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MYELOID DYSFUNCTION IN SICKLE CELL DISEASE

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Background: In sickle cell disease (SCD), profound anaemia and severe hemosiderosis cause functional and physiological abnormalities in various organ systems, including immune system. Infectious complications are common, constitute the second most common cause of mortality and a main cause of morbidity. During the haemolytic crisis, large amount of arginase (s-Arg-1) are released, potentially acting as immunosuppressor molecule. Despite its clinical impact, only a few is known about myeloid dysregulation in SCD. *Aims:* Detecting immunological impairment at the steady state evaluating myeloid and lymphoid cells in peripheral blood of SCD patients. *Materials and Methods:* Between May and June 2014,peripheral blood obtained from 30 consecutive SCD patients at the steady state plus 30 healthy subjects was studied for evaluation of myeloid subpopulations and lymphoid paresis. Myeloiddys function was evaluated as percentage and absolute count of circulating myeloid suppressor cells (MDSC) in peripheral blood assessed by flow cytometry as follows: im-MDSC (CD34+/CD11b+/CD13+/CD14-/HLA-DR-/CD45+), neutrophilic-like N-MDSC (CD11b+/CD13+/CD15+/CD14-/HLA-DR-/Lin-) and monocytic-likemo-MDSC (CD14+/HLA-DRlow/-), phagocytic activityof granulocytes using a commercially available kit (Phagotest R), amount of Arg-1 expressed in mature granulocytes by RT-PCR and circulating s-Arg-1 using a commercially available ELISA kit (Biovendor). *Results:* The capability of phagocytosis of granulocytes wassignificantly reduced compared to healthy subjects (p=0.001). G-MDSC subset was not increased, while mo-MDSC subpopulation was increased in SCD (p=0.001) but not in thalasso-SCD. s-ARG-1 was increased in both SCD and thalasso-SCD (respectively 203±3 ng/mL and 248±6ng/mL, p=0.003) and positively correlated with the amount of HbS (r=0.7, p=0.002). Arg-1 expression in granulocytes was increased (20 times higher than healthy controls, p=0.002) *Conclusions:* SCD and thalasso-SCD caucasian patients exhibiti mmunosuppressive myeloid markers including reduced phagocytosis, increased amount of mo-MDSC, Arg-1 expression in granulocytes and circulating s-Arg-1. Further analysis are ongoing to detect if the same myeloid impairment occurs during vase occlusive crisis and in a different genetic background, like in Afro-Americans.