BACKGROUND:

Severe malarial anemia (SMA) resulting from Plasmodium falciparum infection is one of the leading causes of childhood mortality in sub-Saharan Africa. The innate immune mediator macrophage migration inhibitory factor (MIF) plays a critical role in the pathogenesis of SMA.

METHODS:

To investigate the influence of MIF genetic variation on susceptibility to SMA, haplotypes of the MIF -173G/C and -794CATT5-8 polymorphisms were examined in a cohort of Kenyan children.

RESULTS:

A statistically significant relationship between increasing frequencies of longer CATT repeats at -794 and increasing severity of malarial anemia was observed. In addition, there was a strong association between lower MIF concentrations and longer CATT repeats. Multivariate logistic regression analyses demonstrated that the 6G haplotype (ie, MIF -794CATT6/-173G) was associated with protection against SMA, whereas carriers of the 7C or 8C haplotype had increased risk of developing SMA. Furthermore, carriers of the 7C or 8C haplotype had reduced plasma MIF levels during acute disease.

CONCLUSIONS:

The findings demonstrate that variation in the MIF promoter influences susceptibility to SMA and peripheral MIF production. However, the MIF -173 and -794 polymorphisms appear to have both independent and interactive effects on different measures of disease severity, suggesting that MIF plays a complex role in malarial pathogenesis.