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Research Article

The effects of using lithium on biochemical factors of urinary beta-2 microglobulin, creatinine and urea serum in chronic bipolar patients

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ABSTRACT

In this research, the effects of using lithium on biochemical factors of urinary beta-2 microglobulin, creatinine and urea serum in chronic bipolar patients hospitalized in Razi psychiatric center are investigated. For this purpose, random sampling method was used and among hospitalized patients in Tehran's Razi psychiatric center. Then 87 patients were selected and urinary beta-2 microglobulin tests by ELISA method, urea and blood serum by enzymatic method measured in 42 bipolar patients (including 18 females - 24 males) that using lithium and 45 bipolar patients (including 21 females - 24 males) that using drugs other than lithium. According to studies, lithium-treated bipolar patients have a substantially greater urine beta-2 microglobulin concentration than individuals who are not lithium-treated (Pvale> 0.028). The results demonstrated that the longer time of using lithium will cause higher amount of urinary beta-2 microglobulin secretion (Pval > 0.027). Also, the results showed that the value of creatinine and urea serum were not significantly different between two groups. Finally, it seems that urinary beta-2 microglobulin is a better indicator than urea and creatinine serum to evaluate the side effects of primary kidney damages caused by lithium, and its main role in diagnosis of the disease requires further researches in this field.

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INTRODUCTION

One of the most important psychiatric drugs that causes side effects is lithium, and there is a concern that treatment with lithium can cause kidney problems and, in rare cases, dialysis of patient [1]. Therefore, psychiatrists who use this drug to treat bipolar patients, in order to reduce toxicities and drug side effects, check the blood serum lithium levels of patients on a monthly basis. First, kidney dysfunction in bipolar patients treated with lithium reported in 1970 [2,3].

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Lithium is known as the first-line treatments for the manic and depressive phases of bipolar disorder. It protects against depression and mania as well as being the only therapy known to decrease suicide risk in this patient population [3] with a composite measure of suicide plus deliberate self-harm lowered in patients receiving lithium [4,5]. Even with the availability of newer treatments, lithium is still considered the first-line treatment when prescribing a relapse-prevention drug in bipolar disorder. It has efficacy in the prevention of both manic and depressiveepisode relapse or recurrence [6-10], having the most robust evidence for long-term relapse prevention [11].

In one study, as we need to know about the effect of lithium on the kidney stated that, lithium is a valuable drug in recent decades for the treatment of bipolar patients, although therapeutic use of lithium due to its toxicity in various body systems is problematic. Kidney side effects include polyuria, nephrogenic diabetes, proteinuria, kidney tubular acidosis, and decreased kidney filtration. Pathologically, chronic toxicity of lithium in the kidney is diagnosed by interstitial nephritis with small glomerulus cysts. Although this toxicity is not common, but the risk increases with the dose of lithium usage and the duration of use [12-15]. In an experimental model, lithium has a protective and restorative role in proteinuria diseases. This duality or inconsistency may be due to the short time use or low dose of the drug. However, long term use and high doses of lithium can cause nephrotoxic agents. Short time and low dose of lithium usage may be a point for improving kidney function [9]. In Poznan, Poland, a group of 111 patients (25 male, 76 female) who received lithium for 5-39 (mean 18) years regarding clinical factors associated with the prophylactic efficacy of lithium was assumed. It is found a better effect in patients with later illness onset, no family history of mood disorders, and family members on prophylactic lithium, as well as in women with comorbid anxiety disorders and men who did not abuse alcohol [10]. Recently, British researchers performed a meta-analysis of 71 studies with a total of 12,000 patients regarding clinical factors associated with quality of prophylactic lithium response. They identified such positive features as a mania-depression-remission episode sequence, non-rapid-cycling, no psychotic episodes, a family history of bipolar disorder, short illness duration prior to lithium initiation, and later illness onset. Fewer episodes and hospitalizations prior to lithium treatment, as well as lithium treatment in other family members were also described as favorable factors [16,17].

In a 2020 study, Nunes *et al.*23 assessed 1,266 lithium-treated patients from seven European and Canadian centers. In agreement with previous results, the authors demonstrated that an episodic clinical course and non-rapid-cycling were the most significant factors for a good lithium response [18-20].

Beta-2 microglobulin, is also a small molecule with a molecular weight of 11,800 daltons that is observable on the surface of human nucleated cells and in part of MHC calss1 (Major Histocompatibility Complex). Increased beta-2 microglobulin occurs in kidney malignancies, immune system defects and autoimmune diseases. Beta-2 microglobulin dependence is evident in cardiac death, CKD and hemodialysis as well as thrombotic and vascular diseases. However, the association between MIA syndrome (Malnutrition, Inflammation, and Atherosclerosis) and beta-2 microglobulin has not been well studied [21-24]. Therefore, the diagnosis of drug therapies' side effects, especially the side effects of lithium in patients, and taking timely and effective measures to minimize these side effects in addition to reducing physical and behavioral problems, increases the patient's motivation to use the drug [25-27]. Finally, the objective of this research is evaluating the effects of using lithium on biochemical factors of urinary beta-2 microglobulin, creatinine and urea serum in chronic bipolar patients hospitalized in Razi psychiatric center by conducting several tests on specific persons.

MATERIAL AND METHODS

Materials

This research is a retrospective or comparative scientific research. The statistical population of this research includes all patients with bipolar disorder who are hospitalized in different wards of psychiatric center. The sample size of this study is 87 patients (male and female) with chronic bipolar disorder. Out of the sample number, 43 bipolar patients treated with lithium were randomly selected as experimental group. And 45 bipolar patients treated with drugs other than lithium were placed in the control group. The target group consisted of 24 males and 18 females and the control group included 24 males and 21 females. The method of testing conduction is as follows:

Beta-2 Microglobulin Test

Beta-2 microglobulin can be measured by quantitative luminescence and ELISA methods, we used ELISA method.

Urea Test

Urea can be measured enzymatically (indirectly) and chemically (directly). In this research, the chemical method has been used.

Creatinine Test

Creatinine is similar to urea can be measured in two methods: chemical and enzymatic methods. In this article, we used the chemical method (Pars test kits).

For statistical analysis, SPSS-20 computer software was used and for this purpose, to test the research hypotheses through t-test for independent groups was used.

RESULTS AND DISCUSSION

The linear regression model that used here is also known as covariance analysis models. In this model, the variables

of gender and type of used drug are considered as the factor and the variables of age and duration of drug usage are considered as continuous predictor variables or urgency. Tables (1) to (9) demonstrate the results of fitting the linear regression model with each of the beta-2 microglobulin, creatinine and urea variables as response variables.

Beta-2 Microglobulin

In order to evaluate the variables of gender, duration of use, patient age and type of used drug, the amount of beta-2 microglobulin measured and linear regression model was used. The variance analysis of the regression model to evaluate the relation between mentioned variables and the amount of beta-2 microglobulin in patients is shown in Table (1). The variance of a variable shows the amount of fluctuations or variability of a variable. In a homogeneous population where no factor affects the decrease or increase of beta-2 microglobulin, no variability will be observed in the beta-2 microglobulin variable. These factors can be gender, age of the patient, duration of drug usage and type of drug or even other factors that have not been considered by the researcher. Other factors in the modeling literature are called error or residual factors. Therefore, in the absence of any effective factor on beta-2 microglobulin (factors considered in the research and error factor), the variance of this variable will be zero.

Table (1) demonstrates the contribution of each variable in increasing the variance of the response variable in the sum of square column. If the contribution of one factor is large enough compared to the contribution of other factors (error component), we say that the factor has a significant relation with the response variable, because by changing the response variable (increasing or decreasing it) the variance increases. According to the table above, the effect of drug type as well as the interaction effect of drug type and duration of usage is significant at the test level of 0.05. The effect of other factors is not significant at the test level of 0.05.

It should be noted that the tests carried out in Table (2) are based on hypotheses, the most important of which are the assumption of variance homogeneity of the response variable and the normality of the error component distribution in the regression model. If either of these two hypotheses is not observed, the results presented in the table above will not be valid. Between these two assumptions, deviation from the assumption that the error component is normal when the sample size is large enough has less effect on the validity of the reported results. The variance homogeneity hypothesis states that the variance of the error component is not related to any of the predictor variables in the regression model. This hypothesis can be tested by modeling the quadratic power of the previous regression model with the predictor variables shown in Table (2). If at least one of the predictor variables has a significant relation with the quadratic power of the regression model, the assumption of variance homogeneity will be rejected.

The result of variance homogeneity test is reported in Table (2). The null hypothesis in the hypothesis test performed in this table is the variance homogeneity of the error component. As can be seen, the assumption of variance homogeneity at the test level of 0.05 was not rejected.

Therefore, according to the assumption of variance homogeneity, the results reported in Table (2) can be cited

Table 1. The variance analysis of regression model for evaluating beta-2 microglobulin

Source of variations	Sum of square	Degree of freedom	Mean of square	F	Probability value	Power of the test
Type of drug	4/192	1	4/192	7/682	0/007	0/782
Gender	0/954	1	0/954	1/748	0/190	0/257
Interaction effect between drug type and gender	0/049	1	0/049	0/090	0/765	0/060
Age	0/036	1	0/036	0/067	0/797	0/057
Duration of use	0/001	1	0/001	0/001	0/994	0/050
Interaction effect between drug type and duration of use	2/766	1	2/766	5/069	0/027	0/604
Error	43/652	80	0/546			
Revised total	49/421	86				

Table 2. Test of variance homogeneity hypothesis in regression model

Source of variations	Sum of square	Degree of freedom	Mean of square	F	Probability value
Revised model	436/383	6	72/730	1/033	0/410
Error	5630/157	80	70/377		
Revised total	6066/540	86			

that based on the result, it was observed that the type of drug used as well as the interaction effect between the type of drug used and the duration of the use at the test level of 0.05 is significant. In order to determine the relation between these variables and the level of beta-2 microglobulin in the blood serum of patients, we will refer to the table for estimating the parameters of the regression model. Parameters estimation of this regression model is reported in Table (3). In this test table, the hypothesis related to each of the model parameters is reported in two methods, parametric and non-parametric. The non-parametric tests were performed using the Bootstrap re-sampling algorithm. Bootstrap algorithm is a non-parametric method based on data re-sampling to estimate the analysis distribution of estimators to provide confidence interval, bias calculation, standard error and hypothesis testing. In Table (3), the reported asymptotic result is that if the error component is not assumed to be normal, the results obtained are almost correct if the sample size is large.

According to the table above, the effect of drug type as well as the interaction effect of drug type and duration of usage at the test level of 0.05 was significant with both parametric and non-parametric test methods. According to the estimation of the parameters, it can be inferred that the mean of beta-2 microglobulin in patients who have used lithium-containing drugs is on average 0.759 higher than patients who have used lithium-free drugs.

Given to the parameter estimation of the interaction effect between the duration of use and the type of drug, it can be inferred that with each year of increasing the period of drug use, the effect of lithium drug increases by an average of 0.037 mg / μl.

Creatinine

In order to evaluate the effect of gender, duration of usage, patient age and type of used drug variables on the amount of creatinine measured in the serum of patients, a linear regression model was used. Table (4) demonstrates the result of variance analysis of this regression model.

Table (4) demonstrates the contribution of each variable in increasing the variance of the response variable in the sum of squares column. According to the table above, the probability value of gender effect and age of the patient is close to the test level of 0.05.

The assumption of variance homogeneity in this regression model has been studied by modeling the quadratic power of its residuals and the result is reported in Table (5). If at least one of the predictor variables has a significant

Table 3. Parameters estimation of regression model for evaluating beta-2 microglobulin

		Parametric (asymptotic)			Non-parametric (Bootstrap)	
Parameter	**Estimation**	**Standard error**	**T**	**Probability value**	**Standard error**	**Probability value**
Intercept	0/215	0/409	0/526	0/601	0/353	0/544
Type of drug	0/759	0/339	2/239	0/028	0/365	0/048
Gender (male)	0/268	0/228	1/178	0/242	0/177	0/139
Type of drug (lithium) × Gender (male)	0/103	0/343	0/300	0/765	0/346	0/760
Age	0/002	0/008	0/258	0/797	0/007	0/743
Duration of use	0/019	0/013	1/481	0/142	0/015	0/192
Type of drug (lithium) × Duration of use	0/037	0/017	2/252	0/027	0/018	0/044

Table 4. Variance analysis of regression model for evaluating the creatinine amount in patients

Source of variations	**Sum of square**	**Degree of freedom**	**Mean of square**	**F**	**Probability value**	**Power of the test**
Type of drug	0/043	1	0/043	0/514	0/475	0/109
Gender	0/312	1	0/312	3/685	0/058	0/475
Interaction effect between drug type and gender	0/000	1	0/000	0/000	0/985	0/050
Age	0/318	1	0/318	3/761	0/056	0/483
Duration of use	0/108	1	0/108	1/275	0/262	0/200
Interaction effect between drug type and duration of use	0/075	1	0/075	0/887	0/349	0/154
Error	6/763	80	0/085			
Revised total	8/150	86				

Table 5. Test of variance homogeneity hypothesis in regression model for evaluating the creatinine amount in patients

Source of variations	Sum of square	Degree of freedom	Mean of square	F	Probability value
Revised model	0/137	6	0/023	0/829	0/551
Error	2/206	80	0/028		
Revised total	2/343	86			

Table 6. Parameters estimation of regression model for evaluating the creatinine amount in patients

		Parametric (asymptotic)			Non-parametric (Bootstrap)	
Parameter	**Estimation**	**Standard error**	**t**	**Probability value**	**Standard error**	**Probability value**
Intercept	0/759	0/161	4/713	0/000	0/172	0/001
Type of drug (lithium)	0/071	0/134	0/530	0/597	0/121	0/558
Gender (male)	0/123	0/090	1/367	0/175	0/111	0/272
Type of drug (lithium) × Gender (female)	0/003	0/135	0/019	0/985	0/138	0/976
Age	0/006	0/003	1/939	0/056	0/002	0/044
Duration of use	0/008	0/005	1/523	0/132	0/005	0/115
Type of drug (lithium) × Duration of use	0/006	0/007	0/942	0/349	0/006	0/296

relationship with the quadratic power of the model residues shown in Table (5), the assumption of variance homogeneity will be rejected. Given to the result reported in this table, the hypothesis of variance homogeneity at the test level of 0.05 is not rejected.

In order to determine the relation between the variables of gender and age of the patient with the level of creatinine in the urine of patients, we will refer to the table of estimation parameters of the regression model. Parameters estimation of this regression model is reported in Table (6). In this test table, the hypothesis related to each of the model parameters is reported in two methods, parametric and non-parametric. The non-parametric tests were performed using a Bootstrap sampling algorithm.

According to the result of non-parametric Bootstrap test in the table above, only the effect of patient age is significant at the test level of 0.05. Note that the results reported by the non-parametric method are more conservative than the parametric method. In this study, because the sample size is not large enough, the result reported by the non-parametric method is the decision criterion. According to the estimation of the parameters, it can be inferred that the creatinine level in the serum of patients increases with an average of 0.006 mg / dl with each year of increase in age.

Urea

In order to evaluate the effect of gender, duration of usage, patient age and type of used drug variables on the amount of urea measured in the serum of patients, linear regression model was used. Table (7) demonstrates the result of variance analysis of this regression model.

Table (7) demonstrates the contribution of each variable in increasing the variance of the response variable in the

Table 7. Variance analysis of regression model for evaluating the urea amount in patients

Source of variations	Sum of square	Degree of freedom	Mean of square	F	Probability value	Power of the test
Type of drug	45/382	1	45/382	0/582	0/448	0/117
Gender	32/246	1	32/246	0/413	0/522	0/097
Interaction effect between drug type and gender	0/504	1	0/504	0/006	0/936	0/051
Age	2/418	1	2/418	0/031	0/861	0/053
Duration of use	896/204	1	896/204	11/485	0/001	0/917
Interaction effect between drug type and duration of use	135/550	1	135/550	1/737	0/191	0/256
Error	6242/450	80	78/031			
Revised total	7997/103	86				

Table 8. Test of variance homogeneity hypothesis in regression model for evaluating the urea amount in patients

Source of variations	Sum of square	Degree of freedom	Mean of square	F	Probability value
Revised model	200757/210	6/000	33459/535	1/613	0/154
Error	1659291/998	80/000	20741/150		
Revised total	1860049/208	86/000			

Table 9. Parameters estimation of regression model for evaluating the urea amount in patients

		Parametric (asymptotic)			Non-parametric (Bootstrap)	
Parameter	**Estimation**	**Standard error**	**t**	**Probability value**	**Standard error**	**Probability value**
Intercept	24/911	4/892	5/092	0/000	4/367	0/001
Type of drug (lithium)	-2/494	4/056	-0/615	0/540	3/418	0/461
Gender (male)	-1/426	2/724	-0/523	0/602	2/578	0/575
Type of drug (lithium) × Gender (male)	0/330	4/105	0/080	0/936	4/137	0/933
Age	0/017	0/095	0/176	0/861	0/086	0/839
Duration of use	0/280	0/063	2/254	0/047	0/126	0/025
Type of drug (lithium) × Duration of use	0/261	0/198	1/318	0/191	0/228	0/263

sum of square column. According to the table above, the duration of use effect on urea level in patients' serum at the test level of 0.05 is significant.

The assumption of variance homogeneity in this regression model is evaluated by modeling the quadratic power of the residuals of this model and the result is reported in Table (8). If at least one of the predictor variables has a significant relationship with the quadratic power of the model residues shown in Table (7), the assumption of variance homogeneity will be rejected. According to the result reported in this table, the hypothesis of variance homogeneity at the test level of 0.05 is not rejected.

In order to determine the relation between the duration of use variable and the level of urea in the urine of patients, we will refer to the table of parameters estimation of the regression model. Parameters estimation of this regression model is reported in Table (9). In this test table, the hypothesis related to each of the model parameters is reported in two methods, parametric and non-parametric. The non-parametric tests were performed using the Bootstrap resampling algorithm.

According to the table above, the test performed by non-parametric Bootstrap method also confirms the result obtained in the analysis of variance table. In the table above, only the effect of duration of usage at the test level of 0.05 is significant. According to the parameter estimation column, it can be inferred that the level of urea in the serum of patients increases with an average of 0.28 mg / dl with increase of each year of use.

CONCLUSION

In the present research, the results demonstrated that patients using lithium had a higher mean of urinary beta-2 microglobulin than those who did not use it. Although this difference was not observable for urea and serum biomarkers, but it can also be inferred from this study that the mean of urinary beta-2 microglobulin in bipolar patients using lithium. On average, 0.258 μg / ml was higher in men and 0.283 μg / ml in women than in patients who did not use lithium. A similar study in 2013 reported that women and men who used lithium had an increase in urinary beta-2 microglobulin and a decrease in urinary specific gravity and GFR compared to those who did not use lithium [15]. In our study, it was evident that the longer the lithium is used, the higher the urinary beta-2 microglobulin secretion, and given the significance of interaction effect between the duration of use and the type of drug, it can be inferred that with each year increasing lithium use, the amount of beta-2 microglobulin to 0.037 μg / ml increases. In our study, urinary beta-2 microglobulin amount were lower in women with bipolar disorder than in men but were not significant. In the case of creatinine serum, as mentioned, no significant difference was observed between the two groups, but the effect of age on creatinine serum was greater, i.e. it can be inferred that with increasing age each year, the average of 0.006 mg/dl the amount of creatinine serum increases. In each group separately, creatinine serum was higher in men than women and P value was close to 0.05. In the case of urea, the difference between the two groups was not significant, but the duration of drug usage effect was significant and with the increase of each year of

usage, the amount of urea increases by an average of 0.28 mg/dl. In this study, we also concluded that lithium use increases the secretion of beta-2 microglobulin in urine and the longer it is used, the higher the secretion of beta-2 microglobulin, but this difference was not observed in urea and serum creatinine. These results suggest that urinary beta-2 microglobulin is a better indicator for assessing primary kinery damages caused by using lithium.

AUTHORSHIP CONTRIBUTIONS

Authors equally contributed to this work.

DATA AVAILABILITY STATEMENT

The authors confirm that the data that supports the findings of this study are available within the article. Raw data that support the finding of this study are available from the corresponding author, upon reasonable request.

CONFLICT OF INTEREST

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

ETHICS

There are no ethical issues with the publication of this manuscript.

STATEMENT ON THE USE OF ARTIFICIAL INTELLIGENCE

Artificial intelligence was not used in the preparation of the article.

REFERENCES

[1] Chang CWL, Ho CSH. Lithium use in a patient with bipolar disorder and end-stage kidney disease on hemodialysis: a case report. Front Psychiatry 2020;11:6. [CrossRef]

[2] McKnight RF, Adida M, Budge K, Stockton S, Goodwin GM, Geddes JR. Lithium toxicity profile: a systematic review and meta-analysis. Lancet 2012;379:721–728. [CrossRef]

[3] Davis J, Desmond M, Berk M. Lithium and nephrotoxicity: a literature review of approaches to clinical management and risk stratification. BMC Nephrol 2018;19:305. [CrossRef]

[4] Yatham LN, Kennedy SH, Parikh SV, Schaffer A, Bond DJ, Frey BN, et al. Canadian network for mood and anxiety treatments (CANMAT) and International Society for Bipolar Disorders (ISBD) 2018 guidelines for the management of patients with bipolar disorder. Bipolar Disord 2018;20:97–170. [CrossRef]

[5] Gomes-da-Costa S, Marx W, Corponi F, Anmella G, Murru A, Pons-Cabrera MT, et al. Lithium therapy and weight change in people with bipolar disorder: a systematic review and meta-analysis. Neurosci Biobehav Rev 2022;134:104266. [CrossRef]

[6] Geddes JR, Miklowitz DJ. Treatment of bipolar disorder. Lancet 2013;381:1672–1682. [CrossRef]

[7] Decker BS, Goldfarb DS, Dargan PI, Friesen M, Gosselin S, Hoffman RS, et al. Extracorporeal treatment for lithium poisoning: systematic review and recommendations from the EXTRIP Workgroup. Clin J Am Soc Nephrol 2015;10:875–887. [CrossRef]

[8] Nielsen RE, Kessing LV, Nolen WA, Licht RW. Lithium and renal impairment: a review on a still hot topic. Pharmacopsychiatry 2018;51:200–205. [CrossRef]

[9] Ferensztajn-Rochowiak E, Chłopocka-Woźniak M, Rybakowski JK. Ultra-long-term lithium therapy: all-important matters and a case of successful 50-year lithium treatment. Braz J Psychiatry 2020;43:407–413. [CrossRef]

[10] Dembinska-Krajewska D, Kliwicki S, Chłopocka-Woźniak M, Rybakowski J. The effectiveness of prophylactic use of lithium in bipolar disorder and schizotypal traits. Pharmacother Psychiatr Neurol 2012;28:153–158.

[11] Hui TP, Kandola A, Shen L, Lewis G, Osborn DP, Geddes JR, et al. A systematic review and meta-analysis of clinical predictors of lithium response in bipolar disorder. Acta Psychiatr Scand 2019;140:94–115. [CrossRef]

[12] Nunes A, Ardau R, Berghöfer A, Bocchetta A, Chillotti C, Deiana V, et al. Prediction of lithium response using clinical data. Acta Psychiatr Scand 2020;141:131–141. [CrossRef]

[13] Wu HC, Lee LC, Wang WJ. Associations among serum beta 2 microglobulin, malnutrition, inflammation, and advanced cardiovascular event in patients with chronic kidney disease. J Clin Lab Anal 2017;31:e22056. [CrossRef]

[14] Alsady M, Baumgarten R, Deen PM, de Groot T. Lithium in the kidney: friend and foe. J Am Soc Nephrol 2016;27:1587–1595. [CrossRef]

[15] Rybakowski JK, Abramowicz M, Chłopocka-Wozniak M, Czekalski S. Novel markers of kidney injury in bipolar patients on long-term lithium treatment. Hum Psychopharmacol 2013;28:615–618. [CrossRef]

[16] Sato T, Akatsuka H, Yamaguchi Y, Miyashita K, Tanaka M, Tamaki T, et al. Establishment of β-2 microglobulin deficient human iPS cells using CRISPR/Cas9 system. Integr Mol Med 2015;2:373–377. [CrossRef]

[17] Chen P, Lin WL, Liu XY, Li SJ, Chen RF, Hu ZH, et al. D30 alleviates β2-microglobulin–facilitated neurotoxic microglial responses in isoflurane/surgery-induced cognitive dysfunction in aged mice. Lab Invest 2025;105:102190. [CrossRef]

[18] Baldemir H, Akin A, Akin O. Two modified forms of the SAIR model with a fuzzyfied vaccination effectiveness parameter. Sigma 2025;43:887–898. [CrossRef]

[19] Li L, Dong M, Wang XG. The implication and significance of beta 2 microglobulin: a conservative multifunctional regulator. Chin Med J 2016;129:448–455. [CrossRef]

[20] Meyer JM. Demystifying lithium therapy – A primer for clinicians: lithium-related polyuria. Psychiatr Times 2025;42:1.

[21] Wu HC, Lee LC, Wang WJ. Associations among serum beta 2 microglobulin, malnutrition, inflammation, and advanced cardiovascular event in patients with chronic kidney disease. J Clin Lab Anal 2017;31:e22056. [CrossRef]

[22] Shi F, Sun L, Kaptoge S. Association of beta-2-microglobulin and cardiovascular events and mortality: a systematic review and meta-analysis. Atherosclerosis 2021;320:70–78. [CrossRef]

[23] Abrams Z. Diagnosing and treating bipolar spectrum disorders. Monit Psychol 2022;53:36–41.

[24] Malhi GS, Gessler D, Outhred T. The use of lithium for the treatment of bipolar disorder: recommendations from clinical practice guidelines. J Affect Disord 2017;217:266–280. [CrossRef]

[25] Nguyen T, Seiler N, Brown E, O'Donoghue B. The effect of clinical practice guidelines on prescribing practice in mental health: a systematic review. Psychiatry Res 2020;284:112671. [CrossRef]

[26] Khawagi WY, Steinke DT, Nguyen J, Pontefract S, Keers RN. Development of prescribing safety indicators related to mental health disorders and medications: modified e-Delphi study. Br J Clin Pharmacol 2021;87:189–209. [CrossRef]

[27] Nikolova VL, Pattanaseri K, Hidalgo-Mazzei D, Taylor D, Young AH. Is lithium monitoring NICE? Lithium monitoring in a UK secondary care setting. J Psychopharmacol 2018;32:408–415. [CrossRef]