Supplementary Data

Painful crisis is defined as an acute painful event that required oral/injectable analgesics and that lasted for at least 4 hours when no other cause could explain the symptom. This working definition included hand-foot syndrome, pain in extremities, back and chest. Pain rate [vaso-occlusive crisis (VOC)/patient/year] was calculated by dividing the number of episodes by the number of patients/years [9].

Incidence of anemia was diagnosed on the basis of hemoglobin (Hb): mild (Hb >9.0 g/dL), moderate (6.0-9.0 g/dL) and severe (Hb <6.0 g/dL). On the basis of mean corpuscular volume (MCV): microcytic (MCV <80.0 fL), normocytic (MCV 80.0-100.0 fL) and macrocytic anemia (MCV >100.0 fL). Anemia was also analyzed on the basis transfusion dependence and rate of blood transfusion/patient/year. The rate of blood transfusion (blood transfusion/patient/year) was calculated by dividing the number of patients/years. Patients were evaluated for infections such as malaria, tuberculosis, urinary tract infection (UTI) and respiratory tract infection (RTI).

Malaria diagnosis: quantitative buffy coat (QBC) test, peripheral smear examination and immunochromatography test (ICT). Tuberculosis diagnosis: Montoux test, erythrocyte sedimentation rate (ESR), X-ray, enzyme-linked immunosorbent assay (ELISA) of sputum, acid fast bacilli (AFB) test sputum culture. Respiratory tract infection diagnosis: X-ray chest posteroanterior (PA)-view), sputum culture, gram stain, BAL analysis. Urinary tract infection diagnosis: urine test by routine examination (RE), microscope examination (ME) and culture and sensitivity (C/S). Spleen and liver size, complications (normal *vs.* megaly/atrophied) were assessed clinically followed by ultrasonography in the last 2 years of enrollment. Gastrointestinal/hepatobiliary complicationswere diagnosed by radiologic (ultrasound) evidence of stones (‘hyperechoic with posterior acoustic shadowing’) or sludge (‘hypoechoic mobile matter within the gallbladder’). Diagnosis of avascular necrosis (AVN) of femoral/humeral head was done by radiological examination. Renal failure was diagnosed by estimation of creatinine >1.4 mg and glomerular filtration rate (GFR) <90 mL. Some associated complaints such as epilepsy, epistaxsis, cardiac problem, *etc.* were also included [10,11].