

Correlation Between Hemoglobin Levels, Hematocrit with Serum Erythropoietin in Erythrocytosis Patients

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ABSTRACT

Background: Erythrocytosis is a condition where hemoglobin and hematocrit levels increase, in men (>16.5 g/dL; $>49\%$) and women (>16.0 g/dL; $>48\%$). Erythrocytosis results from an absolute increase in erythrocyte mass (absolute erythrocytosis/polycythemia), either primary or secondary, and as a result of a decrease in plasma volume (relative erythrocytosis). The prevalence of primary erythrocytosis in America is approximately 44 per 100,000 people. The incidence is most common in men, young adults to old age. The prevalence of secondary erythrocytosis is difficult to estimate and is much higher but data are limited and the causes are diverse. The condition of erythrocytosis is at risk of vascular complications and thrombosis. The diagnosis of polycythemia in erythrocytosis patients requires a confirmatory examination of the JAK2 V617F mutation which is expensive and laboratories rarely carry it out, so an alternative erythropoietin examination is needed to differentiate primary or secondary erythrocytosis. **Objective:** This study aims to analyze the correlation between hemoglobin levels, hematocrit and serum erythropoietin in erythrocytosis patients. **Method:** This research is an observational study-cross sectional, with measurements of serum hemoglobin, hematocrit and erythropoietin levels in erythrocytosis patients taken by simple random sampling, in Dr Darsono Hospital, Pacitan Regency. Statistical analysis used the SPSS program with the Pearson correlation test. **Result:** The number of samples was: 56 samples, with characteristics: 89% men and an average age of 46 years. Average hemoglobin level: 17.3 mg/dL, hematocrit: 50.3% and average erythropoietin: 0.67 mIU/mL (reference value: 2.9-5.0 mIU/mL), lowest level 0.01 mIU/mL and highest 4.62 mIU/mL. The results of the correlation analysis found that there was an insignificant correlation between hemoglobin levels and serum erythropoietin ($r= 0.165$ and $p= 0.256$). There was a non-significant correlation between hematocrit and serum erythropoietin ($r= 0.115$ and $p= 0.431$). **Discussion:** There were low mean erythropoietin levels in the erythrocytosis patients in this study. There was an insignificant correlation between hemoglobin levels, hematocrit and serum erythropoietin in erythrocytosis patients. **Conclusion:** Serum erythropoietin examination is needed to screen for primary and secondary causes of erythrocytosis, before carrying out further examination with the JAK2 V617F mutation as confirmation of primary erythrocytosis (polycythemia vera).

Keywords: Erythrocytosis, hemoglobin levels, hematocrit, serum erythropoietin.

INTRODUCTION

Erythrocytosis is a condition of increased hemoglobin and hematocrit levels, in men (>16.5 g/dL; $>49\%$) and women (>16.0 g/dL; $>48\%$).¹ Erythrocytosis is caused by an absolute increase in erythrocyte mass (erythrocytosis absolute/polycythemia), either primary or secondary, and as a result of a decrease in plasma volume (relative erythrocytosis).²

The prevalence of primary erythrocytosis in America is around 44 per 100,000 people.¹ The incidence is most common in men, young adults to old age. The prevalence of secondary erythrocytosis is difficult to estimate and is much higher but the data are limited and the causes are varied.^{1,2} The condition of erythrocytosis is at risk of vascular complications and thrombosis.³

Diagnosis of polycythemia in erythrocytosis patients requires confirmation of the JAK2 V617F mutation. It is still rare for laboratories to do this, so an alternative erythropoietin test is needed to differentiate primary or secondary erythrocytosis.

This study aims to analyze the correlation between hemoglobin levels, hematocrit and serum erythropoietin in erythrocytosis patients.

METHODS

This research is an observational study-cross sectional, with measurements of hemoglobin, hematocrit and serum erythropoietin levels in erythrocytosis patients at Dr Darsono Regional Hospital, Pacitan Regency, taken using simple random sampling. Statistical analysis used the SPSS program with the Pearson correlation test.

RESULTS

The number of samples was: 56 samples, with characteristics: 89% male and average age 46 years. Average hemoglobin level: 17.3 mg/dL, hematocrit: 50.3% and average erythropoietin: 0.67 mIU/mL (reference value: 2.9-5.0 mIU/mL), lowest level 0.01 mIU/mL and highest 4.62 mIU/mL.

Tabel 1: Average Hemoglobin Level

Parameter	N	Minimum	Maximum	Mean	Std. Deviation
Hemoglobin Level (Hb)	56	16.6	22.8	17.313	1.2879

Tabel 2: Average Hematocrit

Parameter	N	Minimum	Maximum	Mean	Std. Deviation
Hematocrit (Hct)	56	35.0	71.0	50.302	5.3481

Tabel 3: Serum Erythropoietin

Parameter	N	Minimum	Maximum	Mean	Std. Deviation
Serum Erythropoietin	49	.01	4.62	.6716	.76328

Tabel 4: Correlation between Hemoglobin Levels and Serum Erythropoietin

Correlation		Hemoglobin Level (Hb)	Serum Erythropoietin
Hemoglobin Level (Hb)	Pearson Correlation	1	.165
	Sig. (2-tailed)		.256
	N	56	49
Serum Erythropoietin	Pearson Correlation	.165	1
	Sig. (2-tailed)	.256	
	N	49	49

Tabel 5: Correlation between Hematocrit and Serum Erythropoietin

Correlation		Hematocrit (Hct)	Serum Erythropoietin
Hematocrit (Hct)	Pearson Correlation	1	.115
	Sig. (2-tailed)		.431
	N	56	49
Serum Erythropoietin	Pearson Correlation	.115	1
	Sig. (2-tailed)	.431	
	N	49	49

The results of the correlation analysis found that there was an insignificant correlation between hemoglobin levels and serum erythropoietin ($r = 0.165$ and $p = 0.256$). There was a non-significant correlation between hematocrit and serum erythropoietin ($r = 0.115$ and $p = 0.431$).

DISCUSSION

The sample for this study was: 56 samples of erythrocytosis patients, with characteristics: 89% male and average age 46 years. The dominant gender of men is in line with previous research conducted by Geyer HL et al.⁶

This study found that the average hemoglobin level: 17.3 mg/dL, hematocrit: 50.3%. Examination of hemoglobin and hematocrit levels increases currently as markers that are widely used for the diagnosis of erythrocytosis. This is because erythrocyte mass examination is rarely done and requires the radioactive substance Chromium-51 reagent which is difficult to obtain.⁷

Erythrocyte production is controlled by the hormone erythropoietin. Serum erythropoietin examination provides information on potential causes of erythrocytosis and helps direct further examination. Serum erythropoietin levels are generally high in erythrocytosis secondary to hypoxic conditions, whereas serum erythropoietin levels are typically low in PV.⁹ This study found that there was a low mean serum erythropoietin level, namely 0.67 mIU/mL (reference value: 2.9-5.0 mIU/mL). Serum erythropoietin levels in patients with primary erythrocytosis are low. 7 Diagnosis of PV using alternative serum erythropoietin tests is very necessary, because the JAK2 V617F mutation test is expensive and laboratories can rarely do it. The WHO 2016 diagnostic criteria for Polycythemia vera (PV) states there are three major criteria, namely: hemoglobin and hematocrit levels, in men (>16.5 g/dL; $>49\%$) and women (>16.0 g/dL; $>48\%$), a picture of hypercellular bone marrow, and the presence of the JAK2 V617F or JAK2 exon 12 mutation. And there is one minor criterion, namely low serum erythropoietin. The diagnosis of PV can be made if 3 major criteria or 2 major criteria plus 1 minor criterion are found.⁷

Diagnosis using serum erythropoietin had been established in previous studies before the discovery of the JAK2 V617F mutation, which showed that low erythropoietin levels were specific for PV.⁷

Correlation between Hemoglobin and Hematocrit Levels with Serum Erythropoietin

This study found that there was an insignificant correlation between hemoglobin levels, hematocrit and serum erythropoietin in erythrocytosis patients. Previous studies reported that the diagnostic performance of serum erythropoietin was comparable to the JAK2 V617F mutation.⁷ The study was conducted on 1090 patients with suspected PV who were referred for erythrocyte mass examination. In patients with high hemoglobin and hematocrit levels, low serum erythropoietin levels and the JAK2 V617F mutation were found. This is demonstrated by comparable positive predictive value, true polycythemia for erythrocyte mass $\geq 125\%$, serum erythropoietin 92.1%, and JAK2 V617F mutation 90%.⁷

Serum Erythropoietin Examination to Screen for Primary and Secondary Causes of Erythrocytosis

Serum erythropoietin examination is needed to screen for primary and secondary causes of erythrocytosis.⁴ In patients with high hemoglobin and hematocrit levels, examination of low serum erythropoietin levels is a true diagnostic modality for polycythemia which has the same efficiency as the JAK2 V617F mutation.⁷ Other studies report that the PV diagnostic method uses mutase. JAK2 V617F is better than serum erythropoietin assay. A serum erythropoietin level < 2 mIU/mL in predicting PV has a specificity of $> 99\%$ and a sensitivity of only 12%.⁸

CONCLUSION

Serum erythropoietin examination is needed to screen for causes of primary and secondary erythrocytosis, before further examination is carried out with the JAK2 V617F mutation as confirmation of primary erythrocytosis or polycythemia vera.

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