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Antiphospholipid antibodies as biomarkers for schizophrenia

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Abstract
Background: Schizophrenia is a neurodegenerative psychiatric disorder causing substantial personal and societal burden, characterized by positive, negative and disorganized symptoms and it is also associated with cognitive impairment. Complex interactions of genetic and environmental factors have been implicated in etiology of schizophrenia. Diagnosis is a challenging problem due to the heterogeneity of this mental disorder and lack of specific effective biomarkers. The antiphospholipid antibodies may have a causal role in the development of some neuropsychiatric conditions such as psychosis, depression and dementia.
Aims: To study the relationship between antiphospholipid antibodies and schizophrenia. In addition, the relationship between the level of these antibodies and psychopathological symptoms were evaluated.
Patients and Methods: Thirty schizophrenic patients compared with 30 healthy people were included in this study. Psychiatric symptoms severity, global cognitive functions and serum levels of antiphospholipid antibodies were evaluated twice in schizophrenic patients with interval one and half month under treatment and compared to the healthy control results.
Results: There were statistically significant differences between case and control groups regarding the studied cognitive domains and antiphospholipid IGM. In the case group, there were a direct correlation between antiphospholipid IGM and positive schizophrenic symptoms, and inverse correlation between cognitive scales and negative symptoms.
Conclusion: The increased levels of antiphospholipid IGM antibodies were correlated with positive schizophrenic symptoms while negative symptoms were correlated with cognitive scales among case group. These results may give an important implication for the usefulness of antiphospholipid antibodies screening in treating schizophrenia in the future.

Keywords: Schizophrenia, cognitive impairment, antiphospholipid antibodies

Introduction
Schizophrenia (SZ) is a severe and frequently chronic mental condition that imposes a significant personal and social burden due to severe and long-term incapacity. Positive (e.g., hallucinations, delusions), negative (e.g., Alogia, Avolition, Anhedonia), and chaotic (e.g., speech, behaviour) symptoms define SZ, which is also linked with cognitive impairment (Legge *et al*., 2021) [1].
Best explains the aetiologies of SZ is a multi-factorial polygenic threshold model with several genetic risk factors changed by the environment. Observed immunological changes in SZ suggest the participation of an immune-related mechanism. Multiple studies have revealed that an active immune system contributes to the genesis of SZ. The significance of immunological dysregulation and changes in neuro inflammatory pathways in schizophrenia suggest the relevance of inflammatory processes (Zamanpoor and Mansour., 2020) [2].
Diagnosis of SZ is a challenging problem due to the heterogeneity of this mental disorder and lack of specific effective biomarkers. In order to diagnose SZ, the clinical symptoms need to be evaluated. Clinical examination includes the main psychiatric assessment that focuses on clinical interviews based on diagnostic and statistical manual (DSM-V) of mental disorders conducted by clinical psychiatrists to diagnose patients with SZ and laboratory tests as well as neuro-imaging (Habtewold *et al*., 2020) [3]. Antiphospholipid syndrome (APS) is an acquired condition defined by an increased incidence of venous or arterial thrombosis and the existence of antiphospholipid antibodies (Selby *et al*., 2022) [4].

Anti-phospholipid antibodies (APL Abs) are heterogeneous family that specifically reacts with serum phospholipid-binding plasma proteins (mainly β2 glycoprotein-I, prothrombin, annexin V, annexin II, protein C, protein S, and oxidized low-density lipoprotein), phospholipid–protein complexes, and anionic phospholipids (Zhang, Yan, *et al*., 2020) [5].

Furthermore, there are currently no clinically recognised and accurate biomarkers for schizophrenia. Several research on biomarkers in SZ advocated the use of blood-based panels containing a collection of markers linked with immunological processes, metabolic abnormalities, and neuroendocrine, neurotrophin, and neurotransmitter changes. The integration of several markers, especially sophisticated multi-marker panels, may aid in the differentiation of individuals with distinct underlying diseases (Belbasis *et al*., 2018) [6].

APL antibodies can directly cause neuronal damage by altering synaptoneurosomes, and APL interacts with GABA ionotropic neuronal receptors. Detailed evidence on a potential pathogenic role for APL in SZ is missing at this moment, however it is known that the antibodies affect a number of cellular and circulatory systems (Mayer, Miroslav, *et al*., 2020) [7].

In schizophrenia, changes in the membrane phospholipids of erythrocytes and platelets have been documented, and such abnormalities have recently been identified in the frontal lobes of drug-naive, first-episode cases, raising the possibility that APL may play some pathogenic role in this disease. It was suggested that IgM antibodies may be more specifically related to disease progression **(**Moray *et al*., 2021) [14].

Aim

This study was done to investigate the relation between schizophrenic symptoms and serum level of antiphospholipid antibodies and. Is it possible to use APL Abs as a biomarker in schizophrenia and the extent to which anti-psychotic drugs may affect it.

Subjects and methods

This study carried out at Neuropsychiatry and Clinical pathology Departments in Tanta University Hospital during the period from March 2021 till May 2022.

Sixty participants recruited in the study and they were selected by convenience sampling and they were divided into two groups:

Group □: 30 schizophrenic patients diagnosed by DSM5.

- A: Firstly, all psychometric and laboratory tests were done to the untreated patients (newly diagnosed or patients who stop the antipsychotic drugs for at least 3 months).
- B: After 1 and half months all psychometric and laboratory tests were done to the same patients after receiving treatment.

Group □□: 30 volunteers matched with patient groups in age, sex and socio-economic standard as control group.

Inclusion criteria

- Age was above 18 years old and less than 60 years.
- Both males and females were included.

Exclusion criteria

- Organic neurological disorders (lacunar infractions, degenerative disorders etc.).
- Patients with autoimmune disorders that has high APL Abs (Rheumatoid arthritis, systemic lupus erythematosus etc.)
- Patients with other psychiatric disorder.

After obtaining an informed written consent, all the participants were subjected to the following during admission in Neuropsychiatric department of Tanta University Hospitals:

A. Psychiatric evaluation using the Arabic version of mini-international neuropsychiatric interview. It involves personal data, complaint of patient, present history, family history, educational history, occupational history, marital history and mental state examination. All these data were obtained by interview of the participant and their relatives (Sadek A., 2000., Wafa A *et al*., 2020) [15-16].
B. Schizophrenic patients were diagnosed according to the diagnostic and statistical manual of mental disorders (DSM 5). (Ross, Colin *et al*., 2010) [8]. and the severity of Schizophrenia assessed by the positive and negative syndrome scale (PANSS). PANSS is a standardized instrument to assess symptom severity in schizophrenia.
C. General examinations and routine investigations to exclude any physical and neurological disorder.
D. Evaluation of cognitive functioning using the mini-mental state examination (MMNSE)
which is a brief measure of five domains of cognition: orientation with regard to time and place, registration of words, attention and calculation, recall, and language.
E. Laboratory work up: antiphospholipid antibodies, determination of antiphospholipid antibodies using enzyme-linked assay (ELISA) technique**.**

Statistical Analysis

Data were analyzed using Statistical Program for Social Science (SPSS) version 22.0 Quantitative data were expressed as mean± standard deviation (SD). Qualitative data were expressed as frequency and percentage.

1 Mean value $\left(\bar{x}\right)$**:** the sum of all observations divided by the number of observations:

$$\left(\bar{X}\right) = \frac{\Sigma x}{n}$$

Where

Σ = sum & n = number of observations.

2 Standard Deviation [SD]

It measures the degree of scatter of individual varieties around their mean:

$$SD = \sqrt{\frac{\Sigma \left|x - x\right|^{-2}}{n-1}}$$

3 Standard student "t test", test of significance of the difference between two means:

$$t = \frac{\bar{X} - \bar{X}_2}{\sqrt{\frac{(SD_1)^2}{n_1} + \frac{(SD_2)^2}{n_2}}}$$

The calculated "t" was compared with tabulated one at different levels of significance at the degree of freedom (DF):

$\bar{X}$ = The mean value of group I
$\bar{x}_2$ = The mean value of group II.
SD_1 = The standard deviation of group I.
SD_2 = The standard deviation of group II.
n1 = The number of observations of group I
n2 = The number of observations of group II.

4 Chi-square: the hypothesis that the row and column variables are independent, without indicating strength or direction of the relationship. Pearson chi-square and likelihood-ratio chi-square. Fisher's exact test and Yates' corrected chi-square are computed for 2x2 tables.

Chi-square test
For comparison between two groups as regards qualitative data.

$$X^2 = \sum \frac{(O-E)^2}{E}$$

Where
Σ = Summation.
O = Observed value.

$$E = \text{Expected value} = \frac{\text{vertical total X Horizontal total}}{\text{grand total}}$$

5- Linear Correlation Coefficient [r]

$$r = \frac{\Sigma (X - \bar{X})(y - \bar{y})}{\sqrt{\{\Sigma (X - \bar{x})2\}\{\Sigma (y - \bar{y})2\}}}$$

Where
X= Independent variable.
Y= Dependent variable.

Results

Socio demographic data
the sociodemographic data of our subjects showed that there was statistically significant difference between case and control groups as regard Occupation (0.001), Residence (0.038), Marital status on contrast, there was no significant difference regard other studied sociodemographic results as showed in table (1)

Table 1: Demographic data of both case and control groups

		Case	Control	Test	p. value
Age	Range	20 – 63	26 – 52	T: 0.129	0.898
	Mean ± S.D	35.70±9.91	35.40±8.01		
Sex	Male (%)	19 (63.3%)	14 (46.7%)	X^2: 1.684	0.194
	Female (%)	11 (36.7%)	16 (53.3%)		
Occupation	Unemployed (%)	23 (76.7%)	8 (26.7%)	X^2: 15.017	0.001*
	Employed (%)	7 (23.3%)	22 (73.3%)		
Residence	Rural (%)	18 (60%)	10 (33.3%)	X^2: 4.286	0.038*
	Urban (%)	12 (40%)	20 (66.7%)		
Marital state	Married (%)	11 (36.7%)	20 (66.7%)	X^2: 5.412	0.020*
	Single (%)	16 (53.3%)	8 (26.7%)	X^2: 4.438	0.035*
	Divorced (%)	1 (3.3%)	2 (6.7%)	X^2: 0.352	0.554
	Widow (%)	2 (6.7%)	0 (.0%)	X^2: 2.071	0.150
Special habits	Smoker (%)	15 (50%)	9 (30%)	X^2: 2.500	0.114
	Nonsmoker (%)	15 (50%)	21 (70%)		
Consanguinity	Positive (%)	11 (36.7%)	6 (20%)	X^2: 2.052	0.152
	Negative (%)	19 (63.3%)	24 (80%)		
Family troubles	Positive (%)	17 (56.7%)	10 (33.3%)	X^2: 3.300	0.069
	Negative (%)	13 (43.3%)	20 (66.7%)		

Clinical Data
As regard clinical data, there was a positive family history of psychiatric disorders in 36.7% and 16.7% in case and control groups respectively. With no statistically significant difference (P value = 0.080) between both groups. The mean duration of illness was 7.20±6.35 years.
However, twenty-seven (90%) of case group were with chronic schizophrenia while only 3 patients 10% were with early schizophrenia.
The majority (46%) of included schizophrenic cases received (Risperidone) only, while 33.3% received Risperidone and ECT therapy. About 6.7% of patients received other antipsychotic drugs (Trifluoperazine or clozapine) and 13.3% received other antipsychotic drugs (Trifluoperazine or clozapine) and ECT.

III) Laboratory results
The level of Antiphospholipid antibodies IgM were positive (≥ 10 U/ml) and higher in case group with mean value 23.55±13.04 than in control group with mean value 6.41±2.96. There was statistically significant difference (P value = 0.001) between both groups regarding this issue as shown in table 2.

Table 2: Results of Antiphospholipid antibodies in both case and control groups:

		Case			Control			t. test	p. value
IgM (U/ml)	Range	4.3	–	62.7	1.6	–	14	7.021	0.001*
	Mean ± S. D	23.55	±	13.04	6.41	±	2.96		
IgG (U/ml)	Range	4	–	22.4	4	–	15.4	0.215	0.830
	Mean ± S. D	9.60	±	5.39	9.85	±	3.21		

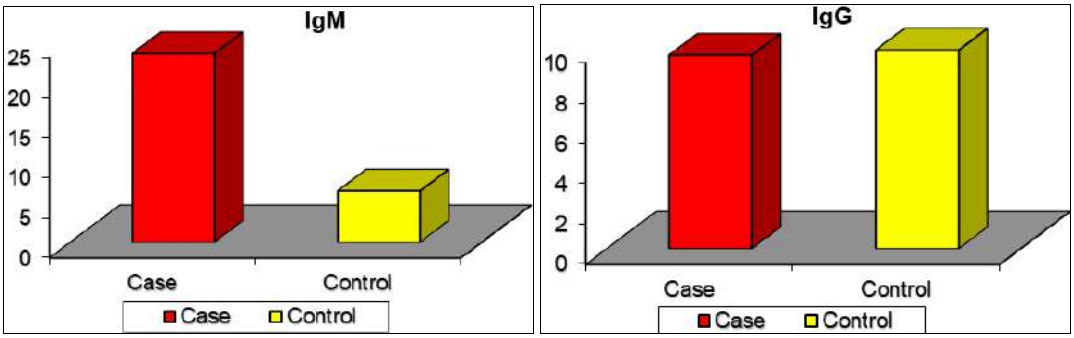

Fig 1: Results of antiphospholipid antibodies in both case and control groups

Table 3: Results of antiphospholipid antibodies in case group before and after treatment

		Pre			Post			t. test	p. value
IgM (U/ml)	Range	4.3	–	62.7	4	–	74.3	0.469	0.641
	Mean ± S. D	23.55	±	13.04	25.19	±	14.16		
IgG (U/ml)	Range	4	–	22.4	4.6	–	27.4	1.023	0.311
	Mean ± S. D	9.60	±	5.39	10.98	±	5.08		

There was no statistically significant difference in case group in pre and post hospitalization stages regarding antiphospholipid antibodies Ig M and Ig G (P value = 0.641 and 0.311 respectively).

Table 4: Result of the total Positive and Negative Syndrome Scale (PANSS) in case group:

	Pre	Post	t. test	p. value
Scale for Assessment of Positive Symptoms	33.13±4.70	18.23±2.86	14.842	0.001*
Scale for Assessment of Negative Symptoms	32.53±4.47	16.97±3.65	14.770	0.001*
general psychopathology scale	67.27±8.69	32.97±5.62	18.162	0.001*
Total	131.47 ± 14.72	68.90 ± 8.32	20.268	0.001*

The mean of the total scale was lower (low symptoms severity) in the post hospitalization stage (68.90 ± 8.32) than in the pre post hospitalization stage (131.47 ± 14.72). The total mean of PANSS scale showed a statistically significant difference (p value = **0.001**) in case group before and after treatment.

As regard the correlation between Scale for Assessment of Positive Symptoms (SAPS) and level of antiphospholipid antibodies in case group

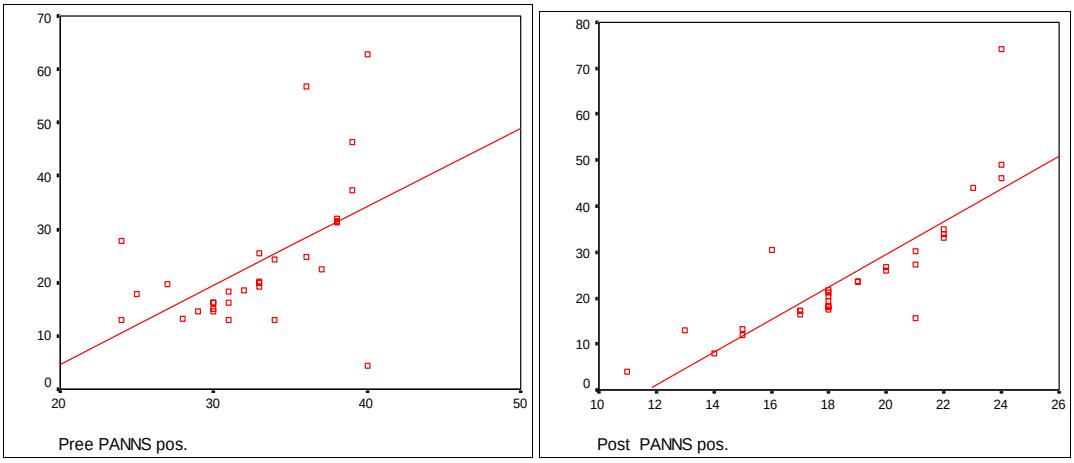

Fig 2: the correlation between SAPS and level of antiphospholipid Ig M antibodies in case group

It was found that the positive symptoms (SAPS) (Delusion, Conceptual disorganization, Hallucinatory behavior, Excitement, Grandiosity, Persecution and Hostility) of the case group in pre and post hospitalization stages had a statistically significant direct correlation ($P< 0.05$) with antiphospholipid Ig M antibodies. There is no correlation

between the positive symptoms (SAPS) and antiphospholipid Ig G antibodies in the case group as shown in figure (2).

As regard the correlation between Scale for Assessment of Negative Symptoms (SANS) and Mini Mental State Examination (MMSE) in the case group

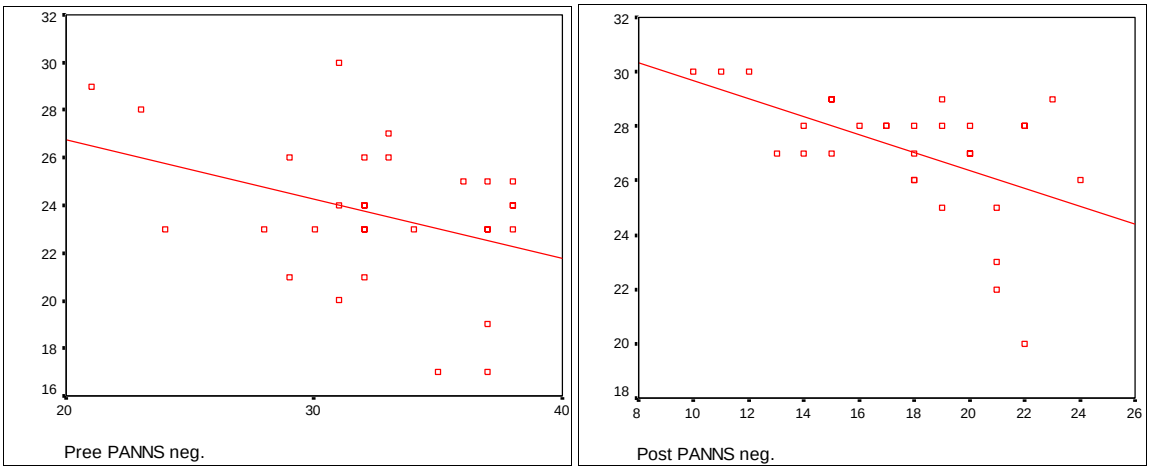

Fig 3: show Inverse correlation between SANS and MMSE (in pre and post hospitalization stages in case group)

It was found that the negative symptoms (SANS) (Blunted affect, Emotional withdrawal, Poor rapport, Apathy, Abstract thinking, Lack of conversation and Stereotyping) of the case group in pre and post hospitalization stages had a statistically significant inverse correlation (p<0.05) with MMSE in the pre and post hospitalization stages.

Table (5) show the Stepwise linear Regression Analysis of demographic data Factors affecting antiphospholipid Ig M antibodies:

Table 5: age and occupation were Significant variables of antiphospholipid Ig M antibodies that having a statistically significant (p<0.05) as shown in table (5).

IgM	Regression analysis	
	OR (95% CI)	P value
Age	0.834 (0.347 – 0.954)	0.039*
Sex	0.821 (0.514 – 2.631)	0.217
Occupation	0.479 (0.221 – 0.616	0.042*
Residence	1.415 (0.449 – 3.534)	0.138
Marital status	1.437 (0.684 – 3.607)	0.274
Special habit	2.418 (0.378 – 4.392)	0.219
Consanguinity	1.754 (0.647 – 2.618)	0.167
Family troubles	0.637 (0.184 – 1.824)	0.126

It was found that age and occupation were Significant variables of antiphospholipid Ig M antibodies that having a statistically significant (p<0.05).

Discussion

The onset of schizophrenia (SZ) often occurs in late adolescence or early adulthood. Among its most prominent symptoms are abnormalities in behaviour, perception of emotions, social connections, and perspective of reality. SZ is the most severe kind of mental disorder, with devastating repercussions on the patient's brain. It creates anomalies in the earliest brain development, which may result in a variety of symptoms including hallucinations, motivational and cognitive difficulties (DeLisi, Lynn E. 2021) [9].

Antiphospholipid syndrome (APS) has been linked to an assortment of neuropsychiatric manifestations. Psychiatric disorders that are resistant to treatment and atypical, severe cognitive impairment, migraines, transient ischemic attacks, and thromboembolic events. Antiphospholipid antibodies (APL abs) may have a role in the aetiology of some neuropsychiatric disorders. Existing APS criteria may not apply to psychiatric patients, resulting in underdiagnosis of APS in psychiatry (Sanil and Charles., 2015) [10].

Consequently, an older age of psychosis beginning and a fast symptoms onset should increase the possibility of APS as a potential underlying cause of psychosis. The majority of female patients is consistent with the greater frequency of SLE and APS in females compared to males (Labad *et al*., 2015) [11].

The aim of this prospective study was to estimate the levels of antiphospholipid antibodies as well as the cognitive performance among control and schizophrenic patients before and after hospitalization. Additionally, the clinical symptoms, as measured by PANSS scale, were also assessed among the studied patients group. Furthermore, the relation between (APL abs) and both the cognitive functions and the clinical symptoms in schizophrenic patients were studied.

As regard the demographic data of both the case and control groups.

This study showed that the majority 76.7% of the schizophrenic patients were unemployed, while the unemployment was encountered in only 26.7% of control group with a significant difference (P value = 0.001) between both groups. Additionally, most of the employed client in case group were working in simple jobs with poor work record, In agreement with these results, Abd El-Rahman *et al*., 2012 [17] found that there was a higher percentage of working people in the control group in comparison with non-working schizophrenic patients**)** These results were expected due to the effect of the schizophrenic symptoms on the patient's ability to perform everyday living skills.

Our findings showed that 60% of case group were rural residence, while 33.3% of control group were rural residence. The urban residence of case group was 40% and was 66.7% in control group with a significant difference (P value = 0.038) between both groups.

In contrast to our study, other studies revealed that increased risk of SZ was found in patients with greater urbanization (Krabbendam and van Os, 2015; Peen *et al*., 2020). Marcelis

et al., 1999 [18] were suggested that environmental factors associated with urbanization increase the risk for SZ before rather than around the time of illness onset.

These discrepancy in previous results were expected as our study was carried out at Tanta University Hospital which provide medical service to several neighboring rural areas. The present study found that the majority 53.3% of case group was single while the majority 66.7% of control group was married. These results are in agree with those reported by Pedersen and Mortensen. 2014 and Newbury *et al*., 2018 [19] who reported low rates of marriage and more single and divorced cases among schizophrenic patients.

It might be explained by the influence of the psychotic disease on the patient's coping strategies and ability to live a regular life and establish social relationships. In addition, the early onset of schizophrenia may account for the poor marriage rates of some individuals. In case group, the majority of divorce and separation cases happened after sickness start.

Regarding, the level of Antiphospholipid antibodies in the case and control groups, it was found that the IgM were positive (≥ 10 U/ml) and higher in case group with statistically significant difference (P value = 0.001) between both groups regarding this issue.

Some research (Schwartz *et al*., 2009) [20] discovered a greater incidence of ACL antibodies and anti-2GP antibodies in their patients, whilst others (Manoubi *et al*., 2015) failed to identify a link between ACL or anti-2GPI antibodies and schizophrenia. Furthermore, assay methodology, different "cut-off points" for positive antibody titers, and the features of the study population itself, such as (clinical status, age, sex, ethnic group, genetic factors, environmental factors, BMI, and smoking) were contributing to heterogeneity across different cohorts. In keeping with our findings, Basma *et al*., 2021 [23], found that the presence of one positive aPL antibody was comparable across their study's schizophrenia patient and control groups (p = 0.60). The frequency of ACL and anti-2GPI antibodies in their patients and controls was comparable. Other research evaluating ACL and anti-2GPI antibodies in schizophrenic patients revealed a broad range of outcomes.

Delluc *et al*. (2014) [24] revealed that 27.1% of their patients had at least one positive aPL abs test. A positive LA test was obtained in 27.6% of patients, and an aPL antibody was revealed in 6.9% of patients using enzyme-linked immunosorbent assay (ELISA). Patients tested positive for IgM anti-B2GP-I, IgM ACL, and IgG ACL in proportions of 3.0%, 1.2%, and 3.0%, respectively. Approximately 2.7% of patients showed positive ELISA results for both LA and aPL.

The role of immune dysregulation in SZ pathophysiology, including (increased expression of complement 4, T helper 1 and 2 disparity, abnormal cytokine levels, and the existence of multiple autoantibodies in serum and CSF) may explain the increased level of antiphospholipid antibodies in SZ cases (Orlovska-Waast *et al*., 2019) [12]. Additionally, SZ has been independently linked to abnormalities in many coagulation pathways (including the fibrinolytic system and plasminogen activators which have been associated with aPL and APS as well). Protease activated are inducible proteases that play a crucial role in clotting dissolution, angiogenesis, and tissue healing, and are also involved in the pathophysiology of schizophrenia by directly altering the hippocampus area and dopamine levels (Ricarte *et al*., 2018) [21]. SZ is among the 'extra-criteria' signs of APS that have been documented (Dahan *et al*., 2018) [22].

The current study showed that, the mean of the total SAPS scale was lower in the post hospitalization stage (18.23±2.86) than in the pre hospitalization stage (33.13±4.70). The conceptual disorganization and the hallucinatory behavior were the most common positive symptoms in the patients of the present study. The total mean of SAPS scale showed a statistically significant difference (p value = 0.001) in case group between pre and post hospitalization stages it may be explained by the efficacy of treatment.

Our results are similar to results of Peen *et al*., 2020 and Scott *et al*., 2018, which reported that the mean value of the SAPS scale in their case group was 27.54±6.82 and 25.54±6.44 respectively with statistically significant difference between their case group and control groups regarding SAPS (P value = 0.001 and 0.002 respectively). The most common positive symptoms in the patients were Persecution**,** Delusion and the hallucinatory behavior.

-Regarding the correlation between Scale for Assessment of Positive Symptoms (SAPS) and level of antiphospholipid antibodies in case group The current study showed that the positive symptoms (SAPS) (Delusion, Conceptual disorganization, Hallucinatory behavior, Excitement, Grandiosity, Persecution and Hostility) of the case group in pre and post hospitalization stages had a statistically significant direct correlation (P value < 0.05) with antiphospholipid Ig M antibodies. There is no correlation between the positive symptoms (SAPS) and antiphospholipid Ig G antibodies in the case group.

As regard, The Correlation between Scale for Assessment of Negative Symptoms (SANS) and Mini Mental State examination (MMSE) in the case group Our study found that the scale for assessment of negative symptoms (SANS) (Blunted affect, Emotional withdrawal, Poor rapport, Apathy, Abstract thinking, Lack of conversation and Stereotyping) of the case group in pre and post hospitalization stages had a statistically significant inverse correlation (P value < 0.05) with MMSE in the pre hospitalization stage.

Patients in the Hallab *et al*., 2018 [25] research tested positively for ANA, IgM ACL, IgG ACL, and LA, all of which indicate a healthy immune system. In 34 unmediated individuals without a documented autoimmune condition who were hospitalized for their first acute episode of psychosis, Fernandes *et al*., 2016 found a correlation between ACL, LA, and psychosis. IgG ACL antibodies were present in 34% of patients, while LA was present in 9%. A sample of 20 healthy people showed no signs of either condition. APS Abs were detected solely in the cerebral fluid of one 12-year-old child, prompting researchers to conclude that these antibodies were CSF origined.

Stepwise linear Regression Analysis of demographic and clinical data Factors affecting level of antiphospholipid Ig M antibodies our study showed that age and occupation were Significant variables of antiphospholipid Ig M antibodies that having a statistically significant.

The 2019 study by Duarte-Garca *et al*. confirmed that women are disproportionately affected by systemic autoimmune illnesses, and that these diseases are often most debilitating in the middle years of life or during pregnancy.

Population-based studies conducted during the last decade indicate that the average age of APS diagnosis is close to 50. Bertero *et al*., 2012 [26] showed decreased mean age of diagnosis such as in the Euro-phospholipid project and the APS piedmont cohort. Cervera *et al*., 2009 [27] observed a peak age for incidence in males of 55-59 years, but for women the incidence peaked at 35-39 years. The prevalence of APS peaked between the ages of 70 and 79 in men alone, according to the study by Hwang *et al*., 2020. In women, the prevalence peaked at ages 30-39 and 70-79. In contrast, the incidence increased between the ages of 55 and 64 for males and 75 and beyond for females in the research by Radin *et al*., 2020. Variations in peak APS occurrence age among studies may be attributable to study-specific factors such as the prevalence of secondary vs primary APS cases or even the racial and ethnic composition of the research populations (Dabit *et al*., 2021) [28].

Shlomo *et al*., 2008 reported occupational APS which is an autoimmune disorder with a clear link to prolonged exposure to photocopy machines; patients who had done so for years typically presented with thromboembolic phenomena and anticardiolipin antibodies as the first autoantibodies to appear, followed by joint and kidney involvement. Occupation-related exposure to UV radiation, ozone emission, and some oxides of heavy metals may have triggered an autoimmune response in these cases.

Limitation and Recommendations

-The prospective study with very short follow up time was the main limitation of this study, it is better if it was with larger numbers in multicenter hospitals are done.

-The schizophrenic patients during hospitalization take different regimens of treatment which may affect in the results of the study.

-Most of schizophrenic patients were non-compliant on treatment and refused the post hospitalization scales and blood sampling.

So we recommend that

-Future studies would need to replicate the findings of the present work with a much larger sample size to understand the relation between antiphospholipid antibodies and schizophrenia.

-Antiphospholipid antibodies screening in patients with first episodes of psychosis.

-Studying of the cognitive functions in unaffected relatives of schizophrenic patients may help in early detection of high-risk individuals for schizophrenia.

-Other antibodies (e.g. ANA, ANCA, and dsDNA) have to be assayed in future studies to determine their impact on symptoms and cognitive functions in schizophrenic patients.

-It is important to determine whether the results of the present study, for patients with mild-moderate schizophrenia, are generalizable to patients with a more severe involvement.

Conclusion

-Schizophrenia is a chronic disease affect mainly adolescents and young adults in both males and females. It has a great effect on life style, work, education and marital status. the level of Antiphospholipid antibodies IgM were positive in case group and there was statistically significant difference between both case and control groups. There was no statistically significant difference between both groups regarding the level of Antiphospholipid antibodies Ig G. The positive symptoms (SAPS) of the cases had direct correlation with antiphospholipid Ig M antibodies while the negative symptoms (SANS) of the cases inverse correlation with MMSE.

Conflict of Interest

Not available

Financial Support

Not available

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