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Assessment of coagulation profiles among Sudanese psychiatric patients under antipsychotic drugs attending Hassan Allob Mental Hospital, Gezira State, Sudan (2020)

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***Abstract*---**Background: Psychiatric disorder is a mental illness diagnosed by a mental health professional that greatly disorders thinking. A psychotropic drug is a chemical substance that crosses the blood brain barrier (BBB) and acts primarily upon the central nervous system (CNS), where it affects brain function, resulting in change in perception, mood, consciousness, cognition, and behavior. It causes changes in platelet function, plasma coagulation, or fibrinolysis seemed more likely to be responsible for the increase in thrombotic events. Objectives: The aim of this study was to assess the coagulation profiles [Prothrombin Time (PT), International Normalize Ratio (INR), Activated Partial Thromboplastin Time (APTT)] in

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psychiatric patients under antipsychotic drug administration. Methodology: This is a case-control hospital-based study carried out in Hassan Allob Mental Hospital, Gezira State, Sudan from January to September 2020. A total of 50 psychiatric patients under antipsychotic drug administration as cases (35.52 ± 11.64 years) and 50 normal healthy individuals as controls (32.68 ± 4.85 years) participated in this study. Two ml of venous blood samples were collected from all participants in trisodium citrate container. Coagulation profiles (PT, INR, and APTT) were measured using a Coatron M4 coagulometer. SPSS computer program (v 22.0) was used for data analysis. Results: The study results showed that the prolonged PT, INR, and APTT account for 92%, 92%, and 40% respectively. Furthermore, the means of PT, INR, and APTT of cases (16.20 ± 0.92 sec, 1.16 ± 0.06, and 39.09 ± 4.12 sec respectively) were higher compared to controls (13.84 ± 0.62 sec, 0.98 ± 0.04, and 32.97 ± 1.99 respectively) giving highly statistically significant differences (P value = 0.000, 0.000, and 0.000) between them. The PT and INR had significant positive correlation within drug usage duration (P value = 0.004; r = 0.483; P value = 0.001; r = 0.453 respectively). Conclusion: The study concluded that the coagulation profiles (PT, INR, and APTT) were significantly prolonged in psychiatric patients under antipsychotic drug administration; so, coagulation profiles (PT, INR, and APTT) should be used as included for assessing and prognosis the psychiatric patients under antipsychotic drug administration.

***Keywords*---**PT, INR, APTT, antipsychotic drugs, psychiatric disorder, Sudan.

Introduction

Psychiatric disorder is a mental illness diagnosed by a mental health professional that greatly disorders your thinking (1). Schizophrenia, Bipolar disorder, Depression, Social phobia, and Anxiety are most common types of psychiatric disorders (2). A psychotropic drug is defined as: a chemical substance that crosses the blood brain barrier (BBB) and such acts primarily upon the central nervous system (CNS), where it affects brain function, resulting in change in perception, mood, consciousness, cognition, and behavior. Antipsychotics are group of medicines that are mainly used to treat mental health illnesses such as Schizophrenia, or mania caused by bipolar disorder, also can treat severe Depression and severe Anxiety (3).

In 2017 it estimated that 970 million persons worldwide suffered of mental, or substance use disorder with largest number suffered from anxiety (4% of the population). In Sudan about 16% suffered from mental or substance use disorders with highest number had anxiety (4.9%) and depression (3.78%) (4). The World Health Organization (WHO) estimates that one of four families worldwide has at least one member suffering from a mental disorder and mental disorders will be the most global burden of disease by the year 2020 (5). The worldwide-pooled prevalence of mental disorders included 41 studies conducted

in 27 countries from every world region was 13.4%, anxiety disorder was 6.5%, depressive disorder was 2.6%, attention-deficit hyperactivity disorder was 3.4%, and any disruptive disorder was 5.7% (6).

There is no national prevalence study has been conducted across the whole country, yet the following are indicative examples of findings from published prevalence studies found that prevalence of depression and anxiety in high-school students in Khartoum State has been estimated to be 12%.6, the prevalence of perinatal psychiatric disorders in primary care settings and communities in the capital city of Sudan has been estimated at 23%.7, higher rates of psychiatric disorders have been found among internally displaced persons (53%) including major depressive disorder (24.3%), generalized anxiety disorder (23.6%), social phobia (14.2%) and post-traumatic stress disorder (12.3%) (7).

Types of antipsychotic drugs (APD) include Typical “conventional” antipsychotics (such as Chlorpromazine, Haloperidol, Molindone, and Thiothixene) and atypical antipsychotics (which are more commonly used than typical agents) (such as Risperidone, Olanzapine, Paliperidone, and Clozapine) (8-9). The common side effects of these drugs include drowsiness, dizziness, restlessness, weight gain (more evident with some atypical antipsychotic drugs), dry mouth, constipation, nausea, vomiting (10).

Although the exact mechanism of a typical antipsychotics is unknown they are thought to block certain chemical receptors in the brain and hence relieve the symptoms of psychotic disorders (11) and the exact biological mechanism for explanation of possible association between antipsychotic drugs and VTE (Venous Thromboembolism) is still unknown (12), but once antipsychotics are administrated, changes in platelet function, plasma coagulation, or fibrinolysis seemed more likely to be responsible for the increase in thrombotic events (13).

There is increasing reports suggest a link between hematological abnormalities (As: risk of venous thromboembolism, platelet, and fibrinolytic abnormalities) and the use of antipsychotic drugs such as: risk of venous thromboembolism (VTE) in a large primary care population, serious ventricular arrhythmias, risk of bleeding and sudden cardiac death (14). During the initial months of treatment with antipsychotic drugs the risk for venous thromboembolism (VTE) seems to be highest although biological mechanisms responsible for this possible adverse drug reaction are unknown till, but a number of hypotheses have been suggested and believed that increased risk may be the result of drug-induced sedation, obesity, hyperleptinemia, antiphospholipid antibodies and increased activity in the coagulation system and the association could also be related to underlying risk factors present in patients with psychosis (15). Thrombotic tendency has been usually associated with psychotropic medication and with immobility, as in restraint or catatonia (16). The increased bleeding risk observed in some patients on serotoninergic anti-depressants which has been related to platelet and fibrinolytic abnormalities (17).

The increased risk was more marked among new users and those prescribed atypical antipsychotic drugs and increased bleeding risk observed in some patients on serotoninergic anti-depressants which has been related to platelet and

fibrinolytic abnormalities (17). Potential etiopathogenetic factors leading to VTE during treatment with antipsychotic agents include sedation, obesity, elevation of anti-phospholipid antibodies, increased platelet activation and aggregation, hyperhomocysteinemia, and hyperprolactinemia (18). The aim of this study is to assess coagulation profiles (PT, INR, and APTT) in patients on psychiatric patients under antipsychotic drug administration to view the susceptibility to hemorrhage or thrombosis.

Materials and Methods

The study was designed as case-control hospital-based study, carried out at Hassan Allob Mental Hospital, Gezira State, Sudan during period from January to September 2020. The samples were collected randomly from 50 psychiatric patients under confirmed usage of antipsychotic drug as cases and 50 normal healthy individuals as controls according to inclusion and exclusion criteria. Ethical approval was obtained from both Research and Ethics Committees (REC) of Ministry of Health, Gezira State and Faculty of Medical Laboratory Sciences, University of Gezira, Sudan. Ethical permission was obtained from Hassan Allob Mental Hospital, Wad Medani, Gezira State. Informed consent was written from each participant.

A 2 ml venous blood sample was collected by clean venipuncture technique in tri sodium citrate container) from each participant. The platelets poor plasma was obtained by centrifugation of blood at 1200 – 2000 rpm for 15 minutes (19). Prothrombin Time (PT), International Normalize Ratio (INR), and Activated Partial Thrombin Time (APTT) were measured using a Coatron M4 coagulometer. The data were analyzed using statistical package for social sciences (SPSS) computer program (Version 22.0).

Results

50 Sudanese psychiatric patients under confirmed usage of antipsychotic drug as cases (mean age 35.52 ± 11.64 years with age range from 20 to 70 years) and 50 normal healthy individuals as control (mean age 30.68 ± 2.85 years) were participated in this study. 45% cases were males, and 60% from rural area (Table 1).

Table 1: Demographic characteristics of study participants

Factors	Cases (N = 50)	Control (N = 50)
Age (years)	35.52 ± 11.64	32.68 ± 4.85
Age group (years)		
Less than 30 years	26 (52 %)	25 (50 %)
More than 30 years	24 (48 %)	25 (50 %)
Gender		
Male	45 (90 %)	30 (60 %)
Female	5 (10 %)	20 (40 %)
Residence		
Urban	20 (40 %)	24 (48 %)

Rural	30 (60 %)	26 (52 %)
Educational level		
Illiterate	4 (8 %)	-
Primary level	17 (34 %)	15 (30 %)
Secondary level	19 (38 %)	20 (40 %)
Graduate level	10 (20 %)	15 (30 %)

A Typical antipsychotics drug was most common drug usage (92%). 54 of cases use Olan. Most cases (92%) take twice dose in day (Table 2).

Table 2: Drug characteristics of study cases

Factors	Cases (N = 50)
Drug group	
Typical antipsychotics	4 (8 %)
A Typical antipsychotic	46 (92 %)
Drug types	
Haloperidol	4 (8 %)
Olan	27 (54 %)
Risperidone	17 (34 %)
Olan and Risperidone	2 (4 %)
Duration of drug usage	
Up to 2 years	23 (46 %)
More than 2 years	27 (54 %)
Drug dose/ day	
Once/ day	9 (18 %)
Twice/ day	41 (82 %)

The prolonged PT, INR, and APTT account for 92%, 92%, and 40% respectively (Table 3).

Table 3: Frequency of coagulation profiles (PT, INR, and APTT) among cases

Parameters	Normal	Prolonged
PT/ sec	4 (8 %)	46 (92 %)
INR	4 (8 %)	46 (92 %)
APTT/ sec	30 (60 %)	20 (40 %)

The means of PT, INR, and APTT of cases (16.20 ± 0.92 sec, 1.16 ± 0.06, and 39.09 ± 4.12 sec respectively) versus controls (13.84 ± 0.62 sec, 0.98 ± 0.04, and 32.97 ± 1.99 respectively) giving highly statistically significant differences (P value = 0.000, 0.000, and 0.000) between them (Table 4).

Table 4: Comparison of coagulation profiles (PT, INR, and APTT) between cases and control

Parameters	Cases (N=50) (Mean ± SD)	Controls (N=50) (Mean ± SD)	P value *
PT/ sec	16.20 ± 0.92	13.84 ± 0.62	**0.000**

INR	1.16 ± 0.06	0.98 ± 0.04	**0.000**
APTT/ sec	39.09 ± 4.12	32.97 ± 1.99	**0.000**

There were no significant differences in PT, INR, and APTT between patients take Typical and A Typical antipsychotics drug (P value = 0.428, 0.401, and 0.470 respectively) (Table 5).

Table 5**:** Comparison of coagulation profiles (PT, INR, and APTT) between Typical and A Typical antipsychotics drug

Parameters	Typical (N=4) (Mean ± SD)	A Typical (N=46) (Mean ± SD)	P value *
PT/ sec	16.45 ± 0.54	16.18 ± 0.95	0.428
INR	1.18 ± 0.04	1.15 ± 0.07	0.401
APTT/ sec	40.95 ± 4.81	38.93 ± 4.08	0.470

There were no significant differences in PT, INR, and APTT between different antipsychotics drugs (P value = 0.674, 0.640, and 0.765 respectively) (Table 6).

Table 6**:** Comparison of coagulation profiles (PT, INR, and APTT) between drugs types

Parameters	Haloperidol (N=4)	Olan (N=27)	Risperidone (N=17)	Olan+Risperidone (N=2)	P value *
PT/ sec	16.45 ± 0.55	16.13 ± 1.01	16.19 ± 0.89	16.90 ± 0.14	0.674
INR	1.18 ± 0.04	1.15 ± 0.07	1.15 ± 0.06	1.21 ± 0.01	0.640
APTT/ sec	40.95 ± 4.81	38.91 ± 4.95	39.13 ± 3.48	37.40 ± 0.84	0.765

There were significant differences in PT and INR between drugs usage duration (P value = 0.000, and 0.001 respectively) (Table 7).

Table 7: Comparison of coagulation profiles (PT, INR, and APTT) between drugs usage duration.

Parameters	≤ 2 years (N=23) (Mean ± SD)	> 2 years (N=27) (Mean ± SD)	P value *
PT/ sec	15.73 ± 1.09	16.60 ± 0.47	**0.000**
INR	1.12 ± 0.08	1.18 ± 0.03	**0.001**
APTT/ sec	38.24 ± 5.00	39.81 ± 3.13	0.184

There were no significant differences in PT, INR, and APTT between drug dose/day (P value = 0.768, 0.868, and 0.742 respectively) (Table 8).

Table 8: Comparison of coagulation profiles (PT, INR, and APTT) between drug dose/day

Parameters	Once/ day (N=9) (Mean ± SD)	Twice/ day (N=41) (Mean ± SD)	P value *

PT/ sec	16.12 ± 0.88	16.22 ± 0.94	0.768
INR	1.15 ± 0.06	1.16 ± 0.07	0.868
APTT/ sec	38.67 ± 2.39	39.18 ± 4.43	0.742

PT and INR had significant positive correlation within drug usage duration (P value = 0.004; r = 0.483; P value = 0.001; r = 0.453 respectively) and age (P value = 0.020; r = 0.310; P value = 0.030; r = 0.306 respectively) (Table 9).

Table 9: Correlation between coagulation profiles (PT, INR, and APTT) and drug usage duration and age

Parameters		**Drug duration**	**Age**
PT/ sec	**Correlation coefficient**	0.483	0.310
	P value*	**0.004**	**0.020**
INR	**Correlation coefficient**	0.453	0.306
	P value*	**0.001**	**0.030**
APTT/ sec	**Correlation coefficient**	- 0.202	- 0.031
	P value*	0.158	0.831

Discussion

Psychiatric disorder is a mental illness diagnosed by a mental health professional that greatly disorders thinking (1). Antipsychotics are a group of medicines that are mainly used to treat mental health illnesses such as schizophrenia, or mania caused by bipolar disorder, also can treat severe depression and severe anxiety (3).

This is a case-control hospital-based study conducted from January to September 2020. It aimed to assess the coagulation profiles (PT, INR and APTT) in patients under antipsychotic drug administration attending Hassan Allob Mental Hospital. The study population consisted of 100 participants, 50 as cases and 50 as normal healthy controls. The present study reflected that male comprise most of the cases (90%) than females (10%) and this disagreed with study done by Mohammed which reported that (60%) were males and (40%) were females (20), but that may be because females in this study were hard to convince to participate. The mean age of cases was 35.52 ± 11.64 years.

According to drug group 4 (8%) were with Typical APDs and 46 (92%) were with Atypical APDs; and that because Atypical APDs had largely substitute Typical APDs due to their ability to reduce EPS like dizziness, rigors, vomiting, .etc. While distribution of cases according to drug type (name), 4 (8%) were using Haloperidol (The most commonly used in the group of typical APDs), 27 (54%) were using Olan (which belonged to atypical drug group and the most commonly wide use in it is group), 17 (32%) were using Risperidone (which too belonged to atypical drug group) and 2 of the cases (4%) used a combination of Olan+Risperidone and again this reflected the wide use of Atypical APDs. As for duration of drug

administration almost half of cases were under usage of APDs up to 2 years (46%) and that may reflect an increase in prevalence of psychotic episodes in the last few years for so many known and unknown causes, where others distributed in the other group of duration. According to daily dosage use, 9 patients (18%) were using APDs once/day, while 41 (82%) were using APDs twice/day usage.

Depending on frequency of coagulation profiles, out of all cases, only 4 (8%) had normal PT, 46 (92%) were having prolonged results readings and none were shorted and the same goes to INR results. On the other hand, 30 (60%) had normal APTT, 20 (40%) were having prolonged readings and none were shorted. The means of PT, INR and APTT levels of cases were significantly higher than controls (P value = 0.000, 0.000 and 0.000 respectively) which stated a case of prolongation; and that agreed with Mohammed (20), Omisakin *et al* (21), Eldaw (22) were there results showed prolongation of the coagulation profiles (PT, INR and APTT) in patients using antipsychotic drugs like the cases of this study and this is may be due to factor deficiency, presence of inhibitors, altered mechanism of coagulation…ect, but the results of this study agreed partially with Zarrabi *et al* who found prolongation in APTT when using Chlorpromazine which belong to Typical APDs for long term (23).

Comparison of coagulation profiles (PT, INR, and APTT) between cases on different drug group (Typical or Atypical) showed no significant differences between cases using typical APDs and cases using atypical APDs (P value >0.05). this agreed with several previous studies (20-23), and that stated the two groups of APDs (Typical and Atypical) had the same impact on the coagulation profile (PT, INR, and APTT) in all previous studies and this study except Mohammed *et al*, 2005 where the effect showed only on APTT.

Regarding drug type (name) there were statistical no significant differences in coagulation profiles (PT, INR and APTT) between drug type (name) used in cases, and this agreed with previous studies (20-22) and partially with Zarrabi et al., (23) on APTT only, and this stated that the prolongation of PT, INR and APTT were the same in case of using any of the drug listed but the effect were much evident with combined drugs (Olan+Risperidone) in this study, which projected higher means of PT and INR but lower mean in APTT comparing to other drug types and this may say that the damage in the hemostatic mechanism (coagulation profile) were greater .

As for comparing coagulation profiles (PT, INR and APTT) with drug duration there were statistically significant differences in PT and INR (P value = 0.001 and 0.000 respectively) and that stated a prolongation in PT and INR with duration of drug administration, but APTT showed statistically no significant difference. This finding disagreed with Zarrabi *et al.,* (23) who found prolongation only in APTT with long term usage of Chlorpromazine and disagreed partially with Eldaw (22) who found statistical no significant difference in PT, INR and APTT and duration and this show that the time counted from the start of APDs administration influenced the coagulation profile later.

There were no statistically significant differences in PT, INR and APTT between drug dosage and this showed that the dose\day wither it was once or twice leave no difference in the coagulation profiles except the initial effect which is prolongation of PT, INR and APTT. This may be due to the different concentrations of the drug itself or wither it is low or high potency drug.

When applied correlation between coagulation profiles (PT, INR and APTT) and drug duration and age. The drug duration showed statistically significant positive but weak correlation with PT and INR (r =0.483 and 0.453 respectively). This means that PT and INR increase with increase drug duration in patients with psychiatric disorder but not APTT. Age showed statistically significant positive but weak correlation with PT and INR (r = 0.310 and 0.306 respectively). This mean that PT and INR increase with age in patients suffering psychiatric disorder and under APDs usage but not APTT. This may be due to that some factors are age dependence, other studies mentioned in literature did a comparison but not a correlation so there were no correlation results to compare.

Conclusion

The study concluded that the coagulation profiles (PT, INR, and APTT) were significantly prolonged in psychiatric patients under antipsychotic drug administration. Furthermore, PT and INR significantly prolonged with increase the drug duration usage. So, coagulation profiles especially PT and INR should be included as follow-up routine test for the psychiatric patients under antipsychotic drug administration.

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References

1. Gross G and Huber G. The history of the basic symptoms concept. *Acta Clinica Croatica*. 2010, 49: 47-59.
2. GBD 2017 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *Global Health Metrics*. 2018, 392(10159): P1789-1858. doi.org/10.1016/S0140-6736(18)32279-7
3. Zornberg GL and Jick H. Antipsychotic Drugs used and the Risk of First-time Idiopathic Venous Thromboembolism: A Case Control Study. *Lancet.*2000, 356(9237):1219-1223. doi: 10.1016/S0140-6736(00)02784-7.
4. Roser M and Ritchie H. Burden of Disease. *Published online at OurWorldInData.org.* Retrieved from: 'https://ourworldindata.org/burden-of-disease' [Online Resource]. 2021.
5. Lopez AD; Mathers CD; Ezzati M; Jamison DT; Murray CJL. *Global Burden of Disease and Risk Factors*. The International Bank for Reconstruction and Development / The World Bank; New York: Oxford University Press. 2006. ISBN-10: 0-8213-6262-3.

6. Polanczyk GV, Salum GA, Sugaya LS, Caye A, Rohde LA. Annual Research Review: A meta-analysis of the worldwide prevalence of mental disorders in children and adolescents. *J Child Psychol Psychiatry*. 2015, 56(3): 345-365. doi: 10.1111/jcpp.12381.
7. Salah TT, Abdelrahman A, Lien L, Eide AH, Martinez P, Hauff E. The mental health of internally displaced persons: an epidemiological study of adults in two settlements in Central Sudan. *Int J Soc Psychiatry*. 2013, 59(8): 782–788. doi: 10.1177/0020764012456810.
8. Allison DB and Casey DE. Antipsychotic-induced weight gain: a review of the literature. *J Clin Psychiatry*. 2001, 62(7): 22-31. PMID: 11346192.
9. Meltzer HY. Update on typical and atypical antipsychotic drugs. *Annu Rev Med*. 2013, 64: 393-406. doi: 10.1146/annurev-med-050911-161504.
10. Dibonaventura M, Gabriel S, Dupclay L, Gupta S, Kim E. A patient perspective of the impact of medication side effects on adherence: result of a cross-sectional nationwide survey patients with Schizophrenia. *BMC Psychiatry*. 2012, *12*:20. doi: 10.1186/1471-244X-12-20.
11. Horacek J, Bubenikova-Valesova V, Kopecek M, Palenicek T, Donkery C, Mohr P, Höschl C. Mechanism of action of atypical antipsychotic drugs and the neurobiology of schizophreneia. *CNS drugs*. 2006, 20(5): 389-409. doi: 10.2165/00023210-200620050-00004.
12. Tripp AC. Nonfatal pulmonary embolus associated with clozapine treatment: a case series. *Gen Hosp Psychiatry*. 2011, 33(1):85.e5-6. doi: 10.1016/j.genhosppsych.2010.11.010.
13. Liperoti R and Gambassi G. Antipsychotics and the risk of venous thromboembolism. *BMJ*. 2010, 341:c4216. doi: 10.1136/bmj.c4216..
14. Ray WA, Chung CP, Murray KT, Hall K, Stein CM. (2009). Atypical antipsychotic drugs and the risk of sudden cardiac death. N Engl J Med. 2009, 360(3):225-235. doi: 10.1056/NEJMoa0806994.
15. Hägg S, Jonsson AK, Spigset O. Risk of venous thromboembolism due to antipsychotic drug therapy. *Expert Opinion on Drug Saftey*. 2009, 8(5):537-547. doi: 10.1517/14740330903117271
16. Ishida T, Katagiri T, Uchida H, Takeuchi H, Sakurai H, Watanabe K, Mimura M. Incidence of deep vein thrombosis in restrained psychiatric patients. *Psychosomatics*. 2014, 55(1):69-75. doi: 10.1016/j.psym.2013.04.001.
17. Bismuth-Evenzal Y, Gonopolsky Y, Gurwitz D, Lancu L; Weizman A, Rehavi M. Decreased serotonin content and reduced agonist-induced aggregation in platelets of patients chronically medicated with SSRI drugs. *J affect Disord*. 2012, 136(1-2): 99-103. doi: 10.1016/j.jad.2011.08.013.
18. Masopust J, Malý R, Vališ M. Risk of venous thromboembolism during treatment with antipsychotic agents. *Psychiatry Clin Neurosci*. 2012, 66(7):541-552. doi: 10.1111/pcn.12001.
19. Bain BJ; Bates I; Laffan M; Lewis S. *Dacie and Lewis practical haematology*. (11th edition): Churchill Livingstone, London. 2011, Pp:394-411.
20. Mohammed SE. *Determination of Coagulation Profile among Patients under Antipsychotic Drugs*. (M. Sc. degree dissertation, University of Shendi. http://hdl.handle.net/123456789/821).
21. Afolabi OI, Adedire OA, Oke OT, Omisakin CT, Esan AJ. Coagulation Activities of Patients on Psychotropic Drugs in Nigeria. *American Journal of*

Medical Sciences and Medicine. 2014, 2 (2): 41-43. doi: 10.12691/ajmsm-2-2-3

22. Eldaw MFM. (2019). *Estimation of Prothrombin and Activated Prothrombin Time among Sudanese Patients Taking Antipsychotic Drugs in Khartoum State*. (M. Sc. degree dissertation, Sudan University of Science and Technology. http://repository.sustech.edu/handle/123456789/24981).
23. Zarrabi MH, Zucker S, Miller F, Derman RM, Romano GS, Hartnett JA, Varma AO. Immunologic and coagulation disorders in chlorpromazine-treated patients. *Ann Intern Med*. 1979, 91(2):194-199. doi: 10.7326/0003-4819-91-2-194.