trophoblastic diseases. Chronic inflammatory diseases like SLE, rheumatoid arthritis etc.

Statistical analysis

Data was compiled in MS Office Excel and results were expressed as Mean±SD and analysed with SPSS 26 software. Comparisons between groups was performed by one-way ANOVA test followed by post hoc analysis with Sidak test. Associations with p value of <0.05 were considered statistically significant.

RESULTS

A total of 200 patients were included in the study. 100 patients with preeclampsia were divided into mild (n=60) and severe preeclampsia (n=40) group while as 100 patients with singleton normal pregnancy formed the control group.

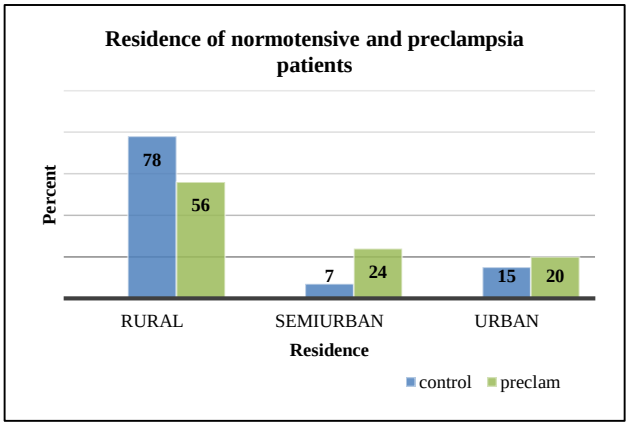

Figure 1: Distribution of patients (preeclampsia and control) as per rural, semi-urban and urban areas of the region.

More than half of the patients [56% (n=56)] in both the preeclampsia and normotensive group (control) [78% (78)] were from the rural areas (Figure 1).

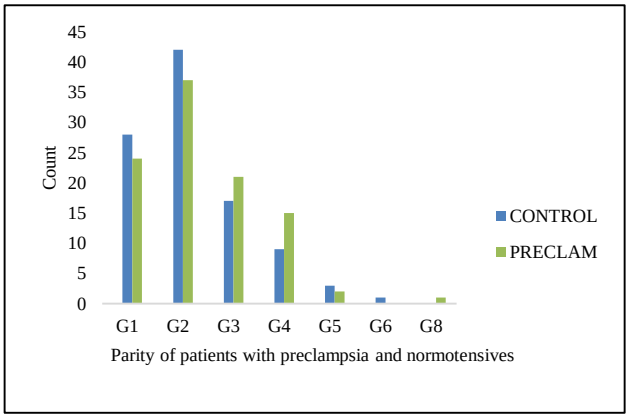

Figure 2: Distribution of patients as per the parity.

Most of the patients in both the groups were having their second pregnancy (G2) (Figure 2).

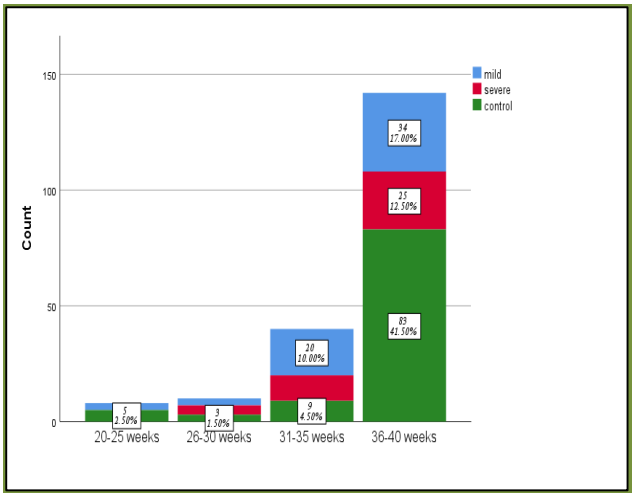

Figure 3: Distribution of patients with severe preeclampsia, mild preeclampsia and control as per the gestational age (in weeks).

Majority of patients in preeclampsia and control group were in the 36-40 weeks gestation (Figure 3).

The average age of control group was 28.95±3.37 years while as in case of severe preeclampsia it was 29.65±3.35 years. Systolic blood pressure (SBP) mean±SD in mild, severe preeclampsia and control groups were 150.73±7.36, 173.00±8.45, 120.63±11.30 mmHg respectively. Diastolic blood pressure Mean±SD were 94.75±10.09, 104.18±10.03, 74.83±6.34 mmHg in mild, severe preeclampsia and control groups respectively. Mild and severe preeclampsia groups exhibited significant elevation in SBP and DBP when compared with the control group (Table 1).

Serum sodium in control group had mean±SD of 135.57±3.29 while as in severe preeclampsia had 134.50±4.24 meq/l, although there was decreased levels of mean sodium level in severe preeclampsia but when ANOVA test was run it did not show any statistical significance. Serum potassium in control group had mean±SD of 4.12±0.53 meq/l, while as in severe preeclampsia it was 4.28±0.74 meq/l. Serum chloride Mean±SD were 106.48±3.41 meq/l in severe preeclampsia group, while as it was 108.20±3.19 meq/l in control group (Table 1).

Table 1: Clinical characteristics and serum electrolytes studied of mild preeclampsia, severe preeclampsia and control group.

Descriptive									
Parameters		**N**	**Mean**	**SD**	**Std. error**	**95% CI for mean**		**Minimum**	**Maximum**
						Lower bound	**Upper bound**		
Systolic BP (mmHg)	Mild preeclampsia	60	150.73	7.36	0.95	148.83	152.64	130.00	160.00
	Severe preeclampsia	40	173.00	8.45	1.34	170.30	175.70	161.00	200.00
	Control	100	120.63	11.30	1.13	118.39	122.87	95.00	168.00
	Total	200	140.14	23.15	1.64	136.91	143.36	95.00	200.00
Diastolic BP (mmHg)	Mild preeclampsia	60	94.75	10.09	1.30	92.14	97.36	70.00	110.00
	Severe preeclampsia	40	104.18	10.03	1.59	100.97	107.38	84.00	124.00
	Control	100	74.83	6.34	0.63	73.57	76.09	60.00	89.00
	Total	200	86.68	14.89	1.05	84.60	88.75	60.00	124.00
Serum sodium (meq/l)	Mild preeclampsia	60	135.82	4.30	0.56	134.71	136.93	126.00	149.00
	Severe preeclampsia	40	134.50	4.24	0.67	133.14	135.86	123.00	142.00
	Control	100	135.57	3.29	0.33	134.92	136.22	127.00	143.00
	Total	200	135.43	3.82	0.27	134.90	135.96	123.00	149.00
Serum potassium (meq/l)	Mild preeclampsia	60	4.47	0.73	0.09	4.28	4.66	2.60	5.90
	Severe preeclampsia	40	4.28	0.74	0.12	4.04	4.51	3.20	5.90
	Control	100	4.12	0.53	0.05	4.02	4.23	3.00	5.30
	Total	200	4.26	0.65	0.05	4.17	4.35	2.60	5.90
Serum chloride (meq/l)	Mild preeclampsia	60	107.92	4.18	0.54	106.84	109.00	99.20	121.00
	Severe preeclampsia	40	106.48	3.41	0.54	105.39	107.57	100.00	112.10
	Control	100	108.20	3.19	0.32	107.56	108.83	100.00	115.60
	Total	200	107.77	3.60	0.25	107.27	108.27	99.20	121.00
Age (years)	Mild preeclampsia	60	28.78	2.91	0.37	28.03	29.54	23	40
	Severe preeclampsia	40	29.65	3.35	0.53	28.58	30.72	24	36
	Control	100	28.95	3.37	0.33	28.28	29.62	21	38
	Total	200	29.04	3.23	0.22	28.59	29.49	21	40

Table 2: A one way ANOVA to compare the means of systolic blood pressure (SBP) diastolic blood pressure (DBP), serum sodium, potassium and chloride in control, mild preeclampsia and severe preeclampsia group.

ANOVA						
Parameters		**Sum of squares**	**df**	**Mean square**	**F**	**Sig.**
Systolic BP	Between groups	87988.31	2	43994.15	465.48	0.000
	Within groups	18619.04	197	94.51		
	Total	106607.35	199			
Diastolic BP	Between groups	30192.74	2	15096.37	213.69	0.000
	Within groups	13917.13	197	70.64		
	Total	44109.87	199			
Serum sodium	Between groups	45.52	2	22.76	1.56	0.212
	Within groups	2865.49	197	14.54		
	Total	2911.02	199			
Serum potasium	Between groups	4.49	2	2.24	5.55	0.004
	Within groups	79.59	197	0.404		
	Total	84.08	199			
Serum chloride	Between groups	86.17	2	43.08	3.40	0.035
	Within groups	2491.37	197	12.64		
	Total	2577.55	199			

Table 3: Post hoc comparisons using the Sidak test for multiple comparisons.

Multiple comparisons using Sidak test							
Dependent variables	**Category**	**Category**	**Mean difference (I-J)**	**Std. error**	**Sig.**	**95% CI**	
						Lower bound	**Upper bound**
Systolic BP	Mild	Severe	-22.26667*	1.98445	0.000	-26.1802	-18.3532
	Control	Mild	-30.10333*	1.58756	0.000	-33.2341	-26.9725
		Severe	-52.37000*	1.81878	0.000	-55.9568	-48.7832
Diastolic BP	Mild	Severe	-9.42500*	1.71568	0.000	-12.8085	-6.0415
	Control	Mild	-19.92000*	1.37254	0.000	-22.6268	-17.2132
		Severe	-29.34500*	1.57245	0.000	-32.4460	-26.2440
Serum sodium	Mild	Severe	1.31667	0.77850	0.092	-0.2186	2.8519
	Control	Mild	-0.24667	0.62280	0.692	-1.4749	0.9816
		Severe	1.07000	0.71351	0.135	-0.3371	2.4771
Serum potassium	Mild	Severe	0.19083	0.12975	0.143	-0.0650	0.4467
	Control	Mild	-0.34533*	0.10380	0.001	-0.5500	-0.1406
		Severe	-0.15450	0.11892	0.195	-0.3890	0.0800
Serum chloride	Mild	Severe	1.44167*	0.72591	0.048	0.0101	2.8732
	Control	Mild	0.27533	0.58073	0.636	-0.8699	1.4206
		Severe	1.71700*	0.66530	0.011	0.4050	3.0290

*The mean difference is significant at the 0.05 level.

A one way ANOVA was performed between subjects to compare the means of systolic blood pressure (SBP) Diastolic blood pressure (DBP), serum sodium, potassium and chloride in control, mild preeclampsia and severe preeclampsia group. There was a significant difference of systolic blood pressure mean at the $p<0.01$ for the three groups [F (2,197) =465.48, p=0.00]. There was also significant difference of diastolic blood pressure mean at the $p<0.01$ for the three groups [F (2,197) =213.69, p=0.00]. There was no such difference in case of serum sodium at $p<0.05$ levels for the three groups [F (2,197) =1.56, p=0.21]. There was significant difference in case of serum potassium mean at $p<0.01$ levels for the three groups [F (2,197)=5.55, p=0.004]. Similarly in case of serum chloride mean levels there was significant difference at $p<0.05$ levels for the three groups [F (2,197) =3.40, p=0.035].

Post hoc comparisons using the Sidak test for multiple comparisons found that there was statistically significant difference in SBP between the means of control, mild preeclampsia and severe preeclampsia group with p=0.00 and 95% confidence interval of (-26.18-18.35) in case of mild versus severe preeclampsia; CI of (-33.23-26.97) in case of control versus mild and CI of (-55.95-48.78) in case of control vs severe group. Same was the case with

DBP having significant statistical difference among the three groups: control versus mild preeclampsia, mild preeclampsia versus severe preeclampsia and control versus severe preeclampsia with p=0.00.

In case of serum sodium there was no statistically significant difference between the means of any group p>0.05, however in case of potassium there was significant difference in means of control and mild group p<0.05. In case of serum chloride there was statistically significant difference in means between mild versus severe (p<0.05) and control versus severe preeclampsia group with p<0.05.

DISCUSSION

This study was conducted to find association between severity of preclampsia and the electrolytes serum sodium potassium and chloride. In the study preeclampsia was more common in second pregnancy (37%) and primigavidae (24%). There was no statistically significant difference between maternal age and preeclampsia.

The mean systolic blood pressure and diastolic blood pressure (SBP and DBP) among the three studied groups showed statistical difference as shown in Table 3 with higher blood pressure observed in preclampsia (both in case of mild and severe preeclampsia) as was previously shown in the study by Macdonald-Wallis et al and Ramasamy et al.[10,11]

The homeostasis of sodium and potassium plays a key role in endothelium-dependent vasodilatation, which is defective in primary hypertension.[7] Sodium retention decreases the synthesis of nitric oxide, an arteriolar vasodilator elaborated by endothelial cells, and increases the plasma level of asymmetric dimethyl L-arginine, an endogenous inhibitor of nitric oxide production.[9] In our study there was mild decrease of sodium mean levels in severe preeclampsia (134.50±4.24) as compared to control group (135.57±3.29) but there was no statistically significant difference in means of serum sodium of the preeclampsia (mild or severe) and control group which is in conformity with other studies like that of Adewolu et al Bera et al but differed from studies that showed statistically significant difference in means of preeclampsia and normotensive with some studies like Prafula et al, showing increase in sodium levels in preeclamptics while others like Indumati et al, which revealed decrease sodium in them.[12-15] Sodium apart from acting at renal tubular level causes activation of the brain renin-angiotensin-aldosterone system (RAAS), which is suggested to increase blood pressure through angiotensin II and aldosterone promoting locally oxidative stress and activating the sympathetic nervous system.[16] Although the role of RAAS in preeclampsia is inconclusive the increase in extracellular volume, the degree of RAAS stimulation and the reduced pressor response to angiotensin II are less marked in preeclampsia. However, animal models displaying increased RAAS activation also result in a pre-eclampsia-like syndrome, and the aldosterone/renin ratio is raised in pre-eclampsia compared with a normal pregnancy.[17]

In our study serum potassium mean showed statistically significance between the mild preeclampsia (n=60) and control group (4.47±0.73 versus 4.12±0.53 mEq/l) as was previously shown by study of Handwerker et al while there was no statistically significance between other groups of mild versus severe preeclampsia or control versus severe preeclampsia.[18] In preeclampsia and pregnancy induced hypertension there is an abnormality in the transport of sodium and potassium across the cell membrane of vascular smooth muscles which regulates blood pressure.[19] A common hypothesis to explain the abnormalities in preeclampsia has been the presence of placenta-derived endogenous digitalis-like factor(s) (EDLFs) in plasma. These factors, which resemble or are identical to cardiotonic steroids, inhibit the sodium potassium adenosine triphosphatase (Na/K ATPase) enzyme transport complex, which functions as the sodium pump (SP) so like digitalis they can cause inhibition of (Na/K ATPase) and hyperkalemia.[20]

Not many studies have been done on chloride levels and preeclampsia but the role of chloride in hypertension has been elucidated by researchers with animal and limited human studies, in our study we found like sodium it followed a trend wherein there was decreased means levels of chloride from control group to severe preeclampsia group and there was statistically significant difference of means of chloride between severe preeclampsia and control group and control versus mild group.[21]

Limitation of the study was the sample size was small, further studies with bigger sample size will throw more light on this hypothesis

CONCLUSION

In our study serum levels of sodium were not significantly different between the three groups although there was decreased levels in severe preeclampsia group as compared to control group. Similarly mean serum potassium levels in control versus mild had statistical significance. While as in case of chloride it followed the trend of sodium levels and mean was lower in severe preeclampsia group as compared to other two groups. These observations suggest a derangement in electrolytes in women with PIH. It is still unclear if this is a consequence of raised blood pressure in observed in preeclampsia or, as advocated by a number of other studies, a consequence of the disorder.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Kuklina EV, Ayala C, Callaghan WM. Hypertensive disorders and severe obstetric morbidity in the United States. Obstet Gynecol. 2009;113(6):1299-306.
2. Abalos E, Cuesta C, Grosso AL, Chou D, Say L. Global and regional estimates of preeclampsia and eclampsia: a systematic review. Eur J Obstet Gynecol Reprod Biol. 2013;170(1):1-7.
3. Brown MA, Magee LA, Kenny LC, Karumanchi SA, McCarthy FP, Saito S, et al. Hypertensive disorders of pregnancy: ISSHP classification, diagnosis, and management recommendations for international practice. Hypertension. 2018;72(1):24-43.
4. Khalil G, Hameed A. Preeclampsia: pathophysiology and the maternal-fetal risk. J Hypertens Manag. 2017;3:024.
5. Granger JP, Alexander BT, Llinas MT, Bennett WA, Khalil RA. Pathophysiology of preeclampsia: linking placental ischemia/hypoxia with microvascular dysfunction. Microcirculation. 2002;9:147-60.
6. Rampersad R, Nelson DM. Trophoblast biology, responses to hypoxia and placental dysfunction in preeclampsia. Front Biosci. 2007;12:2447-56.
7. Panza JA, Quyyumi AA, Brush JE Jr, Epstein SE. Abnormal endothelium-dependent vascular relaxation in patients with essential hypertension. N Engl J Med. 1990;323:22-7.
8. Fujiwara N, Osanai T, Kamada T, Katoh T, Takahashi K, Okumura K. Study on the relationship between plasma nitrite and nitrate level and salt sensitivity in human hypertension: modulation of nitric oxide synthesis by salt intake. Circulation. 2000;101:856-61.
9. Adrogué HJ, Madias NE. Sodium and potassium in the pathogenesis of hypertension. N Engl J Med. 2007;356:1966-78.
10. Macdonald-Wallis C, Lawlor DA, Fraser A, May M, Nelson SM, Tilling K. Blood pressure change in normotensive, gestational hypertensive, preeclamptic, and essential hypertensive pregnancies. Hypertension. 2012;59(6):1241-8.
11. Ramasamy S, Rajagambeeram R, Ramasamy R, Saravanan S. Assessment of serum electrolytes and divalent cation in preeclampsia: a comparative study. J Basic Clin Appl Health Sci. 2020;3(4):154-7.
12. Adewolu O. Serum sodium, potassium, calcium and magnesium in women with pregnancy induced hypertension and preeclampsia in Oredo local Government, Benin Metropolis: a pilot study. Afr J Med Health Sci. 2013;12:1-5.
13. Bera S, Siuli RA, Gupta S, Roy TG, Taraphdar P, Bal R, et al. Study of serum electrolytes in pregnancy induced hypertension. J Indian Med Assoc. 2011;109(8):546-8.
14. Prafula KM. Evaluation of serum electrolytes in preeclamptic pregnant women: a hospital based study. Glob J Res Anal. 2017;6:12-23.
15. Indumati V, Kodliwadmath MV, Sheela MK. The role of serum electrolytes in pregnancy induced hypertension. J Clin Diagn Res. 2011;5(1):66-9.
16. Takahashi H, Yoshika M, Komiyama Y, Nishimura M. The central mechanism underlying hypertension: A review of the roles of sodium ions, epithelial sodium channels, the renin-angiotensin-aldosterone system, oxidative stress and endogenous digitalis in the brain. Hypertens. Res. 2011;34:1147-60.
17. Verdonk K, Visser W, Van Den Meiracker AH, Danser AJ. The renin-angiotensin-aldosterone system in pre-eclampsia: the delicate balance between good and bad. Clin Sci. 2014;126(8):537-44.
18. Handwerker SM, Altura BT, Altura BM. Ionized serum magnesium and potassium levels in pregnant women with preeclampsia and eclampsia. J Reprod Med. 1995;40(3):201-8.
19. Arumanayagam M, Rogers M. Platelet sodium pump and sodium potassium cotransport activity in nonpregnant, normotensive, and hypertensive pregnant women. Hypertens Pregnancy. 1999;18(1):35-44.
20. Graves SW. Sodium regulation, sodium pump function and sodium pump inhibitors in uncomplicated pregnancy and preeclampsia. Front Biosci. 2007;12:2438-46.
21. McCallum L, Lip S, Padmanabhan S. The hidden hand of chloride in hypertension. Pflugers Arch. 2015;467(3):595-603.

Cite this article as: Khan JA, Ashra A, Qureshi WA, Fayaz F. Comparison of serum electrolytes with preeclampsia severity: a cross sectional study. Int J Res Med Sci 2022;10:2586-91.