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BLOOD GROUPING, GENOTYPE AND WHITE BLOOD CELL DIFFERENTIAL AMONGST MIGRAINE PATIENTS ATTENDING UNIVERSITY OF MAIDUGURI TEACHING HOSPITAL, MAIDUGURI, NIGERIA

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ABSTRACT
This study was aimed at assessing the involvement of leukocytes, blood group and genotype during acute migraine attack so as to provide physicians with guidelines for the identification of subjects at risk in clinical practice. One hundred consecutive adult (18 years and above) patients that met the International Headache Society diagnostic criteria for migraine who attended the Neurology Clinic of the Department of Medicine, University of Maiduguri Teaching Hospital, Maiduguri from May, 2010 to October, 2011 and from whom informed consent was obtained were evaluated for this disorder. General, physical and neurological examinations were also conducted at which samples were taken for haematological analysis before acute therapy. Twenty-one, 12, 19 and 48 percent of the patients enrolled in this study had blood group A, B, AB and O respectively. Genotypically, 39% and 61% of the patients had normal (AA) and carrier (AS) genotype respectively. There was a statistical significant difference in the levels of neutrophils ($p<0.01$), lymphocyte ($p<0.05$) and eosinophils ($p<0.05$) among the migraineurs with moderate and severe head pain during acute attack studied. Based on this study, migraine attack was found to increase the levels of lymphocyte and eosinophils above the reference hospital value and is common independent of the blood group or genotypic expression.
Keywords: Migraine, Genotype, Leucocytes, Nigeria

INTRODUCTION

Migraine has been a well known medical problem for long period of time and represents one of the most investigated types of head pain. According to a World Health Organization analysis, migraine alone is responsible for at least one percent of the total US medical disability burden, and severe migraine attacks are as disabling as quadriplegia [1]. Migraine is known to run in families, suggesting a condition that is at least partly regulated by genetics. It occur disproportionately more frequently in association with other inherited disorders. Several large scale epidemiologic studies have confirmed that genetic factors play an important role in migraine [2, 3]. Therefore, searches for genetic predisposition factors to migraine are important because it may be helpful in the identification of subjects at risk. Migraine and sickle cell disease are common diseases and may coexist in the same individual. Such a chance association is potentially dangerous because the two disorders may act synergistically to cause major neurological complications which may be permanent and contribute to the well-known mortality of sickle cell disease [2]. Acute migraine attack significantly increased the levels of APA, ESR and Platelets among migraineurs and acute therapy was able to cause a significant reduction in their levels [4]. Increased platelet activation results in up-regulation of specific binding to leucocytes which promote pro-inflammatory leukocyte secretion and their tethering to endothelium, a mechanism that has been demonstrated in stroke and which could provide a link to migraine [5]. These facts need to be evaluated in our environment. In addition, substantial health care cost associated with migraine (consultations, medications and diagnostic evaluations) and the considerable time often lost from work which has been reported [6, 7, 8, 9] would (if they exist in the manner) contribute negatively to sustainable development in already impoverished economies like Nigeria. These arguments amply justify the current attempt to study the involvement and association of blood grouping, genotype and leucocytes differential in migraine.

MATERIALS AND METHODS

From May, 2010 to October, 2011, one hundred consecutive adult migraine patients that attended the Neurology Clinic of the Department of Medicine, University of Maiduguri Teaching Hospital (UMTH), Maiduguri were prospectively studied with their consents. The study was approved by the Research and Ethics committee of UMTH. Pregnant women, patients with clinical evidence of an organic disease known to cause migraine and those that have a socioeconomic factor were excluded. Personal interviews using a structured questionnaire were conducted individually with the 100 patients. General, physical and neurological examinations were also conducted. Samples were taken for haematological analyses before acute therapy on every study subject. Those patients that did not meet the inclusion criteria were given analgesics and were not enrolled for the study.

Blood Grouping (Tile method): One drop of antisera (Anti-A, Anti-B, Anti –AB and Anti-D) was placed in row respectively. Then one drop of red cells was placed on each antisera and was mixed with applicator stick. The tile was gently rocked and checked for agglutination macroscopically.

Haemoglobin Genotype (Hb electrophoresis): The blood was lysed with lysate by introducing the lysate into the ethylene diammine tetraacetic acid (EDTA) blood sample. The lysed blood sample was applied on a template with the Pasteur pipette. Also the lysed blood sample from the template was applied on the cellulose acetate paper with the applicator. The paper was clamped on the holder and was placed on triphosphate buffer (pH 6.8) in a tank connected to electrophoresis machine (Biosystems BTS-100). The machine was put on and allowed to run for 20 mins. The paper was read macroscopically and the separation of the blood on the acetate paper was observed.

White blood cell differential (Leishman stain): A thin blood film was prepared, flooded with Leishman stain and was allowed to fix for 2 mins. The volume was doubled with buffer solution which was allowed to stain for 8 mins. The back of the slide was washed with water, cleaned and wiped. This was allowed to dry at room temperature. A drop of emersion oil was placed on the tail end of the stained film and was examined under light microscope (Olympus CH) at X100 objective lens. The result was reported in percentage.

Statistical analyses: The data was analyzed using statistical analysis software (SAS) system version 16. Student t-test was used to determine significance of association between non-categorical variables. P values less than 0.05 were considered significant, less than 0.01 highly significant and less than 0.001 very significant.

RESULTS

Twenty-one (21), 12, 19 and 48 percent of the patients enrolled in this study had blood group A, B, AB and O respectively. Two (2) out of the 48 patients with blood group O had rhesus negative blood group. Genotypically, 39% and 61% of the patients had normal (AA) and carrier (AS) genotype respectively (Table 1). The severity of migraine and WBC differential among migraine patients studied is shown in Table 2. The mean ± SD of neutrophils was 53.4 ± 8.6 and 60.2 ± 15.2 during moderate and severe attack respectively; while for lymphocytes it was 52.5 ± 13.0 for moderate attack and 58.8 ± 13.6 during severe attack. Eosinophil has mean ± S.D of 7.0 ± 3.4 and 8.6 ± 3.7 during moderate and severe attack respectively. Linear regression shows a significant difference in the levels of neutrophils ($p<0.01$), lymphocyte ($p<0.05$) and eosinophils ($p<0.05$) among the migraineurs with moderate and severe head pain during acute attack studied. The analysis of variance (ANOVA) among the subjects indicates that WBC levels significantly differ during acute migraine attack ($p< 0.001$).

DISCUSSION

The result of this study indicates that migraine can occur in patients independent of their blood group or genotypical expression. There is insufficient evidence from the patient's blood group or genotype that can reliably predict the chances of having migraine headache. However, carrier of sickle cell gene (61%) predominate those with normal genotype (39%) as observed among the migraineurs studied (Table 1). The distribution of genotype and migraine subtype as common, classic and mixed migraine is a true reflection of the distribution of migraine headache in the general population. For those having the sickle cell traits 43, 17 and 1 had common, classic and mixed migraine head pain respectively. Several large scale epidemiologic studies have confirmed that genetic factors play an important role in migraine [2, 3]. Migraine and sickle cell disease are common diseases and may coexist in the same individual [2].

The result of the white blood cell (WBC) differential during acute migraine attack prior to therapy showed a significant increase in the levels of neutrophils ($p<0.01$), eosinophils ($p<0.05$), and lymphocytes ($p<0.05$) among patients with severe migraine attacks compare to those with moderate attack (Table 2). There was no significant change in the levels of monocytes and basophils among patients with severe or moderate migraine. Studies aimed at assessing the impact of migraine on WBC are scarce, though William et al [10] suggested a need to conduct WBC differential during acute attack. Again, the result of this study agrees with the reports of Timothy et al [4] and Zeller et al [5] in which there was an increased in the levels of platelet among the study subjects that might result in up-regulation of specific binding to leukocytes which promote pro-inflammatory leukocyte secretion and their tethering to endothelium.

CONCLUSION

Migraine attack was found to be common among patients studied independent of their blood group or genotype. Severe migraine attack was found to significantly increase the levels of neutrophils, lymphocyte and eosinophils when compared with those having moderate attack.

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TABLE 1: DISTRIBUTION OF PATIENT'S BLOOD GROUP AND GENOTYPE

Blood parameter		No. / %
Grouping		
	A+	21
	B+	12
	AB+	19
	O+	46
	O-	2
Genotyping		
	AA	39
	AS	61

TABLE 2: WHITE BLOOD CELL DIFFERENTIAL AND SEVERITY OF MIGRAINE

White blood cell differential	Reference value (%)	Severity of migraine attack	Mean ± S.D	P-value[a&b]
Neutrophils	60-70	Moderate	53.4[a] ± 8.6	0.002*
		Severe	60.2[b] ± 15.2	
Lymphocytes	25-40	Moderate	52.5[a] ± 13.0	0.014*
		Severe	58.8[b] ± 13.6	
Monocytes	2-6	Moderate	5.5[a] ± 3.6	NS
		Severe	4.2[b] ± 3.0	
Eosinophils	1-4	Moderate	7.0[a] ± 3.4	0.020*
		Severe	8.6[b] ± 3.7	
Basophils	0-1	Moderate	0.7[a] ± 0.8	NS
		Severe	0.7[b] ± 1.4	

Moderate, N = 48; Severe, N = 52, * = Significant p-value ($p<0.05$) (Student't' test), NS = Not significant, a = means of moderate, b = means of severe

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