Afr. J. Med. med. Sci. (1976) 5, 221–227.

The erythrocyte sedimentation rate in healthy North Nigerian university students

M. A. C. BRECKENRIDGE AND E. OKPANACHI

Department of Physiology, Ahmadu Bello University, Zaria, Nigeria

Summary

The technique recommended by the International committee for Standardization in Haematology (ICSH) was utilized for determination of erythrocyte sedimentation rate (ESR) in 'healthy' young Nigerian students living in the northern part of the country. Ninety-five point eight percent of a sample of 188 cases showed values within the Westergren norm for the first hour viz. 2·6 mm for males and 8·4 mm for females. A detailed follow up during the second hour revealed that 80% were within the norm for the second hour. The second hour elevations in apparently healthy subjects never exceeded 42 mm into the pathological range which would invalidate its use as a screening test in Nigeria for a young student population.

The effects of standardization of technique and the changing age-nutrition parameters of populations on the phenomenon of erythrocyte sedimentation is evaluated in the context of the view that the 'African normal' is higher than in temperate countries.

Résumé

La technique recommandée par le Comité International pour la Standardisation de l'Hematologie (C.I.S.H.) a été utilisée afin de determiner le ESR des jeunes Nigerians de bonne santé qui habitent le nord du pays.

95·8% d'un échantillon de 188 sujets ont revelé pendant la première heure, sous la norme Westergren, viz. 2·6 mm pour les hommes et 8·4 mm pour les femmes. Pendant la deuxième heure, une surveillance minute a démontré que seulement 80% étaient sous les limites normales pour cette deuxieme heure. Ces hausses de la deuxième heure chez les sujets apparemment en bonne santé n'ont jamais excese 42 mm au point de l'état pathologique qui invaliderait son emploi comme examen de selection dans une population de jeunes étudiants au Nigeria.

L'effet de standardisation de la technique et des differents paramètres 'âge-alimentation' des populations sur le phénomène de sédimentation erythrocytique est évalué selon le point de vue que la 'Moyenne africaine' est plus élevée que dans les pays de climat tempère.

Correspondence: Dr M. A. C. Breckenridge, Department of Physiology, Faculty of Medicine, Ahmadu Bello University, Zaria, Nigeria.

On the African continent, with its diverse host-parasite equilibrium, the erythrocyte sedimentation rate (ESR) has been observed to be variable and higher than the Westergren norm of 3–5 mm (males) and 7·12 mm (females) usually accepted for the first hour, (Whitby & Britton, 1969). In a Cape Town study, sixty-nine of 223 Bantus were observed to have higher rates compared to five out of 175 Caucasians and twenty-one of 171 coloured healthy subjects (Bronte-Stewart, Hickley & Ethelston, 1957). In Gambia, Deegan, Gilles & McGregor (1956) not only found the prevalence of high sedimentation rates but also observed significant differences in nearby villages (Kaneba 18 mm ± 11 and Jail 38 mm ± 36). Francis, Odusote & Osuntokun (1971) recording the values of a Nigerian population randomly selected from medical ward in-patients, healthy staff and blood donors at Ibadan reported 'the normal ESR range is 0–26 mm/h, the upper value being thrice that found in temperate countries.'

High prevalence rates of malaria, schistosomiasis, trypanosomiasis and helminthiasis, and high serum gamma globulin patterns have been considered contributory causes for the observed high ESR values. The lower serum albumin—higher gamma globulin pattern of Africans, even thought

to be a genetic feature (Rawnsley, Yonan & Reinhold, 1956) has been observed in Nigeria (Edozien, 1958). Positive correlations between ESR and gamma globulin levels have been recorded in Asia by Sahe & Bannerjee (1971), but Deegan *et al.* (1956) although observing the elevated gamma globulin pattern concluded 'probably the raised fibrinogen level . . . 50–100% higher than the mean of the normal European range . . . exerts the major influence in the increase of ESR in the African normals.'

These observations have contributed to the reluctance to use the test more often as a simple, inexpensive screening device between 'health' and 'disease'. Since its first description by Fahreus (1918) and its popularization by Westergren (1924) ('Die Senkungsreaktion'), the test has apparently stood the test of time with a few refinements enhancing its reliability. Observing the incomparability of ESR values due to variations in methodology the International Committee for Standardization in Haematology (ICSH) in 1970 recommended a standardized technique based on the Westergren method to ensure more meaningful comparisons (Metz, 1973). It also resolved that 'each National Committee should offer a range of values for the normal ESR which should include 90 or 95% of the local healthy population'. This study is presented to satisfy these criteria and to obtain a set of norms for a healthy population of Northern Nigeria.

Materials and methods

Blood samples were obtained from 193 students between the ages of 18 and 34. These included the male and female students of the first and second year medical courses (139), and new entrants presenting for medical examination at the University Health Centre (54).

The more rigid specifications of the ICSH utilized were the following.

(1) The skin of the forearm was cleaned with spirits and allowed to dry before venepuncture, to avoid contamination with spirits.

(2) Blood was collected by venepuncture over a maximum period of 30 s into a syringe (Plastipak BD Sterile Disposable) using a 19G 1½ 40/11 needle (BD Yale microlance sterile disposable propylene), and 2 ml added to 0·5 ml filtered citrate in a conical tube, the two mixed thoroughly by gentle, repeated inversion.

(3) The blood was then drawn into a clean dry Westergren-Katz tube (Blaubrand) with the required specification (overall length 300 ± 15 mm, uniform bore $2{\cdot}55 \pm 0{\cdot}5$ mm, with an etched scale graduated in mm extending over the lower $200 \pm 0{\cdot}35$ mm and a maximal tolerated error of 0·2 mm between two subsequent mm markings). Once filled to the zero mark, the tubes were firmly clamped in a strictly vertical position using the Blaubrand-Westergren rack, the tubes being held in position by a sturdy clamp and a rubber cushion. Before re-utilization the glass tubes were washed in acetone-water system and no detergent mixture or dichromate was used.

(4) The room temperature was in the specified range 18–25°C during December, January and February. In March the test was carried out in an air-conditioned room with the temperature at 22·5°C. Care was taken to see that the tubes were not exposed to direct sunlight, draughts or vibrations.

(5) After varying periods of time, usually after 60 min and 120 min, the sedimentation rates of the aggregated red cells were determined numerically in mm by measuring the distance between the lowest point of the surface meniscus to the upper limit of the red cell sediment. In fifty samples, the sedimentation rate was noted at 15 min intervals for 2 h.

The haemoglobin content and packed cell volumes were also determined in eighty-two of these students. Haemoglobin was determined with the AO Haemoglobinometer (American Optical Corporation, Buffalo, New York) where the absorption of light by the haemoglobin in a layer of haemolysed blood of carefully defined and standardized depth is compared with the absorption of a standardized glass wedge (15·5 G = 100%).

Packed cell volume was obtained by the micro haematocrit centrifugation method (Hawksley) and the MCHC was calculated after making the necessary corrections for trapped plasma.

Results

The ages of the students examined ranged from 18–34 years with an average of 22·3 years.

In a few, grossly elevated ESR values within the pathological range were observed, and these students were carefully examined. Five were excluded from the study as they had obvious upper respiratory tract infections. Three students were apparently healthy at examination and laboratory

TABLE I. Range, Mean ± s.d. ESR values for males and females at the end of the first and second hours. Group A includes all cases; group B includes first hour ESR values below 10 mm for males and below 15 mm for females

	Males				Females			
Group	A		B		A		B	
Time of reading	1st h	2nd h	1st h	2nd h	1st h	2nd h	1st h	2nd h
Number of cases	159	145	153	139	26	22	24	21
ESR mm Range	0–13	0–43	0–10	0–43	0·5–25	4–52	0·5–15	4–45
Mean	2·6	8·9	2·2	8·0	8·4	23·1	7·2	21·7
s.d.	2·8	9·1	2·1	8·1	12·5	12·5	4·3	10·9

investigations of WBC/DC, Hb, PCV, stools and urine showed no abnormality. Repeated tests showed persistently elevated rates 21/55, 20/41, 21/52 for first and second hours; these three were excluded from the study.

The range, mean and standard deviation of the erythrocyte sedimentation rate of the remaining 185 students (159 males and twenty-six females) are shown in Table 1 divided into groups A and B for each of the sexes. Group A includes all the cases. Group B included only those cases which showed a first hour ESR of less than 10 mm for males, or less than 15 mm for females.

Of the 159 males, there were only six (3·7%) with ESR over 10 mm in the first hour. Hence the group B mean ± s.d. of 2·2 ± 2·1 approaches the Westergren standard. The range for all males was [0–13] mm with a mean of 2·6 ± 2·8 mm. Of the twenty-six females, only two (7·7%) showed ESR values of over 15 mm at the end of the first hour. Hence the Group B

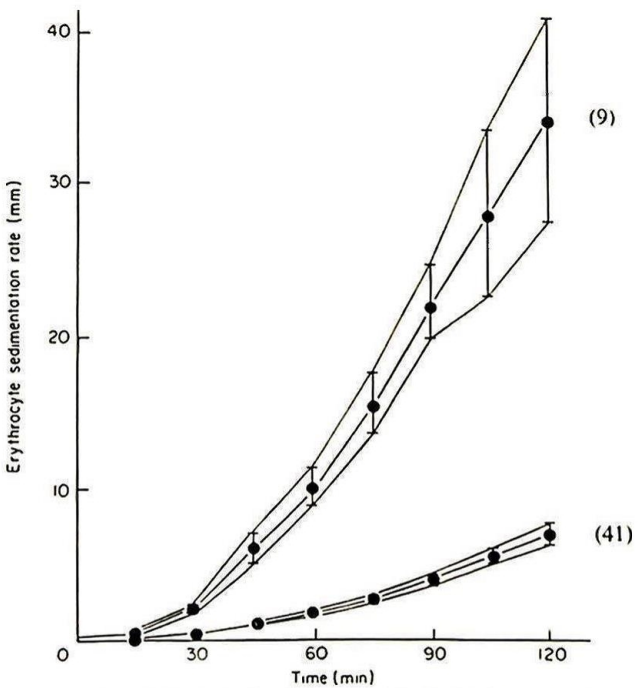

FIG. 1. Mean ESR ± s.e. observed for 120 min in fifty blood samples. Numbers in parentheses represent the size of each group.

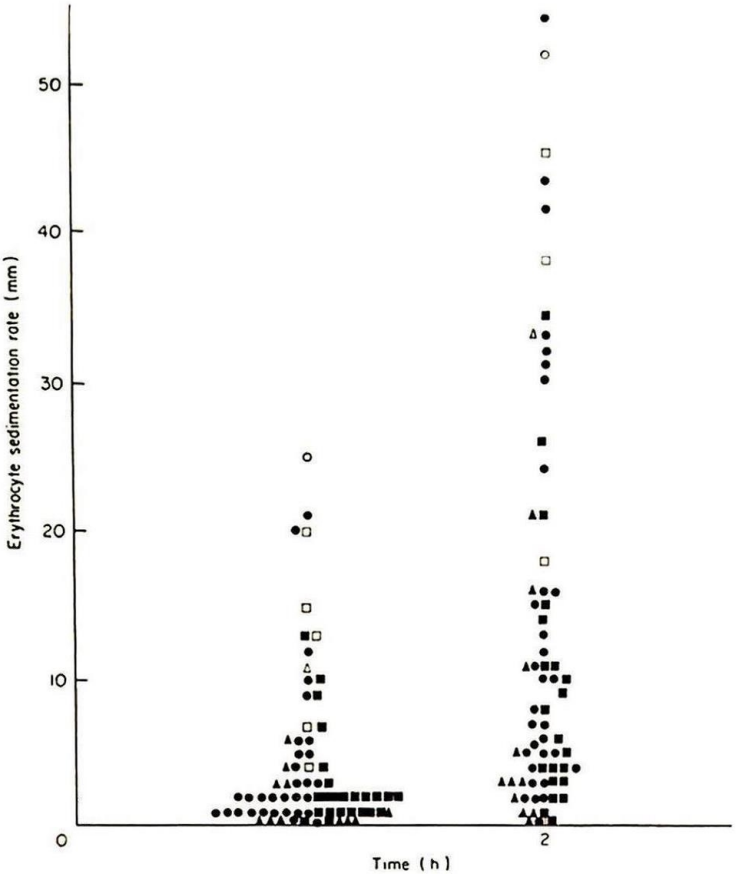

FIG. 2. Scatter diagram of the ESR in three major ethnic groups. ●○ Hausa, ■□ toruba, ▲△ Fulani (closed-males, open-female), at the end of 60 min and 120 min.

mean ± s.d. of 7·2 ± 4·3 for females also approaches the Westergren standard. The range for all females was 0·5–25 mm. with a mean of 8·4 ± 5·9 mm.

Of the second hour values, six males and one female had values over 30 mm and 35 mm respectively, being well in the pathological range defined by the Westergren classification (Whitby & Britton, 1969). The range for the second hour for males was 0–43 mm (mean 8·9 ± 9·1 mm) and for females 0–52 mm (mean 23·1 ± 12·5 mm).

The sedimentation rate was observed at 15 min intervals for 2 h in fifty samples randomly chosen. Forty-one subjects (82%) showed values within the normal range for both first and second hours. In the others (18%) the first hour values were normal, but second hour values were elevated. Figure 1 compares the mean ± s.e. of the ESR at 15 min intervals in these two groups.

Classifying the students according to the community (ethnic/linguistic) identity as declared by them, the distribution of the ESR values for males and females of three major groups within the sample studied, viz. Hausa, Yoruba and Fulani are depicted in Fig. 2. No significant differences were observed in the distribution.

The haemoglobin values for eighty-two students ranged from 12·0–18·8 g/100 ml with a mean of 16·3. As a percentage these values range from 77·4–118% with a mean of 104·5%.

The mean ± s.e. of the PCV was 44 ± 0·3% the

range varying from 33 to 51%. The MCHC calculated from these values ranged from 30·4 to 43·3 with an average of 36·91%.

No correlation was observed between either the haemoglobin or PCV and the first and second hour ESR values.

Discussion

In order to portray the diverse effects of complex host-parasite relationship of home environments, the varying dietary habits and the racial/genetic plasma protein differences relevant to the ESR—the parameters that condemn ESR as an unreliable index of active disease in Africa, this population of university students was selected—homogenous by age, previously medically examined and drawn from the geographical northern areas and its myriad communities.

In the reasonably large sample of 188 students, only 4·2% has ESR values falling outside the defined 'norm' of the Westergren technique, hence the validity of the broad generalization that the 'African normal is higher' needed clearer definition. Such an attempt is made here by considering the contributory roles of (a) the standardization of technique; (b) the variations in blood factors proven to alter the ESR; (c) the factors peculiar to selective populations.

Many values expressed for different parts of Africa have been determined by the Wintrobe method, using different anticoagulants in different series, without meticulous care for control of ambient temperature. Considerations for what might have seemed trivialities of technique have not been rigid and this is what standardization imposes. The theoretical considerations somewhat complicate the simplicity of the test. The use of the Westergren-Katz tube introduces uniformity into the 'geometrical factors' viz. tube length, rube radius, tube surface and tube tilt. This could hardly be overemphasized because calibre has been shown to introduce a significant variation where 27–28% of raised Westergren results showed no elevation with the Wintrobe technique (Gilmour & Sykes 1951). The variety of anticoagulants used probably introduces a variable effect. Heparin increases the ESR particularly if it is alkaline; oxalate shrinks red cells and reduces the rate; with sequestrene results are higher, while citrate alone has minimal effects. The specification of citrate in the technique is therefore a valuable one. The other factor of relevance to the tropical situation is the definition of ambient temperature. Weniger (1968) reported that over the temperature range 16–35°C, increase of 1°C increased the ESR by 1mm/h, the temperature having an aggregating effect on red cells. In Northern Nigeria with its varied Harmattan-Drought temperature fluctuations, this factor was important in the February to March period. The standardization of technique should therefore prove to be useful in obtaining comparable values for the tropical environment.

The observation of normal values in such a large proportion of the sample was somewhat surprising in view of certain theoretical expectations, quite apart from the prejudice that the African normal was higher. Edozien (1958) confirmed that the lower albumin higher gamma globulin pattern observed in other African regions is found in Nigeria and this should theoretically be expected to raise the ESR. Further, considerable fluctuation in red cell mass in Africa, was expected to deviate the ESR from its norm. A 10% change in PCV could alter the ESR by 50% (Dintenfas, 1971), ESR values even needing correction for this factor in anaemia. Drawn largely from the rural environment, these students were expected to show the predisposition to decreased red cell mass from incipient hemolysis (malaria, haemoglobinopathies, glucose-6-P deficiency, drug usage, tropical splenomegaly, hypersplenism) and unnoticed leakage from gastrointestinal and genitourinary tracts (hookworm and schistosomiasis). But on the contrary, the PCV verged on the higher side of normality. In the series the mean ± s.e. of the PCV was 44·01 ± 0·3% with a mean haemoglobin of 16·28 g and MCHC averaging 36·91%. This was similar to the observations on Northern students in an earlier series by Watson & Etta (1973) where the respective values were 45·4 ± 2·96; 15·1 ± 0·95 and 32·8 ± 3·54. If at all the higher red cell mass should have accelerated the ESR but the observed normality in such a large proportion of students was therefore a paradox. It rather potentiates the view of Ruhenstroth-Bauer (1961) that in spite of the observed positive correlation of serum fibrinogen/gamma globulin to raise the ESR, 'the increase in fibrinogen or gamma globin is only coincidental to a high sedimentation' and that the determining factor may be the production of 'agglomerins' (resembling incomplete antibodies) which compete for red cell surface receptors in the presence of a 'high molecular weight non-specific serum supplement'. This hypo-

thesis should also suit to explain the observation that in nearly 20% of this student sample, the first hour values were normal but second hour values abnormal, probably indicating that erythrocytic sedimentation is not a mere mechanical gravitation of red cells through a continuous medium but probably involves red cells receptor-agglomerin competition of the type postulated by Ruhenstroth-Bauer (1961). Fibrinogen, does have agglomerin activity and African populations show 'raised fibrinogen levels, 50–100% higher than the mean of the normal European range' (Deegan *et al.*, 1956). Here again the observed normality of a large proportion of the sample is rather paradoxical. Although fibrinogen contributes to part of the 'agglomerin activity', the total expression of this potentiality is perhaps complex.

The extreme elevations of ESR, i.e. values over 70 mm (Bottiger & Molin, 1964) commonly found in malignancy 58%, collagen disease 25% and renal disease 8% (Zacharski & Kyle, 1967) are associated with complex changes in plasma constituents. In health therefore, it is unlikely for ESR values to be so high not even with the high-fibrinogen, high gamma globulin low albumin serum protein of the healthy African. The highest rate observed in an apparently healthy student in this series was 25 mm for the first hour.

Probably the factors of vital importance in selected populations is homogeneity in age and nutrition. In this sample the average age was 22·3 years and a certain uniformity of nutrition may have been imposed by the hostel environment, particularly during the secondary school growth spurt. There was no difference in values observed among Hausa, Fulani or Yoruba students nor in persons of urban/rural extraction. For the fifty year span 20–70 years, the ESR could rise 2·5–8 mm per hour in males and 7–16 mm in female (Bottiger & Svedberg, 1967) but the more significant factors should be nutritional.

Although the 'healthy student' probably deviates from the concept of the 'normal healthy African' seen in hospital practice, viz. 'an individual living and conducting his normal daily existence in his natural environment, who is apyrexial and not containing malarial parasites in high density' (Deegan *et al.*, 1956), nevertheless the student age group forms a significant bulge in the Nigerian age pyramid and the characterization of a range for normal ESR should help to achieve the aim of the International Committee on Haematology (a value including 90–95% of the local healthy population). In this sample, fourteen of 188 students, i.e. 7·4% were apparently healthy but with ESR values widely dispersed from the Westergren norm. Every population probably has this component, varying in size in the same population from time to time and in different comparable populations. It is the size of this fraction that is probably important in defining a physiological norm. It could be so large in a particular population so as to enhance the view that the 'normal' is high. But with greater uniformity in nutrition, age structure and standards of living it could shrink so that the norm for the community could well be the Westergren norm with a certain percentage tendency to deviation. In this North Nigerian population of young adults between 20–35 years, the expectation of 'high normal' values is probably 5% at maximum 10%. Extreme elevations over 40 mm is occasional. Thus the broad generalization that the 'African normal is higher' is an unsatisfactory one particularly because it tends to reject a simple, inexpensive, quick and efficient screening device of 'health' and 'disease'.

References

Bottiger, L.E. & Molin, L. (1964) Fever and elevated erythrocyte sedimentation rate. A cross study through a medical department. *Acta. med. Scand.* **176**, 639–48.

Bottiger, L.E. & Svedberg, C.A. (1967) Normal erythrocyte sedimentation rate and age. *Brit. med. J.* **2**, 83.

Bronte-Stewart, B., Hickley, J.M. & Ethelston J.D. (1957) Haematological standards for adult South African males; an inter-racial study. *S. Afr. J. Lab. clin. Med.* **3**, 131–41.

Deegan, T., Gilles, H.M. & McGregor, J.A. (1956) Observations on the Erythrocyte Sedimentation Rates and blood protein patterns of Gambian Africans. *Ann. trop. Med. Parasit.* **50**, 451.

Dintenfass, L. (1971). *Blood microrheology—Viscosity Factors in Blood Flow, Ischaemia and Thrombosis*, p. 130–155. Butterworths, London.

Edozien, J.C. (1958) Biochemical 'Normals' in Nigerians. I Blood *W. Afr. med. J.* **1**, 121.

Fahreus, R. (1918) Über die Ursachen der verminderten suspensions-stabilitat der blutkörperchen, während der Schwangerschaft (vorläufige Mitteilung). *Biochem. Z.* **89**, 355.

Francis, T.I., Obusuie, K. & Osuntokun, B.O. (1971). The erythrocyte sedimentation rate in Nigerians. *W. Afr. med. J. JUNE* 1971. 250.

Gilmqur, D., & Sykes, A.J. (1951) Westergren and Wintrobe methods of estimating ESR compared. *Brit. med. J.* **2**, 1496–97.

Metz, J. (1973) Reference method for the erythrocyte sedimentation rate (ESR) test on human blood *S. Afr. med. J.* **47**, 937.

Rawnsley, H.M., Yonan, V.L. & Reinhold, J.G. (1956). Serum protein concentrations in North American Negroid. *Science*, **123**, 991–992.

RUHENSTROTH-BAUER, G. (1961) Mechanism and significance of erythrocyte sedimentation rate. *Brit. med. J.* **1**, 1804.

SAHE, N. & BANNERJEE, B. (1971) Correlation of Erythrocyte Sedimentation Rate with serum composition in the tropics. *Trop. geog. Med.* **33**, 30.

WATSON, R.S. & ETTA, K.M. (1975) Some blood indices in three groups of Nigerians and in severe but ambulatory cases of anaemia. *J. Trop. med. Hyg.* **78**, 13–8.

WENIGER, B. (1968) *Untersuchungen über die Standardisierbarkeit der Erythrozytensenkungsreaktion nach Westergren.* Dissertation; Breisgau, Germany, Albert-Ludwig-Universität zu Freiburg.

WESTERGREN, A. (1924) Die senkungsreaktion. *Ergeb. Inn. Med. Kinderheilk.* **26** 577.

WHITBY, L.E.H. & BRITTON, C.J.C. (1966) *Disorders of the Blood*, 10th edn. Churchill, London.

ZACHARSKI, L.R.& KYLE, R.A .(1967) Significance of extreme elevation of erythrocyte sedimentation rate. *J. Am. med. Ass.* **202**, 264–6.