Original article:

Red cell indices and peripheral blood film findings of anti-Psychotic treatment and treatment naïve Psychiatic patients in a tertiary Hospital in Nigeria.

AO Shittu[1], AO Adewoye[2], HO Olawumi[3]

Abstract:

Background: The overall burden of morbidity and mortality from psychiatric disorders is on the rise. Holistic approach in the care of this group of patients has become inevitable. There is need for collaboration between psychiatrists and other physicians, laboratory physicians inclusive. ***Study design***: cross sectional descriptive case- control study. ***Materials and method:*** A total of 198 patients including controls were recruited for this study. Patients with schizophrenia constituted majority of the respondents, 86.4% of antipsychotic-naïve patients and 90.9% of patients on antipsychotics. A comprehensive medical examination was carried out on every participant. On every sample, automated Full Blood Count was performed using Sysmex2000i and peripheral blood film was made and examined. ***Result:*** 51.5% and 47% of anti-psychotropic-naïve patients and patients on anti-psychotic were 18-40 and 41-60 years respectively. Male (57.6%), predominated the anti-psychotic naïve group while female (51.5%) predominated the group on anti-psychotics. Schizophrenia was the diagnosis in the majority of patients, 86.4% and 91% respectively in anti-psychotic naïve and anti-psychotic treatment groups. Other diagnoses were depressive illness, substance use disorder and dementia. Of all the subjects, one (1.5%) schizophrenic patients and two (3%) of controls had abnormal haemogram results. For the schizophrenic patient with abnormal results, haematocrit was 12g/dl, MCV of 75fl and MCH of 26pg, while the two controls with abnormal results had only haematocrit deranged with value of 12.3g/d. Neutrophil hypersegmentation was seen on the film of five antipsychotic-naïve patients (7.5%) diagnosed with Schizophrenia and one (1.5%) of the controls. Macrocytosis was only seen in three (4.5%) of the five antipsychotic-naïve patients that had neutrophil hypersegmentation. ***Conclusion:*** No significant difference was noted in the Full Blood Counts among the two sets of patients and controls, although there were isolated cases of neutrohil hyperesegmentation and macrocytosis.

Keywards: psychiatric disorders; Schizophrenia; Macrocytosis

Bangladesh Journal of Medical Science Vol. 18 No. 02 April'19. Page :196-205
DOI: https://doi.org/10.3329/bjms.v18i2.40685

Introduction:

The overall burden of morbidity and mortality from psychiatric disorders is on the rise and is becoming a global public health concern[1]. Psychiatric disorders (PDs) have been greatly underscored as causes of disability, but they account for five out of 10 leading causes of disability[2]. Holistic approach to mental health care has therefore become inevitable[3]. For this approach to be implemented there is need for

1. AO Shittu, Department of Haematology, University of Ilorin.
2. AO Adewoye, Department of Haematology, General Hospital, Katsina.
3. HO Olawumi, Department of Haematology, University of Ilorin.

Correspondence to: Dr Shittu AO, Department of Haematology, University of Ilorin, PMB 1515, Ilorin, Nigeria. Email: drakeem06@yahoo.com

collaboration between psychiatrists and other physicians, laboratory physicians inclusive. The importance of laboratory medicine has recently been re-emphasized with advances in biological psychiatry[4]. The laboratory methods available now not only confirm diagnosis, but also help to regulate dosage of medication and response to treatment. Diagnoses of psychiatric disorders are made from both clinical and laboratory features. The clinical features include depression, social withdrawal, Hostility or suspiciousness, extreme reaction to criticism, Deterioration of personal hygiene to mention but a few, while the laboratory ones range from low haematocrit, macrocytosis, anisocytosis, poikilocytosis, elevated Mean Corpuscular Volume (MCV), low serum cobalamin and low red cell folate with megaloblastic erythropoeisis in the bone marrow.

It has been reported that clinical features may precede haematological ones for several years[5]. Even within haematological features, low serum cobalamin symptoms may occur in the absence of anaemia and macrocytosis. This is because when nutritional deficiency is on-going in the body, cobalamin levels in the neuronal tissues falls much earlier than that in the serum[5,6,7]. These facts explain why routine laboratory tests are unreliable for the diagnosis of PDs[5,7].

In view of these, the highly sensitive serum Metyhlmalonic acid (MMA) and Homocystein levels used in detecting cobalamin deficiency and deficiencies of both cobalamin and folate respectively would be more appropriate in the investigations of patients with PDs, but the bottlenecks associated with laboratory analysis of MMA and homocystein[8,9] have limited their routine use in the diagnosis of cobalamin and folate deficiencies- hyperhomocysteinaemia is seen in variety of other disorders like chronic renal failure, alcoholism, smoking and a highly expensive reagents for MMA assay.

Although haematological parameters are not part of the diagnostic criteria for PDs, they may serve as baseline for monitoring treatment and disease progression or as a pointer to an organic basis for PDs. For example, neutropenia has been shown to contribute to immunological factors in the pathogenesis of Obsessive Compulsory Disorders[10]. Neutropenia has also been frequently observed with the use of clozapine[11]. Thrombocytopenia and raised MCV has been observed with the use of sodium valproate dosage level above 80µg/mol especially in females[12]. Auto-erythrocytic sensitization syndrome, a rare mental health problem, characterized by painful and spontaneous purpura especially in female psychiatric patients can be ruled out with Full Blood Count and peripheral blood film examination findings.

There have been conflicting reports on red cell indices and peripheral blood film findings in patients with PDs. The aim of this study was therefore to assess the Full Blood Count and peripheral blood findings of these groups of patients and compare our results with that of other researchers.

Materials and method:

Study Area: This study was carried out at the Psychiatric Out-Patient Clinic and Department of Haematology and Blood Transfusion of University of Ilorin Teaching Hospital (UITH), Ilorin, Nigeria. The hospital is a five star, 504 bedded hospital located at the North Central region of Nigeria. The hospital serves as referral centre for most other hospitals in the region with an estimated population of about 15450084.

General Adult Psychiatric Clinics are run on Mondays, Tuesdays and Thursdays where patients are reviewed by consultant behavioural scientists.

Study Design: it was a cross sectional descriptive case- control study.

Study Population: consisted of

1. Newly diagnosed, anti-psychotic naïve patients.
2. Psychiatric patients already on antipsychotics medication on follow-up.
3. Routine blood donors who were certified fit to donate blood and assessed to be free of psychiatric ailments using General health Questionnaire-12 (GHQ-12) served as case controls.

GHQ-12 is a 12 item versions and self

administered questionnaire used to screen for psychiatric morbidity. Its use has been validated in this environment, with a cut-off of 3[13].

Sample Technique: a multi-staged technique where all newly presenting antipsychotic-naïve patients who certified inclusion criteria were recruited until the required number was obtained. For those on antipsychotics for follow-up, only those registered with even numbers were recruited for the study. The reason for this was because our data showed that patients on follow-up out-numbered newly presenting ones several folds. Equal number of controls was also recruited for the study.

Inclusion criteria for study population

1. Adult newly diagnosed antipsychotic naïve psychiatric patients aged 18-65 years who met ICD-10 criteria[14].
2. Adult psychiatric patients on anti-psychotics who met ICD-10 criteria.

Exclusion criteria for study population:

1. Presence of chronic co-morbidity/ies like hypertension, Diabetes mellitus.
2. Psychiatric patients on haematics or multivitamins.

Inclusion criteria for controls:

1. Blood donors not on haematinics or multivitamins.
2. Blood donors with no physical morbidity/ies.

Exclusion criteria for controls:

1. Blood donors with GHQ-12 >3.
2. Blood donors who did not give consent.

Sample Size: Sixty six (66) each of the study populations and controls were used based on the formular by AraoyeMO[15].

Ethical Issues: Ethical clearance was obtained from UITH Ethical Research Committee. Written permission was also obtained from Heads of Psychiatry and Haematology departments and consultants in charge of the patients. A signed informed consent was obtained from every participant before being recruited.

Every participant was given a number to ensure confidentiality. All pieces of information were kept confidential. There was no harm to participants except for slight discomfort during venepuncture. No financial burden on the participants and no purnitive measure against those that declined to participate in the study.

Methodology: a comprehensive medical examination was carried out on every patients and controls who certified inclusion criteria. Four milliliter of venous blood was obtained aseptically and dispensed immediately into bottle containing EDTA. Automated Full Blood Count was performed on the sample using Sysmex 2000i. Peripheral blood film was made and film stained with May-Graunwald-Giemsa after been air dried. Every film was examined under microscope and morphology of red cells white blood cells and platelets reported.

Data Analysis: Data entry and analysis was done using EPI info version 3.5.1. Results were presented in tabular forms. Chi-square was used to compare two variables while continuous variables were compared using correlation analysis. P-value of <0.05 was regarded as been statistically significant.

Results:

Socio-demographic pattern: About half (51.5%) and slightly lower (47%) of anti-psychotropic-naïve patients and patients on anti-psychotic respectively were young adults, while slightly more (53%) of patients on antipsychotics were middle aged. Two (3%), each of anti-psychotic naïve patients and controls were above 60 years of age, Table 1.

Male (57.6%), predominated the anti-psychotic naïve group while female (51.5%) predominated the group on anti-psychotics, Table 1.

Schizophrenia was the diagnosis in the majority of patients, 86.4% and 91% respectively in anti-psychotic naïve and anti-psychotic treatment groups. Other diagnoses were depressive illness (6.1% of anti-psychotic naïve and 4.5% of patients on anti-psychotics), substance use disorder (3% of anti-psychotic naïve and 4.5% of patients on anti-psychotics) and dementia in 1.5% of anti-psychotic naïve patients, Table 2.

Haemogram: Of all the subjects, only three had abnormal haemogram results, 1(1.5%) schizophrenic patients and 2 (3%) of controls. Other subjects had haemogram results within the

normal reference range, p-value>0.05.

For the schizophrenic patient with abnormal results, haematocrit was 12g/dl, MCV of 75fl and MCH of 26pg, while the two controls with abnormal results had only haematocrit deranged with value of 12.3g/dl, Tables 3 and 4.

Peripheral Blood Film: Neutrophil hypersegmentation was seen on the film of 5 antipsychotic-naïve patients (7.5%) diagnosed with Schizophrenia and one (1.5%) control, p-value >0.05. Macrocytosis was only seen in 3 (4.5%) of the 5 antipsychotic-naïve patients that had neutrophil hypersegmentation, p-value >0.05, Table 5.

Table 1 : Sociodemographic Characteristics of Patients.

Variables	Psychotropic Naïve Frequency n (%)	Patients on Anti-psychotic Frequency n (%)	Control Patients Frequency n(%)
		Age Group	
18-40	**34 (51.5)**	**31 (47.0)**	**33 (50.0)**
41-60	**30 (45.5)**	**35 (53.0)**	**31 (47.0)**
> 60	**2 (3.0)**	**0 (0.0)**	**2 (3.0)**
		Sex	
Male	**38 (57.6)**	**32 (48.5)**	**35 (53.0)**
Female	**28 (42.4)**	**34 (51.5)**	**31 (47.0)**

Table 2: Psychiatric Diagnoses of Patients (Drug-naïve and those on Treatment)

Diagnoses	Drug-Naïve Patients (%)	Patients On Treatment (%)
1. SCHIZOPHRENIA	86.50	91.00
2. DEPRESSIVE ILLNESS	6.10	4.50
3. SUBSTANCE USE DISORDER	3.00	4.50
4. MANIA	3.00	-
5. DEMENTIA	1.50	-

Table 3: Comparing the Hemogram of Anti-psychotic Drug-Naïve Patients with that of Healthy Control

Variables	Patients Mean ± S.D	Control Mean ± S.D	T statistics	df	p- value
PCV (%)	42.00 ± 2.43	42.64 ± 3.83	1.1463	130	0.2538
Range	*35-48*	*36-50*			
Hemoglobin Conc. (g/dl)	14.57 ± 0.76	14.64 ± 1.36	0.3650	130	0.7157
Range	*12.4-16.8*	*12.6-16.8*			
MCH (pg)	29.27 ± 1.27	29.76 ± 1.44	2.0733	130	0.0401
Range	*26.5-33.5*	*27.0-33.0*			
MCHC (g/dl)	33.59 ± 1.83	33.33 ± 1.37	0.9240	130	0.3572
Range	*32.5-36.0*	*32.4-36.5*			
***MCV* (fl)**	89.27 ± 5.91	88.20 ± 6.78	0.9665	130	0.3356
Range	*75-98*	*78-97*			
Reticulocyte Count (%)	1.70 ± 0.29	1.69 ± 0.36	0.1757	130	0.8608
Range	*0.5-2.1*	*0.5-1.8*			
Reticulocyte Index (%)	1.62 ± 0.29	1.62 ± 0.29	0.000	130	1.0000
Range	*0.4-2.1*	*0.4-1.8*			
WBC (x 10^9 /l)	6.64 ± 1.61	6.66 ± 1.70	0.0694	130	0.9448
Range	*2.9-12.1*	*2.8-12.5*			
Platelet Count (x 10^9 /l)	253.18 ±34.65	253.00 ±53.46	0.0230	130	0.9817
Range	*125-331*	*122-328*			
Cobalamin (pmol/l)	160.79 ±1.17	160.77 ±0.89	0.1105	130	0.9122
Range	*140.2-180.5*	*141.3-179.1*			

Table 4 Comparing the Hemogram of Patients on Anti-psychotic Drugs with that of Healthy Control

Variables	Patients Mean ± S.D	Control Mean ± S.D	T statistics	df	p- value
PCV (%)	42.64 ± 3.34	42.64 ± 3.83	0.0000	130	1.0000
Range	*35-48*	*36-50*			
Hemoglobin Conc. (g/dl)	14.36 ± 1.15	14.64 ± 1.36	1.2772	130	0.2038
Range	*12.4-16.8*	*12.6-16.8*			
MCH (pg)	29.58 ± 1.63	29.76 ± 1.44	0.6723	130	0.5026
Range	*26.5-33.5*	*27.0-33.0*			
MCHC (g/dl)	33.59 ± 1.17	33.33 ± 1.37	1.1724	130	0.2432
Range	*32.5-36.0*	*32.4-36.5*			
***MCV* (fl)**	89.55 ± 4.62	88.20 ± 6.78	1.3368	130	0.1836
Range	*75-98*	*78-97*			
Reticulocyte Count (%)	1.71 ± 0.43	1.69 ± 0.36	0.2897	130	0.7725
Range	*0.5-2.1*	*0.5-1.8*			
Reticulocyte Index (%)	1.63 ± 0.44	1.62 ± 0.29	0.1542	130	0.8777
Range	*0.4-2.1*	*0.4-1.8*			
WBC (x 10^9 /l)	6.59 ± 1.82	6.66 ± 1.70	0.2283	130	0.8197
Range	*2.9-12.1*	*2.8-12.5*			
Platelet Count (x 10^9 /l)	252.82 ±33.18	253.00 ±53.46	0.1291	130	0.8975
Range	*125-331*	*122-328*			
Cobalamin (pmol/l)	160.84 ±0.73	160.77 ±0.89	0.4940	130	0.6221
Range	*140.2-180.5*	*141.3-179.1*			
Folate(nmol/l)	370.17 ± 0.70	370.07 ±0.51	0.9380	130	0.3500
Range	*350.5-380*	*357.1-378.5*			

Key: S.D= Standard Deviation

Table 5: Comparison of mean values of parameters in the 3 groups (Analysis of Variance – ANOVA)

Parameters	Study groups	n	Mean ± SD	df	F-test	P-value
PCV (%)	Control	66	42.64 ± 3.83			
	Naive	66	42.00 ± 2.43	2	0.28	0.759
	Treatment	66	42.64 ± 3.34			
Haemoglobin Conc. (g/dl)	Control	66	14.64 ±1.36			
	Naive	66	14.57 ±0.76	2	1.08	0.343
	Treatment	66	14.36 ±1.15			
MCH (pg)	Control	66	29.76 ±1.44			
	Naive	66	29.27 ±1.27	2	1.06	0.402
	Treatment	66	29.58 ±1.63			
MCHC (g/dl)	Control	66	33.33 ± 1.37			
	Naive	66	33.59 ± 1.83	2	0.26	0.801
	Treatment	66	33.59 ± 1.17			
MCV (fl)	Control	66	88.20 ± 6.78			
	Naive	66	89.27 ± 5.91	2	0.91	0.489
	Treatment	66	89.55 ± 4.62			
Reticulocyte Count (%)	Control	66	1.69 ± 0.36			
	Naive	66	1.70 ± 0.29	2	0.68	0.501
	Treatment	66	1.71 ±0.43			
Reticulocyte Index (%)	Control	66	1.62 ±0.34			
	Naive	66	1.62 ±0.29	2	1.01	0.401
	Treatment	66	1.63 ± 0.44			
WBC (x 10^9 /l)	Control	66	6.66 ± 1.70			
	Naive	66	6.64 ± 1.61	2	0.48	0.629
	Treatment	66	6.59 ± 1.82			
Platelet Count (x 10^9 /l)	Control	66	253.00 ± 53.46			
	Naive	66	253.18 ± 34.65	2	0.47	0.521
	Treatment	66	252.82 ± 33.18			
Cobalamin (pmol/l)	Control	66	16.77 ± 0.89			
	Naive	66	16.79 ± 1.17	2	0.45	0.641
	Treatment	66	16.84 ± 0.73			
Folate(nmol/l)	Control	66	37.07 ± 0.51			
	Naïve	66	35.23 ±0.54	2	6.71	0.002
	Treatment	66	37.17 ±0.70			

Key: S.D= Standard Deviation

TABLE 6: Comparing the Peripheral Blood Film of Patients with Psychiatric diagnoses with that of Healthy Control.

	GROUP				
	NAIVE	CONTROL			
PARAMETERS	Freq (%)	Freq (%)	χ^2	df	P-value
Hypersegmented cell					
Present	5 (7.6)	1 (1.5)			
Absent	61 (92.4)	65 (98.5)	1.641*	1	0.200
Total	66 (100.0)	66 (100.0)			
Macrocytosis					
Present	3 (4.5)	0(0.0)			
Absent	63 (95.5)	66 (100.0)	1.364	1	0.243
Total	66 (100.0)	66 (100.0)			
	ON TREATMENT	CONTROL	Freq (%)		Freq (%)
Hypersegmented cell					
Present	0 (0.0)	0 (0.0)			
Absent	66 (100.0)	66 (100.0)	-	-	-
Total	66 (100.0)	66 (100.0)			
Macrocytosis					
Present	0 (0.0)	0 (0.0)			
Absent	66 (100.0)	66 (0.0)	-	-	-
Total	66 (100.0)	66 (100.0)			

= Yates corrected Chi square

Discussion:

A total of 198 subjects were recruited for this study. Patients with schizophrenia constituted majority of the respondents, 86.4% of antipsychotic-naïve patients and 90.9% of patients on antipsychotics. Significant findings were therefore noted amongst this group of patients, probably because other groups were small in the study. One hundred and ninety five (98.5%) of patients had red cell indices within reference interval, meaning there is no significant difference between patients and controls, p-value >0.05. This result is similar to the findings by Lerner V. et al[16] in a study conducted among psychiatric patients in Negev, Israel and that of Lindenbau J. et al[17] in a study conducted at Columbian-Presbyterian Medical Center, Harlem , but differ from that of Bazuaye et[18] and Abiodun et al[19] in Nigeria where low MCV values with hypochromia and microcytosis were reported among psychiatric patients.

Neutrophil hypersegmentation and macrocytosis were recorded mainly among antipsychotic-naïve psychiatric patients but not in any of the psychiatric patients on antipsychotics, although they were not statistically significant when compared with controls. Neutrophil hypersegmentation and macrocytosis are features suggestive of megaloblastic erythropoiesis. These features could precede the development of psychiatric disorder or could arise along the course of psychiatric disorders. Its development during the course of psychiatric disorders could be multifactorial, but commonly due to the effect of the ant-psychotic drugs used in the treatment of psychiatric disorders. If it precedes development of psychiatric disorder, then with treatment it should gradually disappear.

Neutrophil hypersegmentation and macrocytosis recorded among antipsychotic-naïve psychiatric patients in this study could precede development of the disorder. Although macrocytosis is the expected finding in megaloblastic psychosis, some researchers have documented microcytosis in their studies. One of such works is Bazuaye's study of the prevalaence of Cobalamin deficiency in Psychiatric patients in Benin City[18].

This statistically insignificant finding in neutrophil hypersegmentation and macrocytosis in all patients and controls is similar to the

Reports of Lindenbau J. et al[17] on a study of neuropsychiatric disorders caused by cobalamin deficiency in the absence of anaemia and macrocytosis, and study of vitamin B12 levels in hospitalized psychiatric patients by Silver H[20], but differs from the report of Lener and others, where normocytosis[16,21] and microcytosis[19] were reported.

Although no significant difference was noticed in the red cell indices of our patients and controls, positive morphological findings on blood film were noted in few isolated cases.

While request for haemogram should always serves as one of the starting points in the management of psychiatric patients, findings of normal haemogram as in this study does not completely rule out the presence of megaloblastic erythopoeisis.

Conclusion:

There is no significant difference in any of the parameters of Full Blood Counts among the two sets of patients and controls, although there are isolated and insignificant number of cases of neutrohil hyperesegmentation and macrocytosis.

Reccomendation:

Since macrocytosis and neutrophil hypersegmentation are early signs in megaloblastic anaemia, their presence in newly diagnosed patients can be a pointer to a low level of RBC folate. It is therefore advisable to always request for blood film review in newly diagnosed psychiatric patients, especially those with schizophrenia.

Conflict of interest: None declared

Authors' Contribution:

Data gathering and idea owner of this study: AO Adewoye

Study design: AO Shittu, AO Adewoye

Data gathering: AO Adewoye, HO Olawumi

Writing and submitting manuscript: AO Shittu, AO Adewoye

Editing and approval of final draft: AO Shittu, AO Adewoye, HO Olawumi

References:

1. Buka SL. Psychiatric Epidemiology: Reducing the global burden of mental illness. *Am J Epidemiol*. 2008; **168**: 977-979. https://doi.org/10.1093/aje/kwn298
2. Abiodun, OA. The need for a holistic approach to patient care. *East Afr Med J* 1991; **68** : 25-28.
3. Abiodun, OA. The role of Laboratory Medicine in Psychiatry. *East Afr Med J* 1991**; 68** : 389-399.
4. Hughes-Jones NC, Wickramasinghe SN, Hatton C. Macrocytosis and macrocytic anaemia. In: Lecture notes on Haematology. 7th Edition. West Sussex : Blackwell Publishing. 2004: 71-89.
5. Becker M, Axelrod DJ, Oyesanmi O, Markov DD, Martin E, Kunkel EJS. Haematology in The Textbook of Psychosomatic Medicine : Psychiatry Care of the Medically Ill. JL Levenson Ed. American Psychiatric Publication 2011 : 551-569.
6. Hoffbrand AV, Green R. Megaloblastic anaemia. In Hoffbrand AV, Catovsky D, Tuddenham EGD, editors. Postgraduate Haematology. 5th Edition. Massachusetts : Blackwell Publishing 2005 : 60-83. https://doi.org/10.1002/9780470987056.ch5
7. Aaron S, Kumar S, Vijayan J, Jacob J, Alexander M, Gnanamuthu C. Clinical and laboratory features and response to treatment in patients presenting with vitamin B12 deficiency-related neurological syndromes. *Neurol India*. 2005 ; **53** : 55-58. https://doi.org/10.4103/0028-3886.15057
8. Lerner V, Kanevesky M, Dwolatzky T, Rouach T, Kamin R, Miodownik C. Vitamin B12 and Folate serum levels in newly admitted psychiatric patients. *Clin Nutr*. 2006; **25 :** 60-67. https://doi.org/10.1016/j.clnu.2005.08.014
9. Carmel R, Green R, Rosenblatt DS, Watkins D. Update of Cobalamin, Folate, and homocysteine. *Am Soc Hematol Educ Program*. 2003 : 62-81.
10. Paton C. Managing clozapine-induced neutropenia with lithium. *The Psychiatrist*. 2005**; 29** : 186-188.
11. Vasudev K, Keown P, Gibb I, McAllister-Williams RH. Haematological effects of Valproate in psychiatric patients: what are the risk factors? *J Clin Psychopharmacol*. 2010; **30** : 282-285. https://doi.org/10.1097/JCP.0b013e3181db2684
12. Soutar R, Yasmin A, Mckay P, Doig A. Auto-erythrocyte sensitisation syndrome – an unusual cause of bruising. *J R Physicians Edinb*. 2008; **38 :** 311-313.
13. Amoran O, Lawoyin T, Lasebikan V. Prevalence of depression among adults in Oyo state, Nigeria: A comparative study of rural and urban communities . *Aust J of Rural Health* 2007 ; ***15****:* 211-215. https://doi.org/10.1111/j.1440-1584.2006.00794.x
14. Robinson JB. Polydipsia and psychosis in subdural haemorrhage. *Brit Med J Case Rep*. 2009 : **10**: 1-8. https://doi.org/10.1136/bcr.09.2008.0866
15. Araoye MO. Subject selection in Research methodology with statistics for health and social sciences. 1st edition. *Nathadex publishers Ilorin*. 2003 :115-129.
16. Lerner V, Kanevesky M, Dwolatzky T, Rouach T, Kamin R, Miodownik C. Vitamin B12 and Folate serum levels in newly admitted psychiatric patients. *Clin Nutr.* 2006; **25**: 60-67. https://doi.org/10.1016/j.clnu.2005.08.014
17. Lindenbau J, Healton EB, Savage DG, Brust JC, Garrett TJ, Podell ER, et al. Neuropsychiatric disorders caused by cobalamin deficiency in the absence of anemia or macrocytosis. *N Engl J Med*. 1988**; 318** : 1720 – 1728. https://doi.org/10.1056/NEJM198806303182604
18. Bazuaye, GN. Prevalaence of Vitamin B12(Cobalamin) deficiency in Psychiatric patients in Benin City. A dissertation submitted to National Postgraduate Medical College of Nigeria. 2002; viii.
19. Abiodun, OA. Physical Morbidity in a Psychiatric Population in Nigeria. *General Hosp Psychiatry*. 2000 **; 22** : 195-199. https://doi.org/10.1016/S0163-8343(00)00065-7
20. Silver H. Vitamin B12 levels are low in hospitalized psychiatric patients. *Isr J Psychiatry Relat Sci.* 2000; **37** : 41-45.
21. Saedisomeolia A, Djalali M, Moghadam AM, Ramezankhani O, Najmi L. Folate and Vitamin B12 status in schizophrenic patients. *J Research Med Sci*.2011; **16** : 437-41.