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CORRELATION BETWEEN ERITHROCYTES SEDIMENTATION RATE AND HIGH SENSITIVITY C-REACTIVE PROTEIN LEVELS IN PATIENTS WITH CORONARY HEART DISEASE

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Abstract

Coronary Heart Disease (CHD) is one of the diseases that currently threatens public health. One of the biggest triggers for CHD is atherosclerosis or narrowing of the arteries which begins with an inflammatory process. Erythrocyte Sedimentation Rate (ESR) and high sensitivity C-reactive Protein (hs-CRP) are acute phase proteins that will appear when an inflammatory process occurs. This study aims to assess the correlation between ESR and hs-CRP as a marker of inflammation in a total of 30 samples CHD patients. The research method used was laboratory observation with a cross sectional design. The results of the normality test using shapiro-wilk show a value of p>0.05, which means that the data is normally distributed. The average ESR value was 14.25 mm/hour in the male gender category and 26.45 mm/hour in the female gender category. The results of the Spearman-rho correlation test showed that there was a moderate correlation between LED and Hs-CRP (r=0.564). The conclusion of this study is that there is a correlation between ESR and Hs-CRP values in CHD patients. The conclusion of this study is that there is a correlation between ESR and Hs-CRP values in CHD patients.

Keywords*: Erythrocyte Sedimentation Rate, High Sensitivity C-reactive Protein, Coronary Heart Disease*

1. Introduction

Coronary Heart Disease (CHD) is a disease that is now threatening many people's health and is the main and most feared cause of death. The American Heart Association estimates the prevalence of CHD in 2014 to be approximately 13,200,000 in the United States. Worldwide there are 50 million deaths each year due to CHD, 39 million of which are in developing countries (1). In 2018, the World Health Organization estimated that 3.8 million men and 3.4 million women worldwide die each year from CHD (2).

Coronary heart disease is a type of heart disease caused by the process of atherosclerosis. Recent studies have shown that inflammation plays an important role in the development and progression of CHD and other manifestations of atherosclerosis (3). Atherosclerotic vascular disease is a multiple inflammation involving cells, molecules and various substances (4). Atherosclerosis as the main cause of CHD is an inflammatory disease in which immune system mechanisms interact with metabolic risk factors such as obesity, diabetes mellitus, hypertension to initiate, progress and activate lesions in the heart arteries (5).

Erythrocyte sedimentation rate (ESR) is a common inflammatory marker. ESR, also called erythrocyte sedimentation rate (ESR) or *bezinking-snelheid der erythrocyten* (BSE), is the rate at which erythrocyte cells settle in a tube containing anticoagulant blood within one hour (6). The use of ESR as a biomarker for atherosclerosis and coronary heart disease has several advantages, namely that it can be done in first-level health facilities, the procedure is easy and cheap, and can be done as a point of care examination and still has important clinical significance (7). CHD begins with a chronic inflammatory process in the blood vessels, so ESR is a practical parameter used as a screening test for inflammatory markers. Someone with a low ESR has better risk factors for heart attack than someone with a high ESR value, (7.8).

The ESR value is a strong predictor of death from coronary heart disease and can be used as a marker for the course of aggressive heart disease. Research conducted by Fitria et al (2017) reported that the ESR value had clinical significance in coronary artery disease (p=0.001) (9). Another study conducted by Dewi et al (2019) reported that there was a correlation between ESR and the clinical outcomes of acute ischemic stroke sufferers at Sanglah General Hospital (r=0.382) (10). However, because ESR is a general inflammatory biomarker, a more specific and sensitive inflammatory biomarker such as C-reactive protein is needed.

C-reactive protein (CRP) is a prototypical acute phase protein that is synthesized in the liver and secreted by stimulation of interleukin 6 (IL-6) and other proinflammatory cytokines. CRP consists of a 23 kDA subunit which is a pentraxin derivative which plays an important role in the natural immune response. CRP has a long half-life in plasma and is known to be a mediator and marker of atherothrombotic disease (11).

High sensitive CRP (hs-CRP) is CRP with a high level of sensitivity which has prognostic value in patients with acute coronary syndrome, so hs-CRP is used as a primary prevention biomarker (12). Hs-CRP is not only a marker of chronic systemic inflammation, but is also directly involved in the atherosclerosis process because hs-CRP can amplify anti-inflammatory responses

through complement activation, tissue damage and endothelial cell activation, as well as causing component changes in blood vessel wall morphology (13). Research conducted by Horas W (2017) concluded that hs-CRP had an independent and significant effect on the severity of coronary lesions (p=0.02; OR=0.25) (14). Another similar study was reported by Itami et al (2020) who reported that there was a moderate positive relationship between NLR and hs-CRP in non-hemorrhagic stroke patients (r= 0.449; p=0.008) (15).

As previously explained, theoretically ESR and hs-CRP are biomarkers that can be used clinically for early diagnosis of CHD, for this reason the aim of this study is to assess how much correlation ESR has as a general inflammatory biomarker and hs-CRP as a more advanced inflammatory biomarker sensitive to CHD sufferers.

2. Research Methods

This type of research is laboratory observation with a cross sectional research design to determine the correlation between Erythrocyte Sedimentation Rate (ESR) and High sensitivity C-Reactive Protein (hs-CRP) in people with Coronary Heart Disease (CHD), was carried out in June-September 2022 at the Makassar City Regional Hospital. This research received ethical approval from the Health Research Ethics Commission (KEPK) Hasanuddin University Faculty of Medical-UNHAS (RSPTN UH) with ethical number 596/UN4.6.4.5.31/PP36/2022.

The number of samples used in this study was 30 samples of CHD sufferers obtained using the purposive sampling method in accordance with the inclusion criteria including; CHD sufferers who have been clinically diagnosed by a doctor, male and female, aged > 25 years, not having a fever, and willing to take part in the research. We excluded samples that the laboratory technically interfered with the examination results, including serum samples that were hemolyzed, lipemic and icteric.

Erythrocyte Sedimentation Rate Measurement

The sample used in the ESR measurement is EDTA plasma. The method used in the ESR measurement is the Westergren method. The 0.9% NaCl solution was pipetted to the 200 mm scale line on a Westergreen pipette, added with EDTA blood to the 0 mm scale line (ratio 4:1). The pipette is placed perpendicular to the Westergren rack and the LED height reading results are obtained after 1 hour. ESR reference values (men: 0-10 mm/hour, women: 0-20 mm/hour) (16).

High sensitivity C-Reactive Protein Measurement

The sample used in the hs-CRP examination is serum. The method used is immunoturbidimetry with the principle that the hs-CRP protein in the serum sample will

agglutinate with latex particles coated with monoclonal anti-hs-CRP antibodies. The agglutination precipitate formed was measured turbidimetrically. Interpretation of hs-CRP results is categorized as follows; <1.0 mg/L: low heart disease risk level, 1.0 -3.0 mg/L: moderate heart disease risk level, > 3.0 mg/L: high heart disease risk level (17).

3. Results and Discussions

A. Results

Table 1. Subjects characteristics

Characteristics	Frequency (n)	Percentage (%)
Age (years)		
20 - 30	2	7
31 - 40	6	20
41 - 50	10	33
>50	12	40
Total	30	100
Sex		
Male	18	60
Female	12	40
Total	30	100

Table 1 shows the characteristics of the research subjects. The age category is dominated by the >50 year age group at 40%, followed by the 41-50 year age group at 33%, the 31-40 year age group at 20% and the 20-30 year age group at 7%. The male gender category is 60% and female is 40%.

Table 2. Mean ESR and hs-CRP Values in CHD Patients

Variables	Mean
ESR (mm/hour)	
Male (0-10)	14.25
Female (0-20)	26.45
hs-CRP (mg/L)	0.91

Based on table 2, the average ESR value based on male gender is 14.25 mm/hour and female is 26.45 mm/hour. The mean hs-CRP level was 0.91 mg/L. According to the reference values previously explained, the ESR value has increased from the normal value while the average hs-CRP is still in the normal category (<1.0 mg/L).

Table 3. Correlation Test of ESR and hs-CRP in CHD Patients

		hs-CRP
ESR	R	0.546
	P	0.000
	N	30

Notes: R (correlation coefficient), P (significance values <0.001), N (number of samples).
**Spearman-rho test*

Table 3 shows the results of the correlation test between ESR values and hs-CRP levels in CHD patients. The correlation value shows that there is a moderate correlation between ESR values and hs-CRP levels (r=0.546; p<0.001).

B. Discussions

Erythrocyte sedimentation rate (ESR) and High Sensitivity C-Reactive Protein (hs-CRP) are inflammatory markers that can be used to assess the inflammatory process early (18). Coronary heart disease is caused by atherosclerosis or narrowing of the arteries due to plaque buildup in the intima of endothelial cells which triggers inflammation. All subjects involved in this study did not have a fever so as to minimize a bias results due to inflammation or cross infection. Apart from that, we have also ensured that the subject has no history of infectious disease in the last month.

The research results showed that there was an increase in the average ESR value. Bray C et al (2016) Although in certain conditions there are significant changes, the utilization of ESR and hs-CRP plays an important role in the clinical management of many inflammatory and other conditions (19). The same opinion was expressed by Lapic I, et al (2020) who stated that although there is heterogeneity between studies, ESR and CRP have the same diagnostic accuracy in assessing inflammation, especially in orthopedic conditions (20).

Research conducted by Xie, et al (2016) on 89 CHD subjects showed that serum hs-CRP and ESR levels were significantly higher than the control group ($p \leq 0.001$). Gender also had no effect on these biomarkers. Logistic regression analysis showed that hs-CRP and ESR were significantly associated with CHD cases ($p \leq 0.05$) (21). In cases of CHD accompanied by ischemic stroke, Menon B & Krishnan R (2018) reported study results that ESR and hs-CRP increased significantly in stroke patients compared to controls. Correlation analysis between patient groups

showed that serum leptin was positively correlated with hs-CRP ($r=0.41$, $p<0.05$), ESR ($r=0.429$, $p<0.01$) (22).

A recent study correlating hs-CRP with the degree of atherosclerosis in the adult population stated that there was a weak association between coronary atherosclerosis (OR 1.15, 95% CI 1.07–1.24), coronary diameter stenosis ≥ 50% (OR 1.27, 95% CI 1.09– 1.47), ≥ 4 segments involved (OR 1.13, 95% CI 1.01–1.26) and severe atherosclerosis (OR 1.33, 95% CI 1.05–1.69) after adjustment for age, sex and traditional risk factors. The association with high-risk noncalcified plaque, although unlikely to occur via a causal pathway, may explain the association between hs-CRP and clinical events that occurred in many studies (23).

4. Conclussions

Based on the results of the research conducted, it can be concluded that there is a correlation between the erythrocyte sedimentation rate value and the level of High Sensitivity C-Reactive Protein (hs-CRP) in sufferers of coronary heart disease with moderate correlation.

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