Erythrocyte sedimentation rate during steady state, painful crisis and infection in children with sickle cell disease

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ABSTRACT

Objective: To evaluate Erythrocyte Sedimentation Rate in children with sickle cell disease.

Methods: Erythrocyte Sedimentation Rate was performed in 95 children with sickle cell disease during the period from December 1992 to June 1999. Patients were classified into 4 groups. Patients in the steady state (group 1), painful crisis (group 2), mild infection (group 3) and moderate/severe infection (group 4). Comparison between the groups was performed using ANOVA and ANCOVA.

Results: There were 55 males (58%) and 40 females (42%) with a mean age of 79.1 months. The mean Erythrocyte Sedimentation Rate values for the various groups were as follows: Group 1 (n=10); mean Erythrocyte Sedimentation Rate is 5 mm/hr ($\pm$4.6) and was significantly the lowest ($p<0.05$), group 2 (n=44); mean Erythrocyte Sedimentation Rate is 25.8 mm/hr ($\pm$16.3), group 3 (n=18); mean Erythrocyte Sedimentation Rate is 28.1 mm/hr ($\pm$25.8), while group 4 (n=23); mean Erythrocyte Sedimentation Rate is 99.2 mm/hr ($\pm$33.5) and was significantly the highest ($p<0.05$). Two cut-off values for the Erythrocyte Sedimentation Rate ($\geq$ 30 mm/hr then $\geq$ 50 mm/hr) were considered to evaluate their specificity and sensitivity for moderate/severe infection.

Conclusion: Although the Erythrocyte Sedimentation Rate is low in sickle cell disease, it does increase during painful crisis and infection and it is a useful indicator of moderate/severe infection.

Keywords: Sickle cell disease, erythrocyte sedimentation rate, steady state, painful crisis, infections.

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Patients with sickle cell (SCD) disease are known to have unusually low erythrocyte sedimentation rates.[1] Few studies[2,3] have shown that the sedimentation rate may be increased during painful crisis and during infection in patients with SCD and this increase was ascribed to the increased plasma fibrinogen level[2] known to occur during painful crisis.[4,5] We have observed that erythrocyte sedimentation rate (ESR) is underused in evaluating patients with SCD who present with acute or chronic complications the most important of which is significant infection. The reason for this underuse is the misconception that since SCD causes low ESR, infections or complications known to elevate the ESR in patient with HgbA are unlikely to do so in patients with SCD.

The study was performed to evaluate the ESR response in our pediatric patients with SCD during steady state, painful crises, mild infections and moderate/severe infections.

Methods. This study was performed in Asir Central Hospital which is a tertiary hospital in the

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southwest region of Saudi Arabia. The ESR response was studied in patients who have SCD (homozygous for HgbS). Patients were classified into 4 groups. Group 1 included patients who had no crisis of SCD, infection or other diseases (steady state). Group 2 were patients who had painful crises requiring admission. Group 3 were patients who had mild infection and Group 4 were patients who had moderate to severe infection. Examples of mild infections include viral upper respiratory tract infection, mild bacterial pharyngitis, superficial skin infection and mild bronchopneumonia. Examples of moderate to severe infections include patients with positive blood culture, septic arthritis, osteomyelitis, lobar pneumonia, diffuse bilateral broncho-pneumonia, subcutaneous abscess and pyelonephritis.

The blood was collected in EDTA containing tube and the ESR was measured at one hour with the Guest-Westergren method. Hemoglobin level was measured in all patients. Blood culture was performed in all patients whose temperature was >38°C.

The statistical analysis was performed using SPSS package for Windows. The significance of the quantitative differences between groups was assessed with ANOVA and ANCOVA with patient age and hemoglobin level as the covariates.

Results. During the study period (December 1992-June 1999), the ESR was performed in 95 patients with SCD. There were 55 males (58%) and 40 females (42%). Their ages ranged from 6 to 216 months with a mean age of 79.1 months (±58.2) and there was a statistically significant difference in the mean ESR between the different groups (F=66.23, p=0.001). The patient classification were as follows: Steady state (group 1), 10 patients (10.5%), painful crisis (group 2), 44 patients (46%), mild infection (group 3), 18 patients (19%); moderate/severe infections (group 4), 23 patients (24%). The mean ESR for all patients was 41.6 (±39.8) mm/h (Range: 1 to 150 mm/h). The mean ESR values (±SD) for the various groups (Table 1) were as follows: group 1, 5 mm/h (±4.6); group 2, 25.8 mm/h (±16.3); group 3, 28.1 mm/h (±25.8); group 4, 99.2 mm/h (±33.5). The mean ESR values in group 1 (steady state) was significantly lower ($p<0.05$) than its value in any of the other three groups, while the mean ESR value in group 4 (moderate/severe infection) was significantly higher ($P<0.05$) than in any of the other three groups. However, the difference in the mean ESR value between group 2 (painful crisis) and group 3 (mild infection) was statistically not significant.

There was no significant difference between the groups as regards to age ($F=2.46$, $p=0.07$). However, the difference in the mean age between group 3 and group 4 was significant ($p<0.05$). The results also revealed a statistically significant difference in the mean Hgb between the groups ($F=3.34$, $p=0.03$), However, such a significant difference was evident only between group 1 and each of the remaining groups ($p<0.05$).

After adjusting for the differences in age and Hgb values between the groups, the significance of differences in mean ESR values between the various groups remained as stated above, ie. group 1 had significantly lower ESR than the other groups and group 4 had significantly higher ESR than the other groups while the difference in the ESR between group 2 and group 3 was statistically not significant.

For practical purposes, we considered two cut-off values for the ESR (≥30 mm/h then ≥ 50 mm/h) to evaluate their specificity and sensitivity for moderate to severe infection in patients with SCD who present with fever. A cut-off value of ESR ≥30 mm/h had sensitivity of 95% but the specificity was 67%. A cut-off value of ESR ≥50 mm/h demonstrated a sensitivity of 90% and a specificity of 90%.

Table 1 - The mean ESR in SCD patients during steady state, painful crisis and infection.

Group of patients	No. (%)	ESR (mm/h)	
		Mean	SD
Group 1 - Steady state	10 (10.5)	5.0*	4.6
Group 2 - Painful crisis	44 (46)	25.8	16.3
Group 3 - Mild infection	18 (19)	28.1	25.8
Group 4 - Moderate/severe infection	23 (24)	99.2*	33.5
All patients	**95 (99.5)**	**41.6**	**39.8**

*Significantly different from any of the other groups ($p<0.05$). SCD - Sickle Cell Disease ($F=66.23$, $p=0.001$).

Discussion. Patients with sickle cell anemia are considered to be immunocompromised and bacterial infection in them can cause severe morbidity and mortality. Therefore, early identification and appropriate management of bacterial infection cannot be over-emphasised. Fever is not an uncommon finding during vaso-icckysuve (painful) crises[6] in our area and it may be of a high grade in the presence of associated viral infection. Furthermore, patients with painful crises may appear as sick as those with osteomyelitis and hence the difficulty in distinguishing painful crises from osteomyelitis. Also, the leukocyte count may be elevated during painful crises even in absence of infection.[2,3] Some authors have suggested that high ESR is a useful

indicator of bacterial infection[7,8] while others have disputed its value.[3]

Our study has shown that in our group of patients while the ESR was low during the steady state it increases during painful crises and infections, and that ESR response in patients with painful crises is similar to its response during mild infection. However, it has clearly shown that the mean ESR value in the presence of moderate/severe infection is significantly higher than its value during painful crisis or mild infection. Previous study[3] indicated a sensitivity of 38% for infection when a cut-off value of ESR $\geq$30 mm/h was used, while our study has shown a sensitivity of 95% (and a specificity of 67%) when this cut-off value was used. This difference might be attributed to the fact that in our study we evaluated the sensitivity of this cut-off value in identifying moderate/severe infection while in the other study mild infection was included as well. A higher cut-off value (ESR $\geq$ 50 mm/hr) demonstrated a lower sensitivity (90%) and a specificity of 90%. Since infection in patients with SCD can be fatal, one should use the lower cut-off value (30 mm/h) in order not to miss major infections.

The low ESR value in patients with SCD during the steady state is mainly because of the inability of the sickled cells to participate in rouleaux formation.[8] The ESR, however, increases during painful crisis and this is partially related to elevated plasma Fibrinogen level.[2,4,5] During infection, elevated serum globulin level also contribute to the high ESR in patients with SCD.[9]

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