

Erythrocyte sedimentation rate in elderly blacks

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Abstract This study investigated the erythrocyte sedimentation rate (ESR) in an elderly population with the objective of establishing reference ranges and the diagnostic value of the ESR. Elderly blacks were randomly selected from communities in the Orange Free State. ESR determinations were done according to the Westergren method. Total protein, albumin, immunoglobulin and C-reactive protein (CRP) levels were measured on serum. Results were analysed by means of non-parametric statistical methods. In the group with normal CRP and immunoglobulin levels it was found that 99% of values were below 44 mm/h for men and 62 mm/h for women. The sensitivity and specificity for these cut-off values (CRP used as 'gold standard') were 33% and 91% respectively for men and 75% and 89% respectively for women.

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It has been reported that the erythrocyte sedimentation rate (ESR) in apparently healthy elderly subjects is higher than the accepted normal limits.^{1,4} However, no data exist on ESR values in the sub-Saharan indigenous elderly population. Evidence also exists that blacks have higher globulin levels than whites.⁵ Previous studies have shown that plasma proteins have an effect on ESR.^{6,7} The possibility therefore exists that the ESRs of blacks may be higher than known reference values derived from studies of white groups.

Previous studies have shown that C-reactive protein (CRP) is a very sensitive and direct indicator of the acute phase response.⁸⁻¹⁰ It is therefore possible to determine the diagnostic importance of the ESR with regard to the acute phase response in elderly blacks by using the serum CRP concentration as a 'gold standard'.

This study investigated the ESR and the CRP values in a sub-Saharan indigenous elderly population and aimed: (i) to determine ESR reference ranges for this population; and (ii) to determine the possible relationship between the ESR and CRP values in an effort to establish some perspective with regard to the diagnostic value of the ESR.

Subjects and methods

Elderly blacks (65 years and older) were randomly selected from communities in 10 Orange Free State towns with 1 500 or more inhabitants. Subjects were included in the study after informed and written consent was obtained. The selection methods and profile of the selected sample are reported elsewhere.^{11,12}

A blood sample was taken from each person in an ethylenediamine tetra-acetic acid tube for calculation of

ESR, and serum was obtained for CRP and biochemical analysis. ESR values were determined according to the Westergren method, within 2 hours of the sample's being obtained, according to the recommendations of the International Committee for Standardisation in Haematology.^{13,14} All ESRs were calculated in the laboratory of the Department of Haematology at Pelonomi Hospital, Bloemfontein. This laboratory is subject to the quality assurance programme of the South African Institute for Medical Research. Serum CRP concentrations were determined with a laser nephelometer (Behring) after CRP molecules were agglutinated with NA Latex CRP-reagent (Behring). Immunoglobulin levels were determined by means of electrophoretic methods.

The study group was divided into male and female subgroups. Participants with normal immunoglobulin levels and with CRP values of less than 24 mg/l were selected in order to eliminate those individuals with acute phase responses and possible paraproteinaemias. Non-parametric statistical methods were used to evaluate the data because of the distribution types of ESR and CRP values found.

Results

ESR and CRP values were obtained for 302 subjects (136 men and 166 women) with an average age of 73 years (SD 6,5 years, range 65 - 104 years). After participants with abnormal immunoglobulin levels and CRP values above 23 mg/l were excluded, a group of 126 elderly persons (53 men, 73 women) with no paraproteinaemia or acute phase reaction remained. Calculations were made to establish a reference range for ESR on this group.

Frequency distributions of ESR and CRP values followed patterns which resembled the Erlang distribution. Therefore statistical significance of differences between men and women were determined by means of non-parametrical methods (Mann-Whitney test). Table I shows the descriptive statistics for the ESR and CRP values in the 4 different subgroups. Probability values for differences between men and women are also shown in Table I. ESRs in women were significantly higher than those in men, while no significant differences between CRP values were found. The 99th percentiles of CRP values and the selected ESR values found in the study group are shown in Table II, together with the 95% confidence intervals for the percentiles. The confidence intervals were determined by means of non-parametric methods.

Simple linear regression analyses were performed to determine the relationship between ESR and increasing age, CRP, globulin and albumin levels. No direct relationship was found between ESRs and increasing age. CRP values showed a significant correlation with ESRs. It was found that the R^2 values of women were higher ($R^2 = 16,93\%$) than the values of men ($R^2 = 4,24\%$). Serum globulin levels showed a significant positive correlation with ESRs and albumin levels a significant negative correlation.

From the results obtained in this study, we calculated the diagnostic value (specificity, sensitivity, positive predictive value and negative predictive value) of ESR for acute phase response as measured by means of the CRP value (gold standard). Cut-off values used for this exercise were the lower limits of the 95% confi-

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TABLE I.
Descriptive statistics of CRP and ESR values of elderly blacks in the OFS

	Men				Women				P*
	No.	Mean	SD	Range	No.	Mean	SD	Range	
CRP (mg/l)	136	5,2	6,6	2 - 53	166	6,0	6,1	2 - 35	0,2900
ESR (mm/h)	136	17,7	17,6	1 - 20	166	31,6	23,1	1 - 106	< 0,0001
ESR of selected persons (mm/h)†	53	15,0	19,2	1 - 20	73	23,4	16,3	1 - 68	0,0001

* Mann-Whitney test for difference between samples.
† Persons with normal immunoglobulin levels and CRP values less than 24 mg/l.

TABLE II.
Confidence intervals (95%) for the 99th percentile of CRP values and ESRs

	95% CI*
CRP	
Men	24 - 53
Women	24 - 35
ESR	
Men	44 - 120
Women	62 - 68

* Determined by non-parametric methods.

dence intervals of the 99th percentiles (CRP 24 mg/l; ESR men 44 mm/h; ESR women 62 mm/h). Results are shown in Table III. The specificity and negative predictive value were found to be high in both sexes. The positive predictive values and the sensitivity for the men were found to be low.

TABLE III.
Diagnostic value of the ESR for acute phase response in elderly blacks (CRP used as gold standard)

	Men (%)	Women (%)
Sensitivity	33	75
Specificity	91	89
Positive predictive value	8	14
Negative predictive value	98	99
Prevalence	2	2
Accuracy	90	89

Discussion

In a recent editorial in the *SAMJ*, it was concluded that the ESR has an important place in clinical practice.¹⁵ The ESR has been widely used over the past 60 years as a diagnostic tool,⁹ *inter alia* as an indirect method of estimating the acute phase response. The ESR is simple and inexpensive to calculate; it does not need sophisticated equipment and can easily be done at the bedside in most health settings. Sophisticated tests, like that for CRP values, which are better and more direct indicators of the acute phase response, are not always easily accessible to rural medical staff. We therefore considered it important to evaluate the significance of the ESR with regard to diagnoses of acute phase responses in elderly blacks.

In this study the ESRs were investigated in a non-hospitalised elderly black population. Subjects who could have had an acute phase reaction or paraproteinaemia were excluded. This may have biased the group by making it more like a normal elderly black population in respect of ESRs.

Differences between the ESRs of men and women are documented^{3,16} and confirmed in this study. However, only one of the previous studies on elderly populations³ reported this difference. ESRs in women

were significantly higher than those in men. The reasons for this are unknown.

According to the statistical methods used, it can be assumed that 99% of the ESRs of 'healthy' (without an acute phase reaction or paraproteinaemia) elderly blacks will be below the lower limits of the 95% confidence interval (44 mm/h for men and 62 mm/h for women) of the 99th percentile (Table II). These values can therefore be suggested to be upper limits of normal reference ranges in the elderly black population in the Orange Free State. Previous studies on ESR in elderly populations (mainly white populations) reported ranges between 20 mm/h and 69 mm/h (Table IV).^{1-5,17} Gibson¹⁸ concluded that a normal elderly person should have a normal ESR. However, this finding was contrary to reported results from most other workers.^{1-4,17} The findings in this study were not higher than previous reports on white groups¹⁻⁴ and it would seem therefore that higher globulin levels do not raise the ESR.

TABLE IV.
Proposed ESR cut-off values for elderly persons from other studies*

	Men	Women
Olbrich (1948) ¹	14	14
Boyd (1966) ²	40	40
Böttiger (1967) ³	20	30
Sharland (1980) ⁴	69	69
Gibson (1972) ¹⁸	10	10
This study	44	62

* mm/1st h, Westergren method.

In respect of CRP, it can be assumed that 99% of the elderly black population have values of less than 24 mg/l. It was interesting to note that the value of 24 mg/l found in this study was almost the same as the cut-off value of 23 mg/l proposed by Freeman and Cox¹⁹ for elderly people.

To the best of our knowledge the relationship between ESR and CRP in a non-hospitalised population has never been investigated. Both ESR and CRP are known to increase during the acute phase response.⁹ In a study of hospital patients¹⁷ it was reported that CRP is superior to ESR as an objective nonspecific marker for disease activity in the elderly. Simple linear regression analyses in this study showed a significant correlation between CRP and ESR. However, the low R² value confirmed that other factors also have an effect on the predictability of the ESR. In an effort to determine the clinical role of the ESR in elderly blacks as an indicator of acute phase response, the diagnostic value of the ESR was calculated with the CRP used as gold standard.²⁰ Although the CRP was the standard best suited to this purpose, there are known shortcomings. According to Pepys and Baltz,¹⁰ CRP is greatly elevated in cases of infection, immunological complications of infection, inflammatory diseases, malignant neoplasia, ischaemic necrosis such as myocardial infarction, and trauma such

as surgery, burns and fractures. However, only minor elevations are associated with systemic lupus erythematosus, scleroderma, dermatomyositis, Sjögren's syndrome, ulcerative colitis and leukaemia where the ESR still shows a marked response.¹⁰ It is also known that the CRP does not increase in the presence of paraproteinaemias, where the ESR tends to be greatly increased;⁹ this lowers the ESR's specificity and sensitivity for the acute phase response. After tissue injury, the time taken for a detectable increase in plasma protein concentration to occur varies with different proteins. An increase in CRP levels may be detected within 6 - 10 hours; an increase in fibrogen concentrations, which are a major determinant of the ESR, may not occur until 24 - 48 hours have elapsed. Therefore the responses of CRP and ESR to tissue injury are not exactly the same. The diagnostic value of the ESR found in this study must therefore be interpreted against the abovementioned background. From the results it seemed that the ESR values in elderly blacks showed high specificity (the proportion of subjects without an acute phase response who have a normal ESR) but low sensitivity (the proportion of subjects with acute phase response who have a raised ESR). The high negative prediction values (men 98%, women 99%) implied that a high probability exists of an acute phase response not occurring when the ESR value is below the cut-off point. The low positive predictive values (men 8%, women 14%) indicated that only a small proportion of subjects with raised ESRs will prove to have acute phase responses. The information about predictive values in this study could be very useful because the data were gathered from samples in the community and not from hospital populations.²⁰ Statements about predictive values from samples drawn from hospital populations would be misleading because the prevalence of pathology is relatively high.²⁰

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