Summary
Clinico-epidemiological features of pediatric patients with malaria due *Plasmodium vivax* that developed anemia and thrombocytopenia requiring hospitalization are herein reported. Over a 3-year period, 78 children with *P. vivax* infection were admitted to our Hospital in Sucre, Venezuela. Clinical manifestations at admission were 93.59 per cent fever, 41.03 per cent chills and 14.10 per cent headache, among others. On paraclinical evaluations 94.87 percent presented with anemia (10.26 per cent severe), 25.64 percent with malnutrition, and 10.26 percent had intestinal parasitosis. The mean hemoglobin levels on admission were 8.09 g/dl and mean platelet counts 127 402 cells/mm³. Among these patients 58.97 per cent developed thrombocytopenia (24.36 per cent severe) requiring transfusion in 25.64 per cent of patients. After antimalarial treatment with chloroquine and primaquine and supportive care all patients were successfully discharged. No deaths or further complications were seen, except for persistent mild thrombocytopenia in 17.95 per cent of the patients.

Introduction
*Plasmodium vivax* malaria is an endemic infection in northeastern Venezuela (State of Sucre) and is commonly considered a ‘benign’ condition. But in some cases hospitalization is required for complicated clinical conditions. Most reports comment on *Plasmodium falciparum* malaria complications in children, but few studies describe clinical epidemiology of those pediatric patients with moderate to severe malaria due *P. vivax* requiring hospitalization. Children are particularly at risk from malaria since symptoms can be especially severe and can develop rapidly. Symptoms may differ from those in adults and, as children often have febrile illnesses, malaria could not be suspected.¹

For these reasons, we studied all pediatric patients with malaria hospitalized at Santos Anibal Dominicci Hospital, Sucre, Venezuela over a period of 3 years, with the objective to determine clinical features and complications, such as anemia and thrombocytopenia, of malaria due to *P. vivax* in pediatric patients (<12-year-old) which required hospitalization.

Materials and Methods
All pediatric patients (<12-year-old) diagnosed with malaria who required hospitalization, between January 2000 and December 2002, were evaluated and included in this study. All patients in this endemic malaria with fever are suspected to have malaria, due to *P. vivax* given this is the unique species in this zone, and therefore are evaluated and thin and thick blood smears searching for malaria parasites are done. Diagnosis is confirmed with two different external quality control microscopists (one regional and one national). Hematology, blood chemistry and other relevant studies were done in these patients. In the Santos Anibal Dominicci Hospital the criteria for admission of a children with diagnosed malaria is to present with one or more of the following manifestations: anemia, thrombocytopenia, hypoglycemia, acidosis,
hyperlactataemia, renal impairment, jaundice, haemoglobinuria, abnormal bleeding, pulmonary edema, circulatory collapse, respiratory distress, impaired consciousness and prostration. For this study fever was defined as a temperature >37.8°C (in children <3 years old) or >37.4°C (>3 year-old). Anemia was defined as Hemoglobin levels of <12 g/dl (children >6 month-old) or <11 g/dl (<6 months old). Thrombocytopenia was defined as platelet levels <150 000 cells/mm³.

During years 2000 to 2002 a total of 16 810 cases of malaria (99.9 per cent due to P. vivax) were diagnosed in the whole Sucre state, and around 7 per cent (1177) came from the catchment of the hospital.

Differences concerning laboratory data were evaluated using the Fisher exact test and the χ² test. Data were analysed by SPSS for Windows 10.0 and Epi Info v.6.0. All tests were two-sided with differences considered significant at p<0.05.

Results

In the studied period, a total of 78 children with P. vivax malaria infection and criteria for hospitalization were admitted to Hospital Santos Aníbal Dominicci, Sucre, Venezuela.

The mean age of patients was 3.97±3.54 years, being 33.33 per cent prescholars and 32.05 per cent scholars. From total, 52.56 per cent patients were female. Most patients came from the main endemic location for malaria in Sucre state, Yaguaraparo (52.56 per cent).

Clinical manifestations at admission were 93.59 per cent fever, 54.03 per cent chills and 14.10 per cent headache, among others (p<0.05); 63 per cent presented 2–3 clinical manifestations. On para-clinical evaluations 94.87 per cent presented anemia (10.26 per cent severe anemia, Hb<5 g/dl), 25.64 per cent malnutrition and 10.26 per cent intestinal parasitosis (p<0.05).

The mean hemoglobin levels on admission were 8.09±2.65 g/dl and the mean platelet counts 127 402±143 132 cells/mm³. Among these patients 58.97 per cent (46/78) developed thrombocytopenia (including 24.36 per cent with severe thrombocytopenia, <60 000 cells/mm³). There was no difference in the occurrence of anemia and thrombocytopenia in relation to age. Due to severe anemia and thrombocytopenia, transfusion was administered in 25.64 per cent of patients. After antimalarial treatment with chloroquine (25 mg/kg, 10 mg/kg days 1 and 2, 5 mg/kg day 3) and primaquine (>1 month at 3.5 mg/kg, 0.25 mg/kg/day ×14 days) and supportive care all patients were successfully discharged. At outcome, hemoglobin levels increased significantly for a mean of 9.54±1.95 g/dl (p<0.01), as well as for platelet counts 214 583±147 372 cells/mm³ (p<0.01). This group of patients was hospitalized for a mean time of 7.27±4.56 days. No deaths or further complications were seen, except for persistent mild thrombocytopenia in 17.95 per cent of the patients.

Discussion

As stated previously, few studies describe clinical epidemiology of patients with moderate to severe malaria due P. vivax requiring hospitalization, even more in children where most reports correspond to case reports and imported cases series, which are different from those cases seen in P. vivax malaria endemic zones.

Occurrence of anemia and thrombocytopenia in these patients were considerable remarkable, almost 95 per cent and 60 per cent, respectively, which required an appropriate and early management, justifying the hospitalization. These complications are infrequently reported in P. vivax and even more in children and probably are more frequently than reported when are investigated.

Although some authors have indicated the symptoms may differ from those in adults and, as children often have febrile illnesses, malaria may not be suspected, in endemic zones as Sucre is, first suspected diagnosis in a febrile child is malaria. Regard to the occurrence of side effects of antimalarial drugs which has been stated as also different in children, we have no children with these effects receiving treatment with chloroquine and primaquine. An unpublished previous study evaluated the deficiency of G6PD found less than 5 per cent of children with this enzyme defect.

According to World Health Organization, in 2000–2003, six causes accounted for 73 per cent of the 10.6 million yearly deaths in children younger than age 5 years: pneumonia (19 per cent), diarrhoea (18 per cent), malaria (due to P. falciparum) (8 per cent), neonatal pneumonia or sepsis (10 per cent), preterm delivery (10 per cent), and asphyxia at birth (8 per cent). These figures indicate the needs of proper education of people, particularly mothers, on malaria and the presence of health facilities, where treatment is readily available at affordable cost, close to villages, as important strategies that would reduce malaria morbidity and mortality significantly; this is currently being done by the Sucre Regional Office of Malariology. An important issue is to study complications of P. vivax in children, those in WHO report on causes of deaths due to malaria are due to P. falciparum but there is not accurate information about severe disease and possible deaths related to P. vivax infection.
References