Journal of
Blood Disorders & Transfusion

Ahmed et al., J Blood Disord Transfus 2012, 3:2
DOI: 10.4172/2155-9864.1000120

Research Article Open Access

Seasonal Variations in Frequencies of Acute Vaso-Occlusive Morbidities among Sickle Cell Anaemia Patients in Northern Nigeria

Sagir G. Ahmed[1]*, Modu B Kagu[2], Usman A. Abjah[2] and Audu A. Bukar[2]

[1]*Department of Haematology, Aminu Kano Teaching Hospital, PMB 3452, Kano, Kano State, Nigeria.*
[2]*Department of Haematology, University of Maiduguri Teaching Hospital, PMB 1414, Maiduguri, Borno State, Nigeria*

Abstract

Background: Nigeria is the most populous black nation with the heaviest burden of Sickle Cell Anaemia (SCA). The climate in the north is characterized by a short rainy season and a long dry season that can be sub-divided into a cold and dusty harmattan season and a hot non-harmattan dry season. We studied the impact of seasonal variations of climatic factors on the frequencies of acute vaso-occlusive morbidities, including Vaso-Occlusive Crisis (VOC), Acute Chest Syndrome (ACS), priapism and stroke among patients with SCA in northern Nigeria.

Methods: This is a six-year prospective study conducted from 2005 to 2010 in university teaching hospitals of Maiduguri and Kano cities of northern Nigeria. Consecutive patients with SCA who presented with VOC, ACS, priapism and stroke were diagnosed, recruited and enumerated. The monthly and seasonal frequencies of each morbidity (VOC, ACS, priapism or stroke) during the period of study were calculated and graphically evaluated.

Results: The frequencies of VOC showed 3 peaks: during the harmattan dry season in January, during the non-harmattan dry season in April and during the rainy season in August. The frequencies of ACS showed a peak during the harmattan dry season in December. The frequencies of priapism showed a peak during the non-harmattan dry season in April. The frequencies of stroke showed a peak during the rainy season in July/August.

Conclusion: The frequencies of acute vaso-occlusive morbidities in SCA patients could be adversely affected by seasonal variations in climatic factors. There is need for patients and care givers to be adequately educated on how to mitigate the adverse effects of weather on SCA. Moreover, governmental and non-governmental organizations should take seasonal variations of climatic factors into consideration when drafting health care plan for patients with SCA.

Keywords: Sickle cell anaemia; Nigeria; Climate; Crisis; Acute chest syndrome; Priapism; Stroke

Introduction

Nigeria is a sub-Saharan tropical country located just north of the equator lying within latitudes 4°N-14°N and longitudes 3°E-15°E [1,2]. The Nigerian climate varies widely across the country. The climate in the southern region, which is bordering the Atlantic Ocean, is dominated by the tropical rain forest characterized by abundant rainfall, dense and tall vegetation with year round high temperatures and humidity levels [2-4]. The general trend is characterized by rising temperature, decreasing rainfall, reduction in humidity and thinning of vegetation as the climate changes from the southern region towards the inland regions in the midland and the northern part of the country [2-4]. Thus the midland is typically Guinea savannah with relatively sparse vegetation, while the northern region is occupied by Sudan and Sahel savannah characterized by semi-desert climatic features with high temperatures, scanty rainfall, low humidity and scattered vegetations as shown in Figure 1 [2-4].

In contradistinction to the south, the weather in the northern is mainly dry for most of the year with a relatively short rainy season spanning the period between June and September [2,3,5]. The remaining months, October to May, constitute the dry season [2,3,5]. A typical seasonal rhythm of monthly variations in temperature, rainfall and humidity as observed in Kano city in northern Nigeria is shown in Table 1 [3,5]. Unlike the southern part of Nigeria where temperatures are high and relatively constant throughout the year, the weather in northern Nigeria is characterized by significant variations in temperature as a result of the effects of two seasonal air masses [2,3]. The rainy season that covers the period from June to September is dominated by the trans-Atlantic tropical maritime air mass, which brings about rainfall as well as dense cloud cover that blocks sun rays resulting in relatively modest average temperatures of between 29°C to 21°C at the peak of the rainy season in August [3,5]. Thereafter, the dry season sets in during the period October to February when the region comes under the influence of dry and dusty trans-Saharan tropical continental air mass, which is referred to as the Harmattan [2,3]. The harmattan is associated with low atmospheric humidity, increased wind speeds and dusty haze, which partially blocks the sun rays over northern Nigeria with a resultant fall in average temperatures to as low as 13°C with many daily temperature values reaching as low as 3°C especially in the evenings and night times [2,3,5]. The harmattan recedes upon the withdrawal of the tropical continental air mass during the period March to May (non-harmattan dry season), which is characterized by the absence of both haze and cloud in the skies, hence average temperatures escalate to as high as 38°C with many daily temperature values exceeding 40°C [2,3,5]. The temperatures remain

***Corresponding author:** Sagir G. Ahmed, Department of Haematology, Aminu Kano Teaching Hospital, PMB 3452, Kano, Kano State, Nigeria, E-mail: drsagirahmed@yahoo.com

Received December 22, 2011; **Accepted** March 26, 2012; **Published** April 01, 2012

Citation: Ahmed SG, Kagu MB, Abjah UA, Bukar AA (2012) Seasonal Variations in Frequencies of Acute Vaso-Occlusive Morbidities among Sickle Cell Anaemia Patients in Northern Nigeria. J Blood Disord Transfus 3:120. doi:10.4172/2155-9864.1000120

high until the situation is alleviated by the influence of the next trans-Atlantic tropical maritime air mass in June, which marks the onset of the next rainy season in the northern region [3].

It may therefore be surmised that in northern Nigeria there are three distinct seasonal bands. The rainy season that is warm and humid occurs around the middle of the year (June-September), which is preceded by a dry and very hot season (non-harmattan dry season) in the early part of the year (March- May) that is followed by a dry, windy, dusty and relatively cold season (harmattan dry season) in the later part of the year (October- February).

Nigeria is the most populous black nation in the world. With a population of over 160 million and average national prevalence of rates of about 25% and 2% for sickle cell trait and sickle cell anaemia (SCA) respectively, Nigeria carries the heaviest burden of sickle cell disease in the world [6]. It is therefore important to study the effect of climate on the occurrence of acute vaso-occlusive morbidities among patients with SCA in Nigeria. In this paper we studied the impact of seasonal variations of climatic factors on the frequencies of acute vaso-occlusive morbidities, including Vaso-Occlusive Crisis (VOC), Acute Chest Syndrome (ACS), priapism and stroke among patients with SCA in the savannah zone of northern Nigeria.

Materials and Methods

This is a six-year prospective study, which was conducted during the years 2005 to 2007 at University of Maiduguri Teaching Hospital, Maiduguri, northeast Nigeria and during the years 2008 to 2010 at Aminu Kano Teaching Hospital, Kano, northwest Nigeria. The two hospitals in which the study was conducted are sited in cities (Maiduguri and Kano) that are located within the Sudan savannah (Figure 1). In each hospital, patients were recruited from the adult haematology clinics where they were registered for regular clinical care. The subjects studied were diagnosed as SCA based on positive sickling tests and haemoglobin electrophoresis at a pH of 8.6 on cellulose acetate paper [7]. Consecutive patients with SCA who presented at the adult haematology clinic, haematology day care unit or the emergency room with VOC, ACS, priapism or stroke were recruited into the study. In each patient the diagnosis of VOC was based on presentation with acute pain episodes affecting the extremities, back, abdomen, chest or head [8], the diagnosis of ACS was based on presentation with

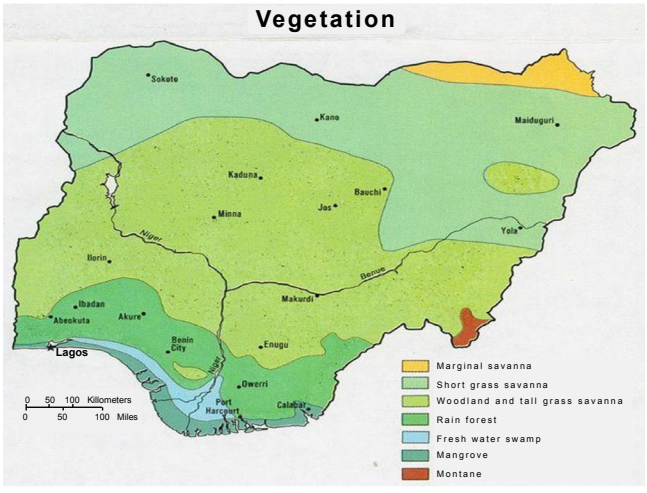

Figure 1: Vegetation of Nigeria.

respiratory distress and finding of new pulmonary infiltrates on chest x-ray [9], the diagnosis of priapism was based on presentation with unwanted painful penile erection, in the absence of sexual activity or desire, that is sustained for more than 2 hours [10] and the diagnosis of stroke was based on presentation with hemiplegia with or without aphasia, seizures, altered consciousness and ischemic features on CT scan [11]. At the point of clinical presentation of VOC, ACS, priapism or stroke, the demographic data of each patient were recorded and the haematological parameters (haematocrit, white blood cell and platelet counts) were determined using automatic blood analyzers with manual correction of white cell counts for the presence of nucleated red cells. In all cases studied every clinical episode of VOC, ACS, priapism and stroke was recorded against the month of the year during which it occurred. The monthly frequencies of each morbidity (VOC, ACS, priapism or stroke) during the period of study were calculated by simple arithmetic as:

[Number of episodes of each morbidity {VOC, ACS, Priapism or Stroke} recorded in a particular month during period of study/ Total number of episodes of each morbidity {VOC, ACS, Priapism or Stroke} recorded during period of study] x 100.

For example, the monthly frequency of VOC for January was calculated as:

[Number of recorded episodes of VOC in the months of January during period 2005-2010/Total number of recorded episodes of VOC recorded during period 2005-2010] x 100.

The data generated was graphically analysed and the monthly and seasonal variations in the frequencies of each vaso-occlusive morbidity (VOC, ACS, Priapism, Stroke) were evaluated and discussed within the context of established seasonal variations of climatic factors as documented in a typical northern Nigerian weather pattern as shown in Table 1. The data was manually analyzed for seasonality of each morbidity by calculating average monthly values and individual monthly seasonal indices. The Chi-square test for the null hypothesis was used to check the statistical significance of the values at $p<0.05$.

Results

During the period of study 987 patients presented with 2652 episodes of VOC, 45 patients presented with 56 episodes of ACS, 21 patients presented with 35 episodes of priapism and 17 patients presented with 17 episodes of priapism. The demographic and haematological profiles of the patients are shown on Table 2. The monthly frequencies of the episodes of VOC, ACS, priapism and stroke during the period of study are shown on Table 3. The variations in monthly frequencies of episodes of VOC, ACS, priapism and stroke are shown graphically in Figures 2, 3, 4 and 5. Each morbidity showed graphically depicted seasonality that was statistically significant with high seasonal peak values ($\chi 2$ test, $p<0.05$). The monthly frequencies of VOC ranged from 4.98% to 11.99% with peaks in January (10.3%), April (11.01%) and August (11.99%). The monthly frequencies of ACS ranged from 3.57% to 16.07% with a single peak in December (16.07%). The monthly frequencies of priapism ranged from 5.71% to 14.29% with a single peak in April (14.29%). The monthly frequencies of stroke ranged from 0% to 17.65% with a single peak in July/August (17.67%).

Discussion

The haematological profiles of the patients showed values indicative of moderate anaemia, leucocytosis and thrombocytosis, which were consistent with SCA [12]. The clinical data accrued revealed that VOC

	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	DEC
Average Maximum Temperature (°C)	30	32	36	38	37	35	31	30	31	34	34	31
Average Minimum Temperature (°C)	13	16	19	22	24	23	22	21	21	19	16	14
Average Rainfall (mm)	0	0	0	10	48	113	200	310	128	13	0	0
Average Relative Humidity (%)	13	13	11	14	33	43	59	68	57	32	16	14
Season	Harmattan Dry Season		Non-Harmattan Dry Season			Rainy Season				Harmattan Dry Season		

Adopted and modified from Reference No. 5.

Table 1: Typical seasonal variations in temperature, rainfall and relative humidity in Kano, northern Nigeria.

	Vaso-occlusive Crisis	Acute Chest Syndrome	Priapism	Stroke
Number of Patients Studied	987	45	21	17
Sex Ratio (M/F)	0.69 (401/581)	0.8 (20/25)	Not Applicable	0.55 (6/11)
Number of Episodes Recorded	2652	56	35	17
Mean Age (years) ± SD	25+6	28+5	27+6	20+2
Mean Haematocrit (L/L) ± S.D.	0.26±0.03	0.27 ± 0.02	0.24 ± 0.03	0.25 ± 0.03
Mean Leucocyte Count (x109/L) ± S.D.	11± 2.7	10.5 ± 3	10.8 ± 2.5	11.5 ± 2
Mean Platelet Count (x109/L) ± S.D.	425 ± 51	420 ± 45	430 ± 50	410 ± 52

Table 2: Demographic and haematological profiles of sickle cell anaemia patients.

	Vaso-occlusive Crisis No of Episodes (%)	Acute Chest Syndrome No of Episodes (%)	Priapism No of Episodes (%)	Stroke No of Episodes (%)
January	266 (10.03)	7 (12.5)	3 (8.57)	1 (5.88)
February	160 (6.03)	5 (8.93)	2 (5.71)	0 (0)
March	239 (9.01)	3 (5.36)	4 (11.43)	1 (5.88)
April	292 (11.01)	4 (7.14)	5 (14.29)	1 (5.88)
May	213 (8.03)	3 (5.36)	4 (11.43)	1 (5.88)
June	134 (5.05)	3 (5.36)	3 (8.57)	2 (11.76)
July	264 (9.95)	2 (3.57)	2 (5.71)	3 (17.65)
August	318 (11.99)	3 (5.36)	3 (8.57)	3 (17.65)
September	211 (7.96)	3 (5.36)	2 (5.71)	2 (11.76)
October	132 (4.98)	6 (10.72)	3 (8.57)	1 (5.88)
November	158 (5.96)	8 (14.29)	2 (5.71)	1 (5.88)
December	265 (9.99)	9 (16.07)	2 (5.71)	1 (5.88)
ALL MONTHS	2652(100)	56(100)	35(100)	17 (100)

Table 3: Monthly frequencies of acute vaso-occlusive morbidities in sickle cell anaemia patients.

was the most common form of acute vaso-occlusive morbidity. The pattern of variations in the frequencies of VOC revealed year-round occurrences with three peaks indicative of periods of increased episodes of VOC. The first peak occurred in January, which approximately coincides with the middle of the harmattan dry season that is associated with the lowest temperature and humidity values and the most windy atmospheric conditions of the calendar year in northern Nigeria [2,3,5]. This finding is consistent with previous studies that had implicated skin cooling due to direct effect of low ambient temperatures or due to rapid evaporation of sweat resulting from the effect of high winds of low humidity as triggers of VOC in patients with SCA [13,14]. The mechanism underlying the pathogenesis of cold induced VOC in SCA is probably related to abnormal neurovascular reflexes leading to intra-medullary vasoconstriction and marrow infarcts resulting in bone pains based on the concept of the 'steal' syndrome hypothesis [15]. It is therefore importance that SCA patients in northern Nigeria should be adequately protected from cold and winds during the harmattan season in order to mitigate the deleterious effect of the season on the frequency of VOC.

The second peak of VOC was observed in April in the middle of the non- harmattan dry season, which is associated with the most intensely hot temperatures of the calendar year in northern Nigeria [2,3,5]. This season is associated with excessive sweating and high rate of insensible water loss resulting in dehydration, which had been reported to be a potent trigger of VOC in patients with SCA [8]. Dehydration would predictably result in increased plasma osmolality, haemoconcentration, microvascular stasis and raised erythrocyte mean corpuscular haemoglobin concentration. These changes would lead to increased HbS deoxygenation and polymerization, which will culminate in enhanced red cell sickling and VOC in patients with SCA [16]. Hence, we interpret the increased frequencies of VOC in the non-harmattan dry season to be a reflection of adverse effects of dehydration associated with the hot temperatures of the season. Furthermore, it must be appreciated that SCA patients are particularly vulnerable to dehydration because sickle cell disease is often associated with recurrent renal papillary necrosis, impaired renal water re-absorption and hyposthenuria [17]. This underscores the need for liberal oral fluid intake by SCA patients during the hot non-harmattan dry season in order to attenuate the risk of VOC.

The third peak of VOC was observed in August in the middle of the rainy season. The rainy season is associated increased stagnant surface water availability and denser agricultural and non-agricultural vegetations, which are conducive for reproduction and survival of mosquitoes in Nigeria [18]. Consequently, the rainy season is a period of intensification of malaria transmission in Nigeria [19]. In addition, malaria infection had also been reported to be the commonest cause

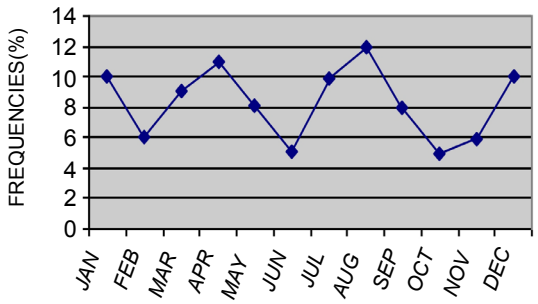

Figure 2: Monthly variations in frequencies of vaso-occlusive crisis among sickle cell anaemia patients.

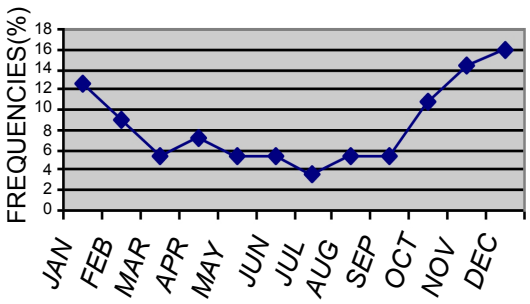

Figure 3: Monthly variations in frequencies of acute chest syndrome among sickle cell anaemia patients.

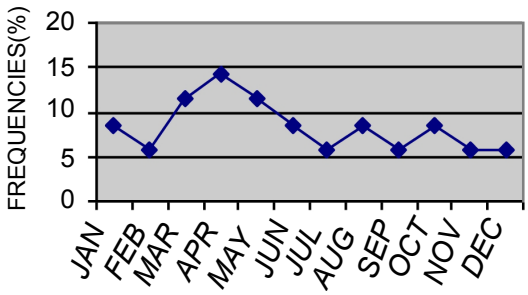

Figure 4: Monthly variations in frequencies of priapism among sickle cell anaemia patients.

of VOC in SCA patients in Nigeria [20]. We therefore surmise that the increased frequencies of VOC seen during the rainy season in this study was due to increased rate of malaria infection among the SCA patients. This data highlights the need for SCA patients in malaria endemic zones to take preventive measures through the use of insecticide treated bed nets and regular administration of anti-malarial chemo-prophylactic drugs in order to reduce the incidence of VOC [21]. The need for anti-malarial prophylaxis in SCA patients is further dictated by the fact that SCA is associated with impaired immunity, which would aggravate patient susceptibility to malaria infection [22]. It is hoped that the recent discovery of the RTSS malaria vaccine would eventually reduce the incidence of malaria, decrease the frequency of VOC and improve the quality of life of many SCA patients in Africa where trials are already underway in selected countries [23].

ACS was the second common acute vaso-occlusive morbidity,

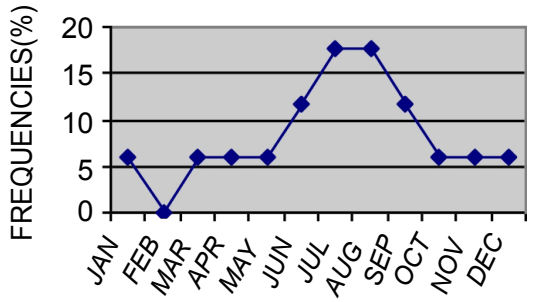

Figure 5: Monthly variations in frequencies of stroke among sickle cell anaemia patients.

which showed a peak in its monthly frequency during the month of December in the middle of the harmattan dry season. The harmattan season is characterized by low ambient temperatures, low relative humidity, dusty winds and atmospheric pollution [2,3,5,24]. These conditions are optimally conducive for acquisition and spread of allergic and infectious diseases of the respiratory system within the community [25]. Consequently, previous studies had reported increased incidence of respiratory diseases in Nigeria during the harmattan season [25]. We therefore interpret the increased monthly frequencies of ACS during the harmattan season to be a reflection of the increased incidence of respiratory infections among SCA patients in whom respiratory infections are known to be potent triggers of ACS [26]. We reckon that the harmattan season would be particularly stressful for the SCA patients because of their background sickle cell related immune dysfunctions, which would accentuate their susceptible to respiratory tract infections [22]. It is therefore strongly recommended that SCA patients in northern Nigeria should be immunized with polyvalent pneumococcal conjugate vaccines as well as other relevant vaccines against common respiratory pathogens in order to reduce the risk of ACS during the harmattan period [27]. The prevention of respiratory tract infection in SCA patients is doubly important because it would reduce the risk of ACS as well as VOC since infections are known to be potent triggers of both morbidities [28]. It is quite possible that the harmattan peak of VOC seen in January, as earlier discussed, was partly accounted for by respiratory infections in addition to the cold induced 'steal' syndrome mechanism.

Priapism, which was the third common morbidity in this study, had a peak monthly frequency in April, which is the hottest month of the non- harmattan dry season in northern Nigeria [2,3,5]. As earlier mentioned, SCA patients are particularly prone to haemoconcentration and hyperviscosity during hot season because of their inability to conserve water due to hyposthenuria [17]. The mechanism of normal erections entails neurovascular mediated increase in arterial flow to the corpora coupled with reduced venous outflow, which lead to relative stasis and tumescence within the corpora [29]. We infer that a vicious concert between blood stasis and hyperviscosity may lead to intra-corporal sickling, which would interfere with the process of detumescence by impeding venous outflow thereby transforming a physiologically initiated erection into priapism. This scenario may underlie the high frequency of priapism observed in the hot non-harmattan dry season in this study. Hence, liberal oral fluid intake during the hot season would prevent hyperviscosity and decrease the risk of priapism in patients with SCA living in hot climates.

Stroke was the least common acute vaso-occlusive morbidity seen

in this study. Nonetheless, our data revealed increased frequencies during the rainy season with peak values in July and August, which as earlier highlighted is a period of increased malaria vector breeding and parasite transmission [18,19]. The fundamental pathology of stroke in SCA is initiated by haemolysis induced nitric oxide depletion and vasculopathy leading to narrowing of intracranial arterial vessels that are associated with high flow velocities typically detectable by trans-cranial Doppler ultrasonography [30]. The final stage in the evolution of stroke in SCA is accomplished by adherence of sickled red cells to the vascular endothelium leading to luminal occlusion of the narrowed vessels resulting in cerebral ischemia and infarctive stroke [30]. We infer that malaria may contribute to the development of infarctive stroke in SCA through its dual role as a potent trigger of red cell sickling and an enhancer of red cell adhesion to vascular endothelium via the effect of knob associated histidine rich protein, which is a tenacious cell adhesion protein expressed on malaria infected red cells [31, 32]. This scenario might explain the increased frequency of stroke that was seen during the rainy season in this study. Hence, this data would imply that intensive anti-malarial prophylaxis may reduce the risk of ischemic stroke in SCA patients. There is therefore the need for detailed investigation of a possible relationship between malaria and stroke in SCA patients living in malaria endemic zones.

Conclusions

This study had shown that the frequencies of acute vaso-occlusive morbidities in SCA patients could be adversely affected directly by seasonal variations in climatic factors such as temperature, rainfall, wind, humidity and atmospheric pollution and indirectly through the effect of climatic factors on prevalence of diseases such as malaria and respiratory infections. There is the need for patients and care givers to be adequately educated on how to mitigate the adverse effects of weather on SCA. Moreover, governmental and non-governmental organizations should take seasonal variations of climatic factors into consideration when drafting health care plan for patients with SCA.

References

1. Ajayi POS (2003) Nigeria- Location, Position, Size and Political Divisions:Comprehensive Geography For Senior Secondary Schools. (2ndedn), A Johnson Publishers, Lagos.
2. http://en.wikipedia.org/wiki/Geography_of_Nigeria#cite_note-10
3. Ajayi POS (2003) The climate of Nigeria: Comprehensive Geography For Senior Secondary Schools. (2ndedn), A Johnson Publishers, Lagos.
4. Ajayi POS (2003) The vegetation of Nigeria: Comprehensive Geography For Senior Secondary Schools. (2ndedn), A Johnson Publishers, Lagos.
5. http://www.climatetemp.info/nigeria/kano.html
6. Akinkugbe OO (1992) Sickle Cell Disease: Non-communicable Diseases in Nigeria. (1stedn), Federal Ministry of Health, Lagos.
7. Dacie JV, Lewis SM, White JM, Marsh GW (1991) Investigation of abnormal haemoglobins and thalassaemia: Practical haematology. (7thedn), Churchill Livingstone, London.
8. Platt OS, Thorington BD, Brambilla DJ, Milner PF, Rosse WF, et al. (1991) Pain in sickle cell disease: rates and risk factors. N Engl J Med 325: 11-16.
9. Taylor C, Carter F, Poulose J, Rolle S, Babu S, et al. (2004) Clinical presentation of acute chest syndrome in sickle cell disease. Postgrad Med J 80: 346-349.
10. Rogers ZR (2005) Priapism in sickle cell disease. Hematol Oncol Clin North Am 19: 917-928.
11. Platt OS (2006) Prevention and management of stroke in sickle cell anemia. Am Soc Hematol Educ Program 54-57.
12. Momodu I, Suleman K, Abdullahi S, Shehu UA (2011) Haematological values in Nigerian children with steady state homozygous sickle cell disease. Int J Acad Res 3: 501-506.
13. Mohan J, Marshall JM, Reid HL, Thomas PW, Hambleton I, et al. (1998) Peripheral vascular response to mild indirect cooling in patients with homozygous sickle cell (SS) disease and the frequency of painful crisis. Clin Sci(Lond) 94: 111-120.
14. Jones S, Duncan ER, Thomas N, Walters J, Dick MC, et al. (2005) Windy weather and low humidity are associated with an increased number of hospital admissions for acute pain and sickle cell disease in an urban environment with a maritime temperate climate. Br J Haematol 131: 530-533.
15. Serjeant GR, Chalmers RM (1990) Current concerns in haematology.1. Is the painful crisis of sickle cell disease a “steal” syndrome? J Clin Pathol 43: 789-791.
16. Eaton WA, Hofrichter J (1990) Sickle cell hemoglobin polymerization. Adv Protein Chem 40: 63-279.
17. Pham PT, Pham PC, Wilkinson AH, Lew SQ (2000) Renal abnormalities in sickle cell disease. Kidney Int 57: 1-8.
18. Oladepo O, Tona GO, Oshiname FO, Titiloye MA (2010) Malaria knowledge and agricultural practices that promote mosquito breeding in two rural farming communities in Oyo State, Nigeria. Malar J 9: 91.
19. Olayemi IK, Ande AT, Ayanwale AV, Mohammed AZ, Bello IM, et al. (2011) Seasonal trends in epidemiological and entomological profiles of malaria transmission in North Central Nigeria. Pak J Biol Sci 14: 293-299.
20. Bolarinwa RA, Akinola NO, Aboderin OA, Durosinmi MA (2010) The role of malaria in vaso-occlusive crisis of adult patients with sickle cell disease. J Med Med Sci 1: 407-411.
21. Oniyangi O, Omari AA (2006) Malaria chemoprophylaxis in sickle cell disease. Cochrane Database Syst Rev 18: CD003489.
22. Salawu L, Orimolade EA, Durosinmi MA (2009) Immuno-haematological characteristics of Nigerian sickle cell disease patients in asymptomatic steady state. Eur J Gen Med 6: 170-174.
23. White NJ (2011) A vaccine for malaria. N Engl J Med 365: 1926-1927.
24. Ogunjobi K, Ajayi V, Balogun I, Omotosho J, He Z (2008) The synoptic and optical characteristics of the harmattan dust spells over Nigeria. Theor Appl Climatol 93: 91-105.
25. Omonijo AG, Oguntoke O, Matzarakis A, Adeofun CO (2011) A study of weather related respiratory diseases in eco-climatic zones. Afr Phys Rev 5: 41-56.
26. Hirani A, Weibel S, Kane GC (2011) Acute chest syndrome and other pulmonary manifestations of sickle cell disease. J Clin Outcomes Manage 18: 211-221.
27. Davies EG, Riddington C, Lottenberg R, Dower N (2004) Pneumococcal vaccines for sickle cell disease. Cochrane Database Syst Rev 1: CD003885.
28. Ahmed SG (2011) The role of infection in the pathogenesis of vaso-occlusive crisis in patients with sickle cell disease. Mediterr J Hematol Infect Dis 3: e2011028.
29. Traish AM (2004) Biochemical and physiological mechanisms of penile erection. Sex Disabil 22: 151-160.
30. Switzer JA, Hess DC, Nichols FT, Adams RJ (2006) Pathophysiology and treatment of stroke in sickle-cell disease: present and future. Lancet Neurol 5: 501-512.
31. Orjih AU (1999) Malaria parasite metabolism in sickle cells. Eur J Haematol 62: 286-292.
32. Rug M, Prescott SW, Fernandez KM, Cooke BM, Cowman AF (2006) The role of KAHRP domains in knob formation and cyto-adherence of P. falciparum-infected human erythrocytes. Blood 108: 370-378.