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The association between crime commitment and viral infection history in male schizophrenic patients*

Filiz Ekim ÇEVİK,[1] Murat ERKIRAN,[2] Hüseyin ÇAKAN,[3] Fatih ÖNCÜ,[2] İbrahim BALCIOĞLU[4]

ABSTRACT

Objective: *Schizophrenia is a significant and common disorder. In neural development, it has been noted that prenatal ve perinatal disruptions result in neuropsychological deficits and these deficits might result in early-onset behavioral problems and criminal behaviors. Taking all these previously completed studies into consideration, we have designed a study to find out whether or not there would be any difference caused by previously acquired viral infections between criminal patients and non-criminal ones. On the other hand, this study compares the socio-demographic characteristics.* ***Methods:*** *Two groups from criminal services and acute psychiatry services participated in the study; the first group consists of 97 male schizophrenic patients with criminal acts and the second group consists of 105 male schizophrenic patients with no criminal acts. ELISA method was used to detect HSV 1-2, and CMV infections. Sociodemographic characteristics of the patients were obtained by scanning patients' files and/or consulting their relatives.* ***Results:*** *The present study was conducted with 202 male patients at the ages of 20 to 76 with a mean age of 40.36±11.33. A logistic regression analysis was conducted by assuming the variables observed as statistically significant or near statistically significant effects as independent variables and the crime commitment status as a dependent variable, in univariant committing crime analyses.* ***Conclusions:*** *These results indicate a statistical significance in some parameters among sociodemographics of schizophrenic patients with criminal acts and without criminal acts as well as non-existence of any significant association between HSV 1-2, and CMV infections and crime commitment in schizophrenic patients.* ***(Anatolian Journal of Psychiatry 2019; 20(4):404-411)***

Keywords: *schizophrenia, ELISA, crime, infection, viral agents*

Erkek şizofreni hastalarında suç işleme ve viral enfeksiyon arasındaki ilişki

ÖZ

Amaç: *Şizofreni önemli ve yaygın bir bozukluktur. Nöral gelişimde, prenatal ve perinatal aksamaların nöropsikolojik defisitlere neden olduğu ve bu defisitlerin erken başlangıçlı davranış problemlerine ve suç davranışlarına neden olabileceği bildirilmiştir. Daha önce yapılan çalışmaları göz önüne alarak, suç işleyen ve suç işlemeyen (şiddet içeren eylemler olmadan) şizofreni hastaları arasında daha önce geçirilmiş viral enfeksiyonların suç işlemeye neden olabileceği yönünden herhangi bir fark olup olmayacağını öğrenmek vebu iki grubun sosyodemografik özelliklerini karşılaştırmak için bir çalışma planladık.* ***Yöntem:*** *Çalışmamıza adli servis ve akut kapalı psikiyatri servislerinde*

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[1] Department of Medicine Sciences, Institute of Forensic Sciences, [3] Department of Sciences Institute of Forensic Sciences, [4] Department of Psychiatry, Cerrahpasa Faculty of Medicine, İstanbul University-Cerrahpaşa, İstanbul, Turkey

[2] Psychiatry Clinic, Bakırköy Prof. Dr. Mazhar Osman Mental Health and Neurological Diseases Education and Research Hospital, İstanbul, Turkey

Correspondence address / *Yazışma adresi:*

Filiz Ekim ÇEVİK, PhD, Department of Medicine Sciences, Institute of Forensic Sciences, İstanbul University-Cerrahpaşa, 34098 Fatih, Istanbul, Turkey

E-mail: fecevik@gmail.com

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yatan erkek hastalardan 97 suç işleyen (adli) 105 suç işlemeyen (adli öyküsü olmayan) şizofreni hastası olmak üzere iki grup alınmıştır. Kanları alınan hastaların serumlarından, HSV 1-2 ve CMV enfeksiyonlarını taramak için ELISA yöntemi uygulanmıştır. Hastaların sosyodemografik özellikleri, hastaların dosyaları taranarak ve yakınlarıyla görüşülerek elde edilmiş ve sosyodemografik değerlendirme formuna kaydedilmiştir. ***Bulgular:*** *Çalışmamız yaşları 20-76 arasında, yaş ortalaması 40.36±11.33 olan toplam 202 erkek hasta ile yapılmıştır. Suç işleme üzerine tek değişkenli analizlerde istatistiksel olarak anlamlıveya istatistiksel anlamlılığa yakın etkileri olduğu gözlenen değişkenler bağımsız değişkenler, suç işleme durumu bağımlı değişken olarak kabul edilerek lojistik regresyon analizi yapılmıştır.* ***Tartışma:*** *Bu sonuçlar, suç işleyen(adli) ve suç işlemeyen(adli olmayan) şizofreni hastalarının sosyodemografik özelliklerinin bazı parametrelerinde istatistiksel olarak anlamlılık kaydedilirken, bir yandan da şizofreni hastalarında araştırılan HSV 1-2 ve CMV enfeksiyonları ve suç arasında anlamlı bir ilişki olmadığını göstermektedir.* ***(Anadolu Psikiyatri Derg 2019; 20(4):404-411)***

Anahtar sözcükler: *Şizofreni, ELISA, suç, enfeksiyon, viral etkenler*

INTRODUCTION

Schizophrenia is a disruptive disorder of the central nervous system.[1] Its pathogenesis involves genetical factors, environmental factors, and psychological etiologies.[2] One of the etiological hypotheses concerning this disease is that it develops as a result of a viral infection or an autoimmune response against the central nervous system tissue following a viral infection.[3-5] The infections exposed during the perinatal period are suggested to increase the risk of developing schizophrenia. The infections and the response of the immune system, particularly in the second and the third trimester, within which the maturation of immune system as well as brain tissue are not completed yet, and early newborn period, are thought to be determining.[6,7]

Also, the cases that are proven to be with viral encephalitis are known to appear together with the symptoms of the schizophrenia.[8] Some viruses are shown to alter the dopamine metabolism, which has been thought to be in change in schizophrenia[9,10] and a few antipsychotic and antimanic drugs, effective in treatment of severe mental illnesses, are shown to be with antiviral characteristics in vivo[11,12] and in vitro.[4,13]

The risk factors, which may be epidemiologically specific to schizophrenia, might be including but might not be limited to the following: infection with toxoplasma gondii and viral agents, genetic polymorphisms, age of onset, gender, birth season, regional variances, urban living, household crowd, lower socioeconomic status, prenatal stress, obstetrical complications, traumatic brain injury,and immigration.[14,15] The association between geographical distribution of schizophrenia prevalence, delivery season,and viral epidemic exposure in prenatal period and schizophrenia are indirect findings supporting this hypothesis.[16,17] At this point, the effects of infections such as HSV 1-2, influenza, CMV, Epstein-Barr Virus (EBV), and Borna Disease Virus (BDV) are mentioned.[18-20] However, social aspects, associ-ation with crime, and not getting a place in the society are substantial concepts for these patients.[1] Schizophrenia is suggested to be a mental illness that has a great association with groups with criminal acts.[21-23] Numerous studies have demonstrated a high rate of violent behavior in patients with schizophrenia compared to a healthy control sample.[24,25]

This is a seroprevalence study, grounding on all of these above mentioned hypotheses.The association between criminal acts, and the seropositive status of anti-(HSV-1,HSV-2, and CMV) in patients with schizophrenia have been investigated. In addition to these risk factors, we also compare the sociodemographic characteristics of schizophrenic subjects with or without the history of crime commitment.

METHODS

Design and setting

The study has been conducted with two groups, one group with criminal acts (homicide, physical assault, attempted homicide, sexual assault, threat etc.) (n=97) and another group of schizophrenic patients without criminal acts (n=105), at the age of 20 to 76 and male, staying at Istanbul University, Cerrahpaşa Faculty of Medicine, Department of Psychiatry and at Prof. Dr. Mazhar Osman Bakırköy Mental Facility Judicial Service and acute psychiatric service between the dates of March, 2015 and May, 2016.

The study has been approved by İstanbul University Cerrahpaşa Faculty of Medicine Ethics Committee by an Ethics Committee decree, No. 264726, dated December 03rd 2014. The patients, whose blood were collected to yellow-cap gel tubes, were verbally informed, and the patients', their first-degree relatives' and/or their custodians' written consents were taken. ELISA method, intended for detecting viral agents, was

used in Acıbadem Labmed Laboratories. The sociodemographic features of the patients were obtained via file scanning or relative consultation and the information gathered was recorded in to the socio-demographic evaluation form.

Participants

Inclusion criteria: 1-Male gender, 2-being diagnosed as a schizophrenic by psychiatry specialists according to the DSM-IV-TR diagnostic criteria and then getting a definitive diagnosis from a health committee, 3-having been informed regarding the participation in the study and given written consent.

Exclusion criteria: 1-Female gender, 2-having another psychiatric disorder diagnosis rather than schizophrenia according to DSM-IV-TR diagnostic criteria, 3-currently having alcohol and substance use.

Sociodemographic Information Form: In the Sociodemographic Information Form used in the study, the details like age, place of birth, occupation and work setting, educational background, civil status, number of siblings, whom they live with, and psychiatric disorder history within family were investigated. Age of onset, number of hospital stays, total duration of stays, history of suicide attempts, type of medication used in the treatment, schizophrenia types, and general medical disease history were recorded. In criminal cases, types of crimes committed, direction of the crimes, number of crimes committed, severity of the crimes, and criminal history within the family were questioned.

Sample collection and laboratory stage

Blood samples were collected to yellow-caps 13x100 pcs 5mL BD Vacutainer plastic gel tubes from patients via vein punctures. The gel in tubes forms a physical obstacle between serum and blood cells after centrifuging and with its silica particles on the tube wall, it speeds up serum coagulation. After about half an hour, the tubes were centrifuged at 4000 rpm for 6 minutes. The serums were stored to -40°C via the serological method ELISA for determining HSV-1, HSV-2, and CMV antibodies. The samples taken from deep-freeze were put at +4°C and let to thaw. Then the antibodies were examined at the laboratory, using ELISA method. Vircell and Vidas Kit were used for HSV-1, HSV-2, and CMV, respectively. Testings were performed by Micro ELISA device (IMM.28).

Statistical analysis

When assessing the findings of the study, the software NCSS (Number Cruncher Statistical System) 2007 Statistical Software (NCSS LLC, Kaysville, Utah, ABD) was used for statistical analyses. When assessing the study data, aside from the definitive statistical methods (mean, standard deviation, median, frequency, and ratio), Student's t-test was used to compare normally distributed inter-group parameters in quantitative data comparisons. Mann-Whitney U test was used for inter-group comparisons of abnormally distributed parameters. Pearson's chi-square test and Fisher's exact test were used to compare qualitative data. Logistic regression analysis was used to inspect risk factors together, affecting committing crime status. The results are in 95% CI, and the significance was at $p<0.05$ level.

Table 1. Distribution of patients' definitive and criminal history characteristics

Characteristics	n	%
Age (years) (Mean±SD)	40.36±11.33	
(min-max)	20-76	
Gender		
Male	202	100.0
Female	0	0
Number of siblings (min-max; 1-11)		
1-2 siblings	22	10.9
3-4 siblings	89	44.1
≥ 5 siblings	91	45.0
Place of birth		
Village	19	9.4
Town	140	69.3
City	40	19.8
Abroad	3	1.5
Educational background		
Illiterate	8	4.0
Literate	15	7.4
Primary school	98	48.5
Elementary school	44	21.8
High school	29	14.4
University	8	4.0
Civil status		
Single	147	72.8
Married	25	12.4
Divorced/widowed	30	14.9
Who they live with		
Homeless	9	4.5
Alone	12	5.9
With someone	181	89.6
Patient's pre-crime work life		
None	80	39.6
Available	122	60.4
Crime		
None	105	52.0
Available	97	48.0

RESULTS

Definitive characteristics

The study was conducted with 202 male patients, 20 to 76 years of age with a mean of 40.36±11.33, staying in Istanbul University, Cerrahpaşa Faculty of Medicine, Psychiatry Department and Bakırköy Prof. Dr. Mazhar Osman Mental Facility Judicial Service and Acute Psychiatry Service (Table 1).

Association between definitive and clinical characteristics with criminal history

The patients' definitive characteristics were inspected per crime status, and the obtained numeric values were shown in Table 2.

Distribution of viral serology presence per groups was shown in Table 3.

Multivariant analysis of risk factors on committing crime

A logistics regression analysis was made by assuming the variables with observed statistically significant ($p<0.05$) or near statistically significant ($p<0.150$) effects as independent variables and the committing crime status as a dependent variable, in univariant committing crime analyses (Table 4). Backward methods (selecting backwards) was used. The model formed because of the assessment was determined to be statistical-

Table 2. Assessment of patients' definitive characteristics per crime status

	Non-criminal		Criminal		
	n	%	n	%	p
Age (years) (Mean±SD)	38.40±11.16		42.48±11.19		[a]0.010
Number of siblings (Mean±SD)	4.62±2.08		4.58±1.84		[e]0.880
Place of birth					
Village	6	31.6	13	68.4	[b]0.061
Town	80	57.1	60	42.9	[b]0.027
City	18	45.0	22	55.0	[b]0.324
Abroad	1	33.3	2	66.7	[c]0.609
Educational background					
Illiterate	3	37.5	5	62.5	[c]0.485
Literate	6	40.0	9	60.0	[b]0.334
Primary school	50	51.0	48	49.0	[b]0.791
Elementary school	27	61.4	17	38.6	[b]0.159
High school	12	41.4	17	58.6	[b]0.217
University	7	87.5	1	12.5	[c]0.067
Civil status					
Single	79	53.7	68	46.3	[b]0.413
Married	16	64.0	9	36.0	[b]0.199
Divorced/widowed	10	33.3	20	66.7	[b]0.027
Patient's pre-disease work life					[b]0.058
None	35	43.8	45	56.2	
Available	70	57.4	52	42.6	
Medication					
Oral typical antipsychotics	90	52.3	82	47.7	[b]0.814
Oral atypical antipsychotics	86	49.7	87	50.3	[b]0.115
Depot antipsychotics	9	31.0	20	69.0	[b]0.015
Other (depot and oral antipsychotics)	15	31.9	32	68.1	[b]0.002
Type of schizophrenia					[b]0.001
Paranoid	79	46.7	90	53.3	
The others	26	78.8	7	21.2	
General medical disease					[b]0.095
None	95	54.3	80	45.7	
Available	10	37.0	17	63.0	
Hospital stay duration (months)					[e]<0.001
Min-max	10 days-22 months		15 days-348 months		
Median	2		48		
Mean±SD	2.97±3.66		64.48±69.77		

[a]: Student's t-test; [b]: Pearson's chi-square test; [c]: Fisher's exact test; [e]: Mann Whitney U-test

Table 3. Assessment of outcomesof virus (HSV-1, HSV2, and CMV) positivity in schizophrenic subjects on committing crime

	Non-criminal		Criminal		
	n	%	n	%	p
HSV-1	96	51.1	92	48.9	[a]*0.339*
HSV-2	3	37.5	5	62.5	[b]*0.485*
CMV	100	51.5	94	48.5	[b]*0.723*

[a]*: Pearson's chi-square test;* [b]*: Fisher's exact test*

Table 4. Assessment of risk factors affecting crime

	Univariant analyses			Multivariate analyses		
	β	p	OR (95% CI)	β	p	OR (95% CI)
Age	0.033	0.012	1.03 (1.01-1.06	-0.023	0.311	0.98 (0.94-1.02)
Place of birth		0.130		0.000	0.967	0 (0-0)
Place of birth (village)	1.061	0.042	2.89 (1.04-8.04)	-0.195	0.875	0.82 (0.07-9.26)
Place of birth (city)	0.488	0.176	1.63 (0.80-3.30)	0.195	0.794	1.22 (0.28-5.27)
Place of birth (abroad)	0.981	0.428	2.67 (0.24-30.10)	0.668	0.699	1.95 (0.07-58.05)
Civil status		0.062		0.000	0.656	0 (0-0)
Civil status (single)	0.425	0.343	1.53 (0.64-3.68)	-0.290	0.714	0.75 (0.16-3.53)
Civil status (divorced/widowed)	1.269	0.026	3.56 (1.17-10.84)	0.464	0.624	1.59 (0.25-10.13)
Educational background		0.194		0.000	0.628	0 (0-0)
Educational background (literate)	-0.105	0.907	0.90 (0.15-5.26)	0.770	0.554	2.16 (0.17-27.8)
Educational background (primary sch.)	-0.552	0.467	0.57 (0.13-2.54)	-0.217	0.848	0.8 (0.09-7.38)
Educational background (elementary s.)	-0.973	0.220	0.38 (0.08-1.79)	-0.935	0.438	0.39 (0.04-4.17)
Educational background (high school)	-0.163	0.843	0.85 (0.17-4.26)	-0.853	0.508	0.43 (0.03-5.32)
Educational background (university)	-2.457	0.058	0.09 (0.01-1.08)	-20.976	0.999	0 (0-0)
Pre-disease work life (none)	0.549	0.059	1.73 (0.98-3.06)	1.144	0.017	3.14 (1.22-8.07)
Alcohol (available)	0.609	0.117	1.84 (0.86-3.93)	0.975	0.166	2.65 (0.67-10.54)
Medication (OAA)	0.653	0.119	1.92 (0.84-4.37)	-0.040	0.956	0.96 (0.24-3.92)
Medication (depot)	1.019	0.018	2.77 (1.19-6.43)	0.356	0.686	1.43 (0.25-8.01)
Medication (other)	1.083	0.002	2.95 (1.48-5.90)	0.271	0.684	1.31 (0.36-4.84)
Suicide (available)	0.586	0.096	1.80 (0.90-3.58)	0.649	0.315	1.91 (0.54-6.79)
Type of schizophrenia (paranoid)	1.443	0.001	4.23 (1.74-10.28)	1.476	0.043	4.38 (1.05-18.23)
Organic factor (available)	0.702	0.099	2.02 (0.87-4.66)	0.716	0.300	2.05 (0.53-7.92)
Disease duration	0.064	<0.001	1.07 (1.03-1.10)	-0.015	0.759	0.98 (0.89-1.08)
Number of hospital stays	-0.079	0.035	0.92 (0.86-0.99)	-0.404	0.001	0.66 (0.52-0.85)
Duration of hospital stays	0.181	<0.001	1.20 (1.11-1.29)	0.444	<0.001	1.56 (1.25-1.95)

ly significant (χ^2=164.65, p<0.001). The model's sensitivity, specificity, and accuracy were found to be 76.3%, 98.1%, and 87.6% respectively.

Reference categories: born in town for place of birth, married for civil status, illiterate for educational background, working for work life, not abusing alcohol for alcohol, not using this medication for medication (OAA), not using this medication for medication (depot), not using this medication for medication (other), no suicide attempt for suicide variable, the others for types of schizophrenia, not having this factor for organic factor variable.

As a result of the assessment, the variables tending to get a significant place in the model were found to be pre-crime work life, types of schizophrenia, total number of hospital stays, and duration of hospital stays (p=0.017, p=0.043, p=0.001, p<0.001, respectively). Although other variables turned out to have significant or near-significant affects in univariant analyses, they became statistically insignificant in multivariate analyses. In those not working before the crime occurrence, the crime rate appears to be 3.14 times as much as those working [OR (95% CI): 3.141 (1.223-8.068),

p=0.017]. In those with paranoid type schizophrenia, the crime rate appears to be 4.37 times as much as those of the others [OR (95% CI): 4.376 (1.050-18.235), p=0.043]. It was found that a unit increase in total number of hospital stays results in folding the crime rate by 0.66 (decreased to about two-thirds) [OR (95% CI): 0.664 (0.520-0.850), p=0.001]. It was found that a unit increase in total duration of hospital stays results in folding the crime rate by 1.56 [OR (95% CI): 1.559 (1.246-1.950), p<0.001].

DISCUSSION

The factors held responsible for the etiology of this disease might not be found in all patients in its entirety, and schizophrenia might not occur in every individual with these risk factors and/or laboratory findings. Therefore, various hypotheses on potential factors resulting in this disease could be formed and there are many ongoing researches, along with the development of examination methods in biological psychiatry.

In the recent years, the interaction between biological and psychosocial factors (gene-environment correlation model) has become important. Neurotransmitter model, neurodevelopmental model, contribution of inheritance, and psychosocial and environmental reasons are examples thereof.[26,27] In another hypothesis, it has been thought that an exposure to various viral infections at 2nd and/or 3rd trimesters and which affect central nervous system play an important role in the etiology of schizophrenia.[18,19]

In this study, some viruses(HSV-1,HSV-2, and CMV), which might cause latent infections in central nervous system, have been inspected via serological methods in terms of IgG in order to find out whether or not a patient has had a prior infection. The patients have been grouped as one with criminal acts and the other one without criminal acts, and these schizophrenic groups have been compared. Also, in order for the disease to appear phenotypically, the data obtained from the retrospective study information scanning form, which inquiries the roles of environmental and psychosocial factors, judicial personal history of the patients containing sociodemographic features, and familial history features have been compared between two above mentioned groups.

In studies investigating the factors affecting tendency towards violent and criminal acts in schizophrenic patients, the association of these behaviors with socioeconomic factors are also highlighted.[28] There are numbers of publications stating that in psychiatric and non-psychiatric cases, the factors such as gender (male gender), work status (unemployment), poor educational background, and lower socioeconomic levels result in increased risk of crime commitment.[29-35] This study has found that the mean age of the criminal cases are statistically significantly older than the non-criminal ones. The statistically significantly different age levels appear to be associated with the fact that the patients with criminal backgrounds have been selected among the existing patient groups, who have been under protection and treatment especially for a long period.

Two studies have shown that individuals who are born[36] or raised[37] in cities (towns) have increased risks of developing schizophrenia compared with those who are born or raised in rural areas.[38] This complies with the studies of psychiatric hospital stays resulting from serious mental disorders, which indicates a greater possibility of hospital stays in countries with more urbanized populations.[39] The use of depot antipsychotic drugs is recommended in the literature and in related guidelines, it is preferred mostly for patients with poor oral medication compliance. Regarding this, patients who are non-compliant with oral medication intake might have higher crime rates.

In this study, in compliance with the literature one might come up with the fact that in those cases who are born in towns, the crime rate was statistically significantly higher than the others were, and patients who are non-compliant with oral medication intake might have higher crime rates.

In addition to these, Herpes class virus antibodies have been reported to be at higher values in psychotic patients' serum and cerebrospinal fluid samples.[40,41] Besides, in schizophrenic patients, HSV-1 serum antibody levels have been shown to increase when compared to healthy controls.[42,43] It has been reported that HSV-1 antibodies have been increased in 42.3% of cases via neutralization test in cerebrospinal fluid samples, however, there has been no significant difference with complement fixation[5] test.[44,45]

In a study, the qualitative serologic test of CMV and HSV-1 infection did not show a significant difference between schizophrenic patients and control group. As a result, it has been stated that the HSV-2 infection has a similar prevalence rate in the control group.[7]

In another study, the mean HSV-1, HSV-2 and CMV IgG levels in a patient group and in a control group, and the difference between two groups was not found to be significant.[39,44] Finding different results against HSV and CMV in different studies may result from the use of different methods.[40,46,47]

In this study, the potential effects of schizophrenia with viral infection etiology have been investigated and although, it has been pre-thought that the serological parameters of the previously mentioned viruses might be used as predictor markers for tendency towards criminal acts, no statistically significant difference between the group with criminal acts and without criminal acts has been shown in terms of the presence of viral antibody in the collected samples.

Because of the assessment, the variables tending to get a significant place in the statistics were found to be pre-criminal act work life, type of schizophrenia, total number of hospital visits, and duration of hospital stays. This could indicate that the duration of disease and hospital stays were longer in the group with criminal acts, thus the overall wellbeing of the patients were lower in this group. Socio-demographic features and disease-related details in this study appear to be supportive of the relevant literature. Detection of higher psychiatric disease frequency in family history within both groups (47% and 43%) supports the role of genetic tendency in schizophrenia.

However, the study has a few certain limitations. Since there has been an insufficient number of female patients with criminal acts, particularly in schizophrenia patient group, the study has been conducted with male patients. Considering the prenatal passage of viruses, it has been suggested, but could not have been included in the study of ours, that serological scanning of serums collected from patients' mothers might be of importance in order to be able to make a confirmation of the neurodevelopmental hypothesis in schizophrenia. The serological markers in serums have been used within the study. Cerebrospinal fluid or postmortem brain tissue sample studies are assumed to be presenting higher period of viral retention in central nervous system. As the serological method materials are expensive, only HSV-1, HSV-2, and CMV have been investigated. It is important to highlight the fact that the study is to be developed in terms of variety of microbiological etiology in schizophrenia with an inclusion of various other microbial agents (Toxoplasma Gondii, Chlamydia spp., Epstein-Barr Virus, Influenza virus etc.) in the serological study panel. On the other hand, it is suggested that researching microorganism-associated etiology in schizophrenia through genetic sub-typology studies with different microbiological agents would make a great contribution to the literature.

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