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Neutrophil/lymphocyte ratio: Can a non-specific marker of inflammation helps to confirm the inflammatory hypothesis of the serious mental diseases? A case-control study

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ABSTRACT

Background: The hypotheses of autoimmune, allergic or infectious etiology of severe mental illness have been reported in the scientific literature repeatedly. The main objective of this work is to study the relationship of inflammatory, autoimmunity or recent infection markers with the fact of suffering Severe Mental Disorders (SMD).

Methods: In the present case-control study, adult patients with a diagnosis of SMD were compared with controls who underwent routine health checks that included analytical control. Cases with psychosis substance-induced and controls with diagnosis of any psychiatric illness were excluded. In both groups, patients with chronic inflammatory diseases or intercurrent infectious disease were also excluded. A set of common analytical parameters, markers of infectious diseases and inflammatory markers were retrieved for both groups, as well as demographic and clinical data.

Results: A total of 212 subjects (81 cases and 131 controls) were recruited. From cases, 70 (86.4%) have a diagnosis of Schizophrenia Disease (SD) and 11 (13.6%) of Schizoaffective Disorder (SAD). In the multivariate model the female sex (OR 0.24, 95% CI 0.12–0.46) and the neutrophil-lymphocyte ratio (OR 3.00, 95% CI 1.91–4.70) were associated with the fact of being case.

Conclusions: Patients with SMD seem to have higher inflammatory markers compared to the general population, being the neutrophil-lymphocyte ratio, the marker associated with more strength. The role of inflammatory processes in the etiology of this type of disorders, if confirmed, opens interesting and innovative therapeutic possibilities.

Introduction

The hypothesis of the infectious etiology of severe mental illness is already reported in the scientific literature since bacteriae began to be known. It was in 1874 when the American Journal of Insanity published an article entitled “On the Germ-Theory of Disease” [1] that postulated this theory. After a stage of change of the scientific focus, in which the orientation of the etiology shifted towards genetics, this research path was resumed thanks, in part, to a work on slow and latent viruses in schizophrenic disorder (SD) and bipolar disorder (BD) [2].

When the hypothesis of mild underlying encephalitis [3] was described in a subgroup of severe psychiatric disorders, it is postulated that low-level neuroinflammation plays an important role in the pathogenesis of severe mental illness.

In the search for peripheral biological markers of this inflammation, different parameters have been found in the population of mental patients, such as C-reactive protein [4–7], as well as elevation of neutrophil count, decrease in lymphocyte count, increased neutrophil-lymphocyte ratio (NLR), and increased monocyte-lymphocyte ratio (MLR) in patients with Severe Mental Disorders (SMD) [8–10].

The leukocyte count is a common test in clinical practice, so we believe it may be an accessible inflammatory marker to initiate the

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clinical search of the etiology of this inflammation in patients affected by severe mental illness in which high figures are detected of the NLR.

Hypothesis

Our hypothesis is that a non-specific marker of inflammation, neutrophil/lymphocyte ratio, could help to confirm the inflammatory hypothesis of the serious mental diseases. Markers of past or recent infections by some viruses and bacteria can increase the likelihood of serious mental illness. The search for a nonspecific marker of inflammation associated with severe mental illness may be a first step in the detection protocol of an underlying infection in these pathologies.

Methods and materials

A case-control study was designed that, after authorization by the Research and Ethics Committee of the Francesc de Borja Hospital (Gandia, Valencia), was carried out with patients belonging to the Gandia Health Department, whose reference attended population is approximately 150,000 inhabitants. According to this design and the guidelines for reporting observational studies, The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement were followed (http://www.equator-network.org/reporting-guidelines/strobe/).

The cases were adult patients, attended in the Mental Health Unit of Gandia Health Department, with a diagnosis of SMD (codes included in sections F20-29 of the ICD-10) [11] and who voluntarily accepted to participate in the study. People with psychosis suspected to be induced by toxics consumption were excluded.

The National Institute of American Mental Health (NIMH) presented the most representative definition, and has reached a greater consensus, on SMD [12]. This definition includes three dimensions: 1) Diagnosis referred to psychotic disorders (excluding organic) and some personality disorders; 2) Duration of the disease and treatment considering a time exceeding two years; 3) Presence of disability referred to an impairment of moderate to severe labor, social and family functioning.

The controls were patients referred by their family doctor, attended at the Corea Health Center (Gandia, Valencia, Spain) by routine health check-ups that included analytical control and who voluntarily agreed to participate in the study. The exclusion criteria in the controls were the diagnosis or antecedents of any psychiatric illness, well suffered by the patient himself, or by an ascending relative. In both groups, patients with chronic inflammatory diseases or intercurrent infectious disease were excluded.

During the design phase, a sample size estimation was performed beforehand and, accepting an alpha risk of 0.05, a beta risk of 0.2 in a two-sided test and a proportion of exposed subjects in the control group around 60%, 76 cases and 152 controls were needed to recognize as statistically significant an odds ratio greater than or equal to 2.5.

The data sources were the Laboratory Information System (Gestlab Cointec-Indra®) and, exclusively for the cases, the clinical records through the official electronic record system (Orion Clinic V10). From them, the following variables were collected for the entire sample: age (years), gender (male or female), glucose (mg dL), urea (mg/dL), creatinine (mg/dL), glomerular filtration rate (FGE) (mL/min/1.73 m^2), sodium (mEq/L), potassium (mEq/L), chlorine (mEq/L), triglycerides (mg/dL), cholesterol (mg/dL), proteins total (g/dL), albumin (g/dL), aspartate aminotransferase (AST; U/L), alanine aminotransferase (ALT; U/L), gama glutamyl transpeptidase (GGT; U/L), C-reactive protein (mg/L), TSH (μU/mL), glycosylated hemoglobin (%), absolute neutrophil count (10^9/L, absolute lymphocyte count (10^9/L), absolute monocyte count (10^9/L), absolute platelet count (10^9/L), neutrophil–lymphocyte ratio (NLR; quotient of neutrophil and lymphocyte counts; continuous variable), platelet-lymphocyte ratio (quotient of platelet and lymphocyte counts; continuous variable) and monocyte-lymphocyte ratio (quotient of monocyte and lymphocyte counts; continuous variable). The aforementioned analytical parameters were determined in serum and whole blood, with the usual units of the clinical laboratory.

The techniques used for the detection of infectious serology were almost all qualitative, except for two of them, cytomegalovirus (CMV) which was in UA/ml (arbitrary units/ml) and Toxoplasma IgG (IU/ml); these are the only ones of those studied in which the luminescent reading is transformed into units. For all other infectious immunoglobulins, readings were made by chemiluminescence or fluorescence that transform into a value, which is not in international units. Each of the techniques corresponded to the reading values of the test provided by the Cobas (Roche) and Vidas (bioMerieux) teams. In the daily laboratory work we report qualitatively (positive/negative/indeterminate), but for this study we have collected the reading values because we think that, at least initially, the higher the reading value, the greater the amount of antibodies. The following variables were collected for the whole sample: Immunoglobulin (Ig) A (less than or equal to 400 mg/dL or greater than 400 mg/dL); Total Ig (mg/dL); Total IgG (Less than or equal to 1600 mg/dL/greater than 1600); total Ig M (less than or equal to 230 mg/dL/greater than 230 mg/dL IgM); antinuclear antibodies (UI/mL: less than or equal to 0.69/greater than 0.69), antibodies IgG against Toxoplasma gondii (UI/mL: positive/negative/indeterminate), IgM antibodies against *T. gondii* (positive/negative/indeterminate), IgG antibodies against human CMV (UA/mL: positive/negative/indeterminate), IgM antibodies to CMV (negative/indeterminate/positive), IgG antibodies to the Epstein Barr -VCA viral capsid of the EBV – (positive/negative/indeterminate), IgM antibodies to the EBV VCA (negative/indeterminate/positive), IgG antibodies to the EBV nuclear antigen-EBNA – (Negative/indeterminate/positive) and IgG antibodies to varicella zoster virus -VVZ- (negative/indeterminate/positive).

For the patients included in the case group, the following were also collected: Diagnosis (Schizophrenia/schizoaffective), Level of studies (Primary/Secondary/Universitary), marital status (single/separated/divorced/married), active work (No/Yes), degree of mental disability according to criteria of the Disability Assessment Team of the National Institute of Social Security (Less than 67%/Higher or equal to 67%), disability benefit (No/Yes), number of episodes (1,2,3,4, 5 or more), total PAS scale score [13] (less than 7 points/greater or equal than 7 points), EEAG score [14] (equal or less than 60 points/greater than 60 points).

Data were entered into a MySQL database hosted on a secure server with access control. From it, the base used for the analysis was created, which did not contain personal information that would allow the identification of the patients. The statistical analysis was organized in two phases. In the first one all the aforementioned variables were described. Quantitative variables were summarized by arithmetic mean, median and standard deviation. In qualitative variables, absolute and relative frequencies were calculated. In the second phase, of an analytical nature, the relationship of the different variables with the fact of being case or control was studied. For the quantitative variables, the Student's T test or Mann-Whitney U (when normality could not be assumed) were utilized; for the qualitative variables, the Pearson Chi-square test or its exact alternative was used when applicability criteria were not met. As a preliminary step to the multivariate analysis, a univariate non conditional logistic regression model was adjusted with the result variable being the case and all the explanatory variables collected. Finally, a non-conditional multivariate logistic regression model with dependent variable was constructed, whether it was a case or not and as independent variables those that showed a significant association with it in the previous step. The SPSS program, version 18, was used for the analysis. The level of confidence was 95% and all contrasts were bilateral.

Table 1
Descriptive characteristics of the cases (n = 81).

Variable	Category	N (%)
Diagnosis	Schizophrenia	70 (86.4)
	Schizoaffective	11 (13.6)
Level of Education	Primary	63 (77.8)
	Secondary	17 (21.0)
	Superiors	1 (1.2)
Marital status	Single	67 (82.7)
	Separated/divorced	10 (12.3)
	Married	4 (4.9)
Active Work	No	80 (98.8)
	Yes	1 (1.2)
Degree of mental disability	Less than 67%	20 (43.5)
	Greater than or equal to 67%	26 (56.5)
	Lost	35 (43.2)
Disability benefit	No	18 (22.2)
	Yes	63 (77.8)
Number of episodes	1	12 (25.0)
	2	5 (10.4)
	3	5 (10.4)
	4	12 (25.0)
	5 or more	14 (29.2)
	Lost	33 (40.7)
PAS score	Less than 7 points	43 (53.1)
	Greater than or equal to 7 points	38 (46.9)
EEAG Score	Equal or less than 60 points	51 (65.4)
	Greater than 60 points	27 (34.6)
	Lost	3 (3.7)
Degree of mental disability (points)*		66.2 (67.0; 14.2)
Time since first episode (years) *		19.7 (20.0; 9.9)
Time since last episode (years) *		4.7 (3.0; 4.6)
Number of episodes *		3.7 (4.0; 2.3)
Total score PAS scale (points) *		6.6 (6.0; 3.4)
EAGG score (points) *		56.0 (60.0; 14.0)

* Mean (Median, Standard deviation).

Results

A total of 212 subjects were recruited, with a mean age of 48.7 years (standard deviation 49.0) and of which 111 (52.4%) were men. Regarding the control case status, 131 (61.8%) were controls and the rest, 81 (38.2%), cases. Of the latter, 70 (86.4%) had a diagnosis of SD and 11 (13.6%) of SAD. The rest of the descriptions referring to the cases are shown in Table 1.

In the bivariate analysis, the following variables were associated with psychotic disorders: female sex (OR 0.23, 95% CI 0.13–0.42), CMV IgG serum levels (OR per change in 10 units) 0.88, 95% CI 0.82–0.95) urea (OR 0.94, 95% CI 0.91–0.97), creatinine (OR 8.77, 95% CI 1.63–47.27), glomerular filtration rate (OR 0.97, 95% CI: 0.95–0.99), cholesterol (OR by change in 10 units 0.91, 95% CI 0.85–0.97), total proteins (OR 0.45, 95% CI 0.23–0.92), absolute neutrophil count (OR 1.51, IC95% 1.22–1.88), absolute lymphocyte count (OR 0.58, 95% CI 0.39–0.87), absolute platelet count (OR by change in 10 units 0.92, 95% CI 0.88–0.98), NLR (OR 2.98, 95% CI 1.93–4.60), lymphocyte monocyte ratio (OR 86.94, 95% CI 5.46–1385.33).

They remained associated with psychotic disorders in the multivariate model the female sex (OR 0.24, 95% CI 0.12–0.46) and the NLR (OR 3.00, 95% CI 1.91–4.70) (Tables 2 and 3).

Discussion

The main finding of the present study is the association between different markers of inflammation and the fact of suffering a SMD. Among them, the NLR stands out specially, tripling the probability in patients with SMD for each increment of one unit of this marker. On the other hand, no association was found between the different markers of infection with the fact of suffering a SMD, indeed, the only association that has been detected was that of CMV, whose antecedent of past infection was, against what was expected, more prevalent in the controls.

These results are consistent with those obtained by other authors and reveal the elevation of neutrophil counts, the decrease in lymphocyte numbers and the increase in NLR in patients with SMD [8–10]. In our opinion, it seems clear the concomitance of inflammatory processes in at least a part of the patients diagnosed with severe mental illness. In other studies, possible hypotheses explaining this relationship have already been suggested, Specifically, three groups of factors with the capacity to produce brain inflammation: infections, allergic diseases and autoimmune processes. As far as the infectious etiology is concerned, there are already antecedents that try to associate the Herpes simplex virus [15,16], the Epstein-Barr virus [17], the *Toxoplasma gondii* [18], the virus of the disease of Borna [19], Cytomegalovirus [20], *Chlamydophila pneumoniae* [21], *Borrelia burgdorferi* [22] or *Candida albicans* infections [23] with pathology of the mental sphere. With regard to allergic reactions, there have already been published studies in which food antigens [22–25] or mast cells [26] are considered factors to be taken into account for the presentation of psychiatric symptoms. Finally, among the autoimmune processes associated with psychosis, it is worth mentioning the positive association established between autoimmune diseases and schizophrenia [27]; some studies find a significantly higher prevalence of positive titers for twenty different autoantibodies in patients with schizophrenia compared to controls, highlighting the anti-cardiolipin IgG and IgM, the nerve growth factor, the ANA and the anti-NMDA [28].

Among the studies aimed at the assessment of inflammatory markers as evaluators of the evolutionary course of the psychopathological process, we highlight the study by Ivković et al [29], which assesses the usefulness of NLR as a biological indicator of suicide risk in patients diagnosed of Bipolar Disorder (BD). The aim of this study was to explore the relationship between NLR and the risk of suicide in euthymic patients with BD, and a significant relationship was found between the NLR score and the Revised Suicide Behavior Questionnaire (SBQ-R). Increases in NLR were observed in BD suicide attempts compared to healthy controls. In addition, important moderating effects of family history on the relationship of NLR with suicide risk were found, this quotient being a significant positive predictor of suicide risk only in patients with a positive family history of suicide attempts. Therefore, the authors suggested that NLR exerted an enhancing effect on the positive family history of attempted suicide.

The determination of causality is one of the central objectives of epidemiological and biomedical research, and the differentiation between mere association and causation is crucial in this regard [30]. On the other hand, although the quality of the evidence offered by the case-control studies is limited due to their vulnerability to biases, they can sometimes provide reasonable evidence of causality if they meet the criteria proposed by Sir Austin Bradford-Hill [30]. In the case at hand, our study satisfies the criteria of strength of the association, consistency and biological plausibility, and the confirmation of the rest should be the objective of future research.

Deepening the possible sources of bias, we can consider those that affect the choice of cases and the controls. In the design phase it was decided to select known cases of SMD, that is, prevalent cases, in order to achieve a feasible study in a field where knowledge is scarce. This choice presents problems, since cases, chronic patients with approximately two decades of evolution and where schizophrenia is overrepresented, may not be a true reflection of the entire spectrum of patients with psychotic disorders. On the other hand, when selecting controls, both the possibility of selecting controls matched by age and sex and the possibility of finding controls with some degree of kinship or relationship with the case that made their recruitment easier were assessed. Finally, it was decided to select the controls from the user population of a health center in Gandía with the hope that they would represent the relatively healthy population of the department. The most relevant difference found between the cases and the controls has been

Table 2
Bivariate analysis: comparison of categorical variables (Chi-square test).

Variable	Category	Controls N (%)	Cases N (%)	Significance
Sex	Man	45 (34.4)	56 (61.1)	less than0.001
	Woman	86 (65.6)	25 (30.9)	
Ig A	Less than or equal to 400 mg/dL	124 (94.7)	58 (93.5)	0.757
	Greater than 400 mg/dL	7 (5.3)	4 (6.5)	
Ig G	Less than or equal to 1600 mg/dL	130 (99.2)	61 (100.0)	> 0.999
	Greater than 1600 mg/dL	1 (0.8)	0 (0.0)	
Ig M	Less than or equal to 230 mg/dL	124 (94.7)	59 (96.7)	0.722
	Greater than 230 mg/dL	7 (5.3)	2 (3.3)	
ANA	Less than or equal to 0,69	114 (87.0)	53 (86.9)	0.979
	Greater than 0,69	17 (13.0)	8 (13.1)	
IgG Toxoplasma	Negative	75 (57.3)	28 (43.9)	0.142
	Positive	56 (42.7)	33 (54.1)	
IgM Toxoplasma	Negative	129 (98.5)	61 (100.0)	0.564
	Indeterminate	2 (1.5)	0 (0.0)	
	Positive	0 (0.0)	0 (0.0)	
IgG Cytomegalovirus	Negative	22 (16.8)	19 (31.1)	0.024
	Positive	109 (83.2)	42 (68.9)	
IgM Cytomegalovirus	Negative	129 (98.5)	60 (98.4)	> 0.999
	Indeterminate	1 (0.8)	1 (1.6)	
	Positive	1 (0.8)	0 (0.0)	
IgG Epstein-Barr virus	Negative	2 (1.5)	1 (1.6)	0.818
	Indeterminate	2 (1.5)	2 (3.3)	
	Positive	127 (96.9)	58 (95.1)	
IgM Epstein-Barr virus	Negative	128 (97.7)	59 (96.7)	0.225
	Indeterminate	2 (1.5)	0 (0.0)	
	Positive	1 (0.8)	2 (3.3)	
Anti EBNA	Negative	5 (3.8)	4 (6.8)	0.582
	Indeterminate	4 (3.1)	1 (1.6)	
	Positive	122 (93.1)	56 (91.8)	
IgG varicella zoster virus	Negative	7 (5.4)	3 (5.6)	> 0.999
	Indeterminate	6 (4.7)	2 (3.7)	
	Positive	116 (89.9)	49 (90.7)	

Ig: Immunoglobulin.

the prevalence of the male sex among the cases and the female among the controls. Undoubtedly, this association may reflect a higher prevalence of psychotic illness in men or a higher prevalence of females in the use of health services provided by a health center. Despite this, the possible confounding effect of this variable in the study of the relationship of interest (markers of inflammation and psychotic illness) seems to be controlled by having no effect on the coefficient of the regression model. Another aspect to be considered in this section of limitations is that, although it is a case-control study, design has an important component of transversality, that is, the analytical one with which cases and controls are compared is after diagnosis of disease, which cannot ensure the role of this inflammation in the etiology of these disorders. Finally, one might wonder if the cause of this inflammation could reside in some other factor that differentiates the cases from the controls, such as the treatment of the underlying disease itself. In this regard, the anti-inflammatory effect of antipsychotic drugs is known, which has been shown to be able to normalize values of the CRP and the erythrocyte sedimentation rate [31], to increase the levels of anti-inflammatory cytokines and to decrease the levels of proinflammatory cytokines [32]. In addition, they could reduce the concentrations of ferritin, interleukin-6, interleukin-1α, tumor necrosis factor-α and plasminogen activator inhibitor [33] and other inflammatory markers [34].

For all of the above, and for future lines of research, it would be worthwhile to focus on the evaluation of the NLR's discriminatory capacity and the study of the factors that could explain the reason for this greater inflammatory activity present in patients with disorders psychotic. Other aspects to consider, although in the longer term, would be to evaluate the possible therapeutic alternatives that are opened if this hypothesis is confirmed, such as the use of concomitant anti-inflammatory treatments with the usual psychopharmacological therapy.

A recent review study [35] points out that perinatal exposure to infections during critical periods of development is a promising area of study in autistic spectrum disorder (ASD), as a higher prevalence of infections has been found in cases of ASD; infections during pregnancy, infections during the first month after birth, infections during the first year after birth, and even later infections in early childhood. This line of research has also been developed in SMD [36–40].

Our results suggest that there is a greater degree of systemic inflammation in patients with SMD compared to the general population. The best associated marker has been the NLR, which is why it is worth considering it within the parameters used to assess this type of patients. It remains to evaluate the role of this inflammation in the etiology of this type of disorders and the therapeutic possibilities that are opened in these patients if an important role of inflammation in the etiology or maintenance of SMD is confirmed.

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Conflict of interest statement

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Table 3
Bivariate analysis: comparison of quantitative variables.

Variable	Controls Mean (Deviation)	Cases Mean (Deviation)	Significance
Age (years)	48.2 (15.3)	49.4 (10.3)	0.484 [T]
Glucose (mg/dL)	93.1 (21.3)	94.1 (21.6)	0.912 [U]
Urea (mg/dL)	32.2 (8.1)	27.6 (9.7)	< 0.001 [T]
Creatinine (mg/dL)	0.75 (0.15)	0.81 (0.20)	0.010 [T]
EGF (mL/min/1,73 m^2)	99.7 (15.5)	91.6 (15.8)	< 0.001 [T]
Sodium (mEq/L)	141.7 (2.0)	141.3 (10.3)	0.415 [T]
Potassium (mEq/L)	4.5 (0.3)	4.5 (0.3)	0.542 [T]
Chlorine (mEq/L)	101.02 (2.18)	100.08 (3.72)	0.073 [U]
Triglycerides (mg/dL)	116.6 (97.1)	145.6 (109.0)	0.005 [U]
Cholesterol (mg/dL)	192.4 (41.7)	171.9 (40.3)	0.001 [T]
Total proteins (g/dL)	7.0 (0.4)	6.9 (0.5)	0.026 [T]
Albumin (g/dL)	4.5 (0.3)	4.4 (0.3)	0.131 [T]
ALT (U/L)	20.8 (8.1)	21.6 (13.7)	0.327 [U]
AST (U/L)	22.2 (14.8)	22.9 (20.3)	0.110 [U]
GGT (U/L)	28.4 (28.1)	35.2 (48.5)	0.057 [U]
C-reactive protein (mg/L)	2.6 (3.1)	5.0 (7.9)	0.028 [U]
TSH (μU/L)	3.2 (0.5)	3.1 (0.6)	0.012 [U]
Glycosylated hemoglobin (%)	5.3 (0.7)	5.4 (0.6)	0.059 [U]
Total IgA (mg/dL)	241.0 (118.9)	224.4 (90.9)	0.334 [T]
Total IgG (mg/dL)	1029.8 (204.9)	981.4 (249.1)	0.188 [T]
Total IgM (mg/dL)	120.8 (62.0)	92.6 (52.8)	0.002 [T]
ANA (UI/mL)	0.5 (0.7)	0.4 (0.4)	0.003 [U]
Absolute neutrophils (10^9/L)	3.7 (1.1)	4.6 (1.8)	< 0.001 [T]
Absolute lymphocytes (10^9/L)	2.5 (0.8)	2.2 (0.8)	0.007 [U]
Absolute monocytes (10^9/L)	0.6 (0.3)	0.6 (0.2)	0.051 [U]
Absolute platelets (10^9/L)	248.7 (49.5)	224.0 (68.4)	0.006 [T]
Neutrophil-lymphocyte ratio	1.56 (0.56)	2.31 (1.17)	< 0.001 [T]
Platelet-lymphocyte ratio	105.6 (36.0)	115.8 (61.0)	0.177 [T]
Monocytes-Lymphocytes ratio	0.24 (0.12)	0.32 (0.18)	< 0.001 [U]
IgG Toxoplasma (UI/mL)	173.3 (248.5)	195.2 (233.0)	0.295 [U]
IgM Toxoplasma (UI/dL)	0.3 (0.1)	0.3 (0.1)	0.036 [U]
IgG Cytomegalovirus (UA/mL)	266.2 (197.5)	216.4 (205.7)	0.065 [U]
IgM Cytomegalovirus (UA/mL)	0.3 (0.2)	0.3 (0.1)	0.013 [U]
IgG Epstein-Barr virus (UA/mL)	3.6 (5.7)	3.3 (1.6)	0.464 [U]
IgM Epstein-Barr virus (UA/mL)	0.1 (0.7)	0.0 (0.0)	0.276 [U]
Anti EBNA (UA/mL)	4.7 (3.2)	4.6 (3.0)	0.968 [T]
IgG Varicella Zoster virus (UA/mL)	1.9 (0.7)	2.0 (0.9)	0.285 [T]

EGF: Estimated Glomerular Filtration. Ig: Immunoglobulin. [T]: T: Student's *T* test. [U]: U: Mann-Whitney *U* test.

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