

## Hemoglobin level and cardiothoracic ratio in children with chronic severe anemia

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### Abstract

**Background** Chronic severe anemia is known to increase cardiac output when the hemoglobin levels are  $\leq 7$  g/dL for more than three months. Chronic severe anemia is also associated with a high incidence of cardiac enlargement and congestive heart failure.

**Objective** To determine the relationship between hemoglobin level and cardiothoracic ratio in children with chronic severe anemia.

**Methods** We conducted a cross-sectional study in Haji Adam Malik Hospital, Medan, Indonesia from October to December 2009. Subjects had chronic severe anemia and were aged 1 to 15 years. Hematological data was collected at the beginning of the study. The heart was considered enlarged if the cardiothoracic ratio (CTR) was greater than 50% (0.50) by chest roentgenogram. We used simple linear regression to analyze the relationship between hemoglobin and CTR values.

**Results** Thirty subjects enrolled in our study. Their mean age was 115.7 months (SD 56.95). Hemoglobin levels ranged from 2.1 to 6.9 g/dL. The mean hemoglobin level and duration of anemia were 4.71 g/dL (SD 1.48) and 3.9 months (SD 0.70), respectively. Heart enlargement was observed in 23 patients (76.6%). The CTR ranged from 0.52 to 0.69, with a mean of 0.54 (SD 0.06). We found a significant correlation between CTR and hemoglobin levels with Pearson's correlation coefficient, ( $r = -0.612$  and  $P = 0.001$ ).

**Conclusion** Low hemoglobin levels significantly correlated with high CTR values in children with chronic severe anemia. [Paediatr Indones. 2011;51:262-5].

**Keywords:** severe anemia, cardiac enlargement, cardiothoracic ratio

Anemia is a global public health problem affecting both developing and developed countries with major consequences for human health.<sup>1</sup> Anemia, depending on its severity, can affect myocardial function.<sup>2</sup> Severe anemia is associated with a high incidence of cardiac enlargement and may result in congestive heart failure.<sup>3,4</sup>

Chronic severe anemia is known to increase cardiac output when hemoglobin levels drop to  $\leq 7$  g/dL for three months or more duration.<sup>5</sup> Cardiac enlargement in patients with chronic severe anemia has been reported in necropsy studies. Roentgenogram studies have also shown cardiac enlargement that disappeared with correction of the anemia. In addition, cardiac enlargement has been attributed to dilatation or hypertrophy.<sup>3</sup>

Chest roentgenogram is routinely used to assess the presence cardiac enlargement. The aim of our study was to determine the relationship between

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## Methods

We conducted a cross-sectional study in Haji Adam Malik Hospital, Medan, Indonesia from October to December 2009. We recruited 30 participants aged 1 to 15 years with chronic severe anemia by consecutive sampling. The minimum number of subjects required was 29. Hematologic data was collected at the beginning of the study. Included subjects had chronic severe anemia with hemoglobin levels of  $\leq 7$  g/dL for at least for three months. Informed consent was obtained from parents or guardians. We excluded patients with acute hemorrhage, congenital or acquired heart disease, and those receiving regular transfusions. This study was approved by the Medical Ethics Committee, University of North Sumatera Medical School.

Subjects underwent interviews and physical examinations to assess their health histories. Height, body weight and blood pressure were measured by using a 2M stature meter, Camry® scales and a Riester® sphygmomanometer, respectively. We obtained demographic and hematologic data including age, duration of anemia and hemoglobin level. Duration of anemia was defined as the time from estimated onset of anemia (obtained from parental history-taking) to the time of enrollment in our study. The diagnosis of anemia was made by clinical assessment and hemoglobin levels were estimated by cyanmethemoglobin method. Cutoff for diagnosing severe anemia was hemoglobin level  $\leq 7$  g/dL. Chronic severe anemia was defined as suffering from anemia for three months or more.

Routine blood assessment was done by Sismex Hitachi 2009. CTR measurement is a simple way to estimate heart size in children. Chest roentgenograms were taken on admission in posteroanterior position with Siemens chest roentgenogram machine. The heart was considered enlarged if the CTR was  $> 50\%$  (0.50). CTR was obtained by comparing the largest transverse diameter of the heart to the widest internal diameter of the chest.<sup>5-7</sup> CTR was calculated by radiologic clinician, blinded to the subjects' hemoglobin levels.

Data was analyzed with SPSS version 14.0. Statistical significance was accepted as  $P < 0.05$ , with 95% confidence interval (95% CI). Means, SDs of age and anthropometric variables were analyzed. Pearson's correlation coefficient was used to determine the relationship between hemoglobin level and CTR in subjects with chronic severe anemia.

## Results

Of the 30 subjects enrolled, there were 15 males and 15 females. Subjects' characteristics are shown in **Table 1**.

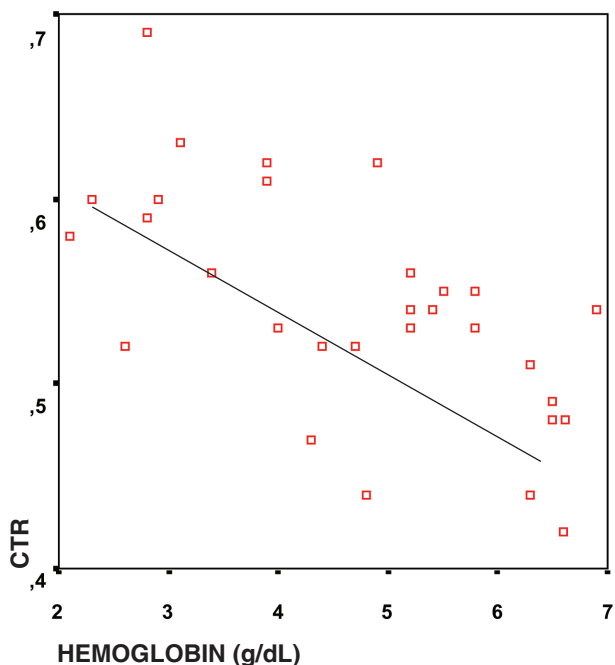
The mean age of the subjects was 115.7 months. Hemoglobin levels ranged from 2.1 to 6.9 g/dL. We observed 23 subjects had tachycardia, with an overall mean heart rate of 122.5 beats/minute. In addition, we found cardiac enlargement in 23 patients (76.7%). The incidence of cardiac enlargement was nearly equal in males and females. The CTRs in patients with cardiac enlargement ranged from 0.52 to 0.69, with a mean of 0.54 for all subjects.

We evaluated the relationship between hemoglobin level and CTR with Pearson's correlation coefficient. There was a significant, inverse correlation between hemoglobin levels and CTR,  $r = -0.612$  and  $P = 0.001$ . (**Figure 1**) The lower the hemoglobin values, the higher the CTR, and vice versa.

We obtained a simple equation for this relationship, namely  $Y = 0.66 - 0.03(\text{Hb})$ . Based on the line equation, Y represents CTR. This equation may be used to predict CTR in chronic severe anemia pediatric patients, once the hemoglobin level is available.

**Table 1.** Subjects' characteristics

Characteristics	Mean (SD)
Gender, n (%)	
Male	15 (50%)
Female	15 (50%)
Age, months	115.7 (56.95)
Weight, kg	24.1 (11.65)
Height, cm	125.6 (27.37)
Systolic blood pressure, mmHg	106.2 (13.88)
Diastolic blood pressure, mmHg	66.9 (10.5)
Heart rate, beats per min	122.5 (15.01)
Respiratory rate, times per min	32.5 (5.85)
Hemoglobin, g/dL	4.7 (1.48)
Duration of anemia, months	3.9 (0.70)
Cardiothoracic ratio	0.54 (0.06)



**Figure 1.** The relationship between Hb level and CTR in chronic severe anemia

## Discussion

In this cross-sectional study of children with chronic severe anemia aged 1 to 15 years, we found that hemoglobin level had a significant, inverse relationship with CTR. The mean age of our subjects was 115.7 months, with the youngest aged 12 months and the oldest aged 178 months. Cardiac enlargement incidence did not differ between boys and girls. Three months or more duration of anemia was used to define chronic anemia, with a mean duration of 3.9 months. Anemia duration ranged from three months to one year.

Satou *et al.* evaluated cardiac enlargement in 95 consecutive outpatients by comparing chest radiograph to echocardiography. Their median age of their subjects was 5 years.<sup>8</sup> Brannon *et al.* studied 51 patients with anemia of at least four months duration and hemoglobin values of 1.5 to 6.5 g/dL. 80% of these patients had cardiac enlargement.<sup>9</sup> In contrast, Sanghvi *et al.* found that the incidence of cardiac enlargement had no relation to age, sex, duration, and the etiologic factor of anemia.<sup>3</sup>

We found the mean hemoglobin level to be 4.7 g/dL and majority of participants (23 children) had cardiac enlargement with a mean CTR of 0.54 for all subjects. Generally anemia was due to malnutrition and iron deficiency. Although some studies report anemia as a common condition, it is also associated with chronic infection in children.<sup>10,11</sup> The prevalence of anemia in preschool-aged children in Indonesia, according to World Health Organization (WHO) from 1993 to 2005, was 44.4%.<sup>1</sup> In Indonesia, anemia generally occurs due to lack of nutrients, especially iron. A household survey in 2001 reported the prevalence of iron deficiency anemia in Indonesia as 48.1% in infants. Therefore, about half the Indonesian infant population had anemia, mainly due to iron deficiency.<sup>12</sup> Cardiovascular adjustments in chronic severe anemia have been the subject of several studies.<sup>13</sup>

Our results were in agreement with previous reports on the hemodynamic consequences of chronic severe anemia showing that cardiac output increases when hemoglobin levels fall below 7 g/dL.<sup>14-18</sup> These subjects have tachycardic values in their resting heart rates. These findings can be explained based on hemodynamic mechanisms. Chronic severe anemia increases cardiac output because hypoxia stimulates chemoreceptors and increases sympathetic activity to fulfill the oxygen demand and perfusion of vital organs.<sup>13</sup>

We found systolic blood pressure (SBP) and diastolic blood pressure (DBP) ranged from 80 to 140 mmHg and from 50 to 90 mmHg, respectively. The average pressure was 107.3/68.3 mmHg. According to age-specific percentiles of SBP and DBP in boys and girls, these values were slightly high (between P<sub>50-75</sub>).<sup>19</sup> Hemodynamic compensation in chronic severe anemia may be activated to maintain blood pressure in order to provide adequate perfusion to vital organs.

Clinicians have shown that increased heart size (assessed by x-ray measurement) can decrease with resolution of anemia.<sup>14,20</sup> The return to normal size may occur within a few weeks.<sup>14</sup> Other studies have also shown definite cardiac enlargement during anemia, and a return to normal size following appropriate treatment.<sup>18,20</sup> Furthermore, children with hemoglobin levels of less than 6 g/dL due to iron deficiency had significantly higher cardiac indices.<sup>6,21</sup>

We found a significant, inverse relationship between hemoglobin level and CTR in chronic severe anemia patients. Our results indicated that lower hemoglobin values correlated to higher CTR. However, we did not monitor heart size after treatment of anemia. Based on the line equation,  $Y = 0.66 - 0.03$  (hemoglobin), with Y representing CTR, we can predict CTR in chronic severe anemia, once the hemoglobin level is available. Low hemoglobin level is associated with greater alteration in CTR.

Children with congenital or acquired heart disease were not included in this study due to the cardiac disease effect on CTR values in chest radiographs. To better assess risk factors that may affect the hemoglobin concentration and CTR, univariate and multivariate analyses are needed. Our use of only simple linear regression test and Pearson's correlation is a limitation of this study. We attempted to avoid research bias by other risk factors in our exclusion criteria. Other limitations were the small sample size and the inaccurate determination of duration of anemia, since the latter obtained by history-taking.

In conclusion, we found a significant, inverse relationship between hemoglobin levels and CTR in pediatric patients with chronic severe anemia. Further research is needed to examine other factors affecting this correlation.

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