

## HEMATOKRİTE GÖRE DÜZELTİLMİŞ ERİTROSİT SEDİMENTASYON HIZI, C-REAKTİF PROTEİN İLE DAHA İYİ BİR KORELASYONA SAHİPTİR

### HEMATOCRIT-ADJUSTED ERYTHROCYTE SEDIMENTATION RATE HAS A BETTER CORRELATION WITH C-REACTIVE PROTEIN

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#### ÖZ

**AMAÇ:** Eritrosit sedimentasyon hızı (ESR) klinik uygulamada yaygın olarak kullanılan bir laboratuvar belirteçidir. ESR, temel olarak iki faktörden etkilenir: fibrinojen gibi plazma proteinleri ve hematokrit gibi eritrositler ile ilişkili bazı durumlar. Hematokritin ESR üzerindeki etkisini ortadan kaldırarak ESR'yi yorumlayabilmek için bazı formüller geliştirilmiştir. Bu çalışmanın amacı, hematokrite göre düzeltilmiş ESR formüllerinin C-reaktif protein (CRP) ile daha iyi bir korelasyonunun olup olmadığını belirlemektir.

**GEREÇ VE YÖNTEM:** Hastanemiz veri tabanından Şubat 2018'e ait veriler alındı. Aynı anda elde edilen kan örneklerinde ölçülen ESR, CRP ve hematokrit değerlerine ait toplam 1206 hastanın sonuçları, bu parametreler arasında bir korelasyon olup olmadığı açısından analiz edildi. Hematokrite göre düzeltilmiş ESR değerleri, aşağıdaki formüllerle hesaplandı: (a) Hematokrite göre düzeltilmiş sedimentasyon-1 (HA-ESR-1) =  $[(15)/(55-\text{hematokrit})] \times \text{sedimentasyon}$ , (b) Hematokrite göre düzeltilmiş sedimentasyon-2 (HA-ESR-2) =  $(\text{hematokrit}/45) \times \text{sedimentasyon}$ .

**BULGULAR:** HA-ESR-2 standart ESR ölçümlerine kıyasla CRP ile daha iyi bir korelasyona sahipti, ancak HA-ESR-1, CRP ve ESR arasındaki ilişkiyi iyileştiremedi.

**SONUÇ:** HA-ESR-2'nin CRP ile standart ESR'den anlamlı olarak daha iyi bir korelasyon gösterdiğini bulduk. Bu nedenle, söz konusu formül klinik uygulamada yararlı olabilir.

**ANAHTAR KELİMELER:** Eritrosit sedimentasyon hızı; hematokrit; C-Reaktif protein

#### ABSTRACT

**OBJECTIVE:** Erythrocyte sedimentation rate (ESR) is a laboratory marker widely used in clinical practice. It is affected primarily by two factors following: plasma proteins such as fibrinogen and some conditions associated with the erythrocytes such as hematocrit. Some formulas have been developed so as to interpret the ESR by eliminating the effect on the ESR of the hematocrit. The purpose of our research was to determine whether the formulas for ESR adjusted with hematocrit levels have a better correlation with C-reactive protein (CRP).

**MATERIAL AND METHODS:** The data belong to February 2018 were obtained from database of our hospital. A total of 1206 patients' results including ESR, CRP, and hematocrit, which had been measured in blood samples simultaneously obtained, were analyzed in terms of whether there is a correlation between these parameters. Hematocrit-adjusted ESR values were calculated by formulas following: (a) Hematocrit-adjusted sedimentation-1 (HA-ESR-1) =  $[(15)/(55-\text{hematocrit})] \times \text{sedimentation}$ , (b) Hematocrit-adjusted sedimentation-2 (HA-ESR-2) =  $(\text{hematocrit}/45) \times \text{sedimentation}$ .

**RESULTS:** While HA-ESR-2 had a better correlation with CRP compared to standard ESR measurements, HA-ESR-1 didn't make good the association between CRP and ESR.

**CONCLUSIONS:** We found that HA-ESR-2 has significantly a better correlation with CRP than that of standard ESR. Therefore, this formula may be useful in clinical practice.

**KEYWORDS:** Erythrocyte sedimentation rate; hematocrit; C-Reactive protein

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## INTRODUCTION

Erythrocyte sedimentation rate (ESR) is a laboratory marker widely used in clinical practice in order to support a suspected diagnosis and to predict the course and severity of the diseases such as inflammatory conditions, infections, and malignancies, even psychiatric disorders (1-3). It is affected mainly by two factors: (a) plasma proteins such as fibrinogen and immunoglobulins and (b) conditions associated with quality and quantity of the erythrocytes (4). Although the hematocrit levels have an enormous effect on the ESR values (5), this interference is usually disregarded by the health care providers.

Some researchers have suggested a couple of formulas for ESR adjusted with hematocrit levels (5,6), however, none of which have gained wide validity. It has been shown that there are various common triggers (e.g. IL-6) that stimulate the synthesis and release of both C-reactive protein (CRP) and fibrinogen in hepatocytes (7).

Thus, it can be seen that there is a correlation between CRP and ESR levels in most instances (8, 9), even though the consistency is not complete at all times (1). The aim of this study was to determine whether the formulas for ESR adjusted with hematocrit levels have a better correlation with CRP.

## MATERIALS AND METHODS

The data belong to February 2018 were obtained from the database of our hospital. A total of 1206 patients' results including ESR, CRP, and hematocrit, which had been measured in blood samples simultaneously obtained, were analyzed in terms of whether there is a correlation between these parameters.

ESR, CRP, and hematocrit had been measured by SDM-100 (Berkhun, Turkey), Cobas c501 (Roche, Germany), and ABX Pentra DX 120 (Horiba, Japan), respectively.

Hematocrit-adjusted ESR values were calculated by formulas following: (a) Hematocrit-adjusted Sedimentation= $[(15)/(55-\text{hematocrit})] \times$  sedimentation (5), which works in the range of 10 to 50 for hematocrit, and thus the results of patients with hematocrit values over 50% were

not included in the this study (b) Adjusted sedimentation= $(\text{hematocrit}/45) \times$  sedimentation (6). In the rest of the article, we will name the first of these as HA-ESR-1 and the second as HA-ESR-2.

HA-ESR-1= $[(15)/(55-\text{hematocrit})] \times$  sedimentation

HA-ESR-2= $(\text{hematocrit}/45) \times$  sedimentation

## ETHICS COMMITTEE

The study was approved ethically by the Local Ethics Committee of our university (27.02.2019/10).

## ISTATISTICAL ANALYSIS

Spearman test was used to evaluate whether there is a correlation between ESR, HA-ESR-1, HA-ESR-2, CRP, and hematocrit. Whether there is a difference between the correlations was evaluated by Hotelling's t-test using the FZT Computator software. This test was performed on the purpose of comparison of correlations from dependent samples used correlations of two predictors both with the variable and with each other.

## RESULTS

ESR, CRP, and hematocrit values were in between 1 and 137 mm/hours; 0 and 40.43 mg/dL; and 18.4% and 49.9%, respectively. The ages of the patients varied from 2 to 94. Correlations between ESRs (measured ESR, HA-ESR-1, and HA-ESR-2) and other parameters (CRP and hematocrit) were as in Table 1. HA-ESR-2 had a better correlation with CRP compared to standard ESR measurements, however, HA-ESR-1 didn't make good the association between CRP and ESR (**Table 1**).

**Table 1:** Correlations between ESRs and other parameters.

	CRP	Hematocrit
ESR	$r_1=0.551$ $p=0.000$	$r=-0.452$ $p=0.000$
HA-ESR-1	$r_2=0.541^a$ $p=0.000$	$r=-0.020$ $p=0.479$
HA-ESR-2	$r_3=0.559^b$ $p=0.000$	$r=-0.340$ $p=0.000$
	$z=0.860, p>0.05$ $\chi^2=2.489, p<0.05$	

ESR: Erythrocyte sedimentation rate; HA-ESR-1: Hematocrit-adjusted erythrocyte sedimentation rate-1; HA-ESR-2: Hematocrit-adjusted erythrocyte sedimentation rate-2; CRP: C-reactive protein.

<sup>a</sup>difference between  $r_1$  and  $r_2$  values (for  $n=1206$  and correlation between ESR and HA-ESR-1=0.881).

<sup>b</sup>difference between  $r_1$  and  $r_3$  values (for  $n=1206$  and correlation between ESR and HA-ESR-2=0.991).

## DISCUSSION

Erythrocytes have a negative charge due to the carboxylate groups of the N-acetyl neuraminic acids on the surfaces of their membranes (10).

The negative charge forms a repulsive force called zeta potential (10). Positively charged plasma proteins such as fibrinogen and immunoglobulins increase ESR by disrupting the repulsive effect (11). The sedimentation occurs at three steps following: (a) rouleau formation, (b) sphere formation with uniform size, and (c) the falling down (5). As hematocrit increases, ESR decreases because the radius of the spheres reduces (5). Some charts (Gram, Rourke and Ernstene, Wintrobe and Landsberg, etc.) and formulas have been developed in order to interpret the ESR results by eliminating this effect on the sedimentation rate of the hematocrit (5, 6, 12-14). Although these have been practiced in several scientific researches and it has been reported that they may be useful in the monitoring of many diseases, adjusted/corrected formulas have not gotten a chance with regard to widespread use in clinical practice (15-18).

In recent years, researches have increased to find new inflammatory markers (19-21), but the candidates are inefficient in terms of cost, applicability, and practicality, none of which has become widespread in the hospital or clinical laboratory setting. Also, there is an endeavor to develop better ones through a number of calculations by using formerly known markers (22-24). Even though ESR is an inexpensive, simple, and easily feasible test, it is seen as more cumbersome and disadvantageous compared to the others because of that it is affected by many factors unrelated to inflammation status (25).

There are two main factors that affect ESR: factors associated with the inflammation (e.g. fibrinogen and immunoglobulins) and characteristics relating to erythrocytes, mainly hematocrit (4, 5). So, eliminating the effect of hematocrit on ESR can make this simple and inexpensive test more purposive and handy.

We found that the HA-ESR-2 formula has a better correlation with CRP than that of standard ESR measurement. Thus, we speculate that using HA-ESR-2 to adjust the sedimentation may be useful in clinical practice.

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