

## Original Research Article

# High density lipoprotein as prognostic indicator in patient with diabetic foot

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### ABSTRACT

**Background:** Diabetic is a chronic metabolic disease with vascular disorder and HDL (High Density Lipoprotein) is a vascular protector acting agent. One of the most difficult complication of diabetics are diabetic foot with often lead to an amputation due to vascular disorder. Objective of this study aims to determine the relationship of HDL levels with diabetic foot severity by comparing HDL levels in each diabetic foot grade according to the Wagner classification.

**Methods:** This is a cross sectional study, with new inpatient and outpatient with diabetic foot ulcer that never received therapy in Wahidin Sudirohusodo Hospital as a study population in April 2018 to June 2018 time period. Frequency distribution, Spearman's Correlation, Anova, and Chi Square statistical analytic was done with  $p < 0.05$  considered as significant.

**Results:** HDL level was wound highest in Grade I and lowest in Grade IV and V. HDL level comparison according to Wagner comparison shows significant difference,  $p < 0.001$ .

**Conclusions:** There were a negative correlation as an analysis results shows between HDL level and Wagner classification, whereas the lower HDL level, the higher diabetic foot grade and HDL can be used as a prognosis predictor and planning therapy.

**Keywords:** Diabetic foot, High density lipoprotein, Prognostic indicator

### INTRODUCTION

Diabetes melitus is a chronic metabolic disease which characterized with a micro and macro vascular complication with global prevalence about 5-6%. International Diabetes Federation (IDF) has predicting that current patients with diabetic in the world are 285 million and will reach to 438 million at the year of 2030.<sup>1</sup> WHO also reporting that more than 347 million patients in the world suffered for diabetes mellitus.<sup>2</sup> Diabetic foot ulcer is the main factor of non-traumatic amputation, about 85% of the amputation, due to it's complications, infection spreading and gangrene.<sup>1,3</sup> Lower extremities amputation become one of the most feared complication by patients which will take effect to their health and

quality of life.<sup>4</sup> The risk of amputation increasing because of the perifer neuropatic which cause losing of sensibility and capability to identify problems on the foot, lead to foot deformity and ulceration.<sup>5</sup>

HDL has a pleiotropic effects, anti-oxidant and anti-inflammation, which promote cholesterol moving out from cells. Previous reports clearly shown that there was a relation of the low HDL's content in blood and the increasing of chronic complications such as renal disease and cardiovascular disease in diabetic patients. It also has a role in patient immune system, response to infection and sepsis. From the past studies, they compared HDL serum and the degree of the diabetic foot according to Wagner's classification, pre and post therapy with

unevenly samples in each groups.<sup>4</sup> In this study, we examine those samples once before therapy and authors take samples evenly in each group. HDL serum can be a marker for a vascularization disorder which will worsen the diabetic foot so it can be used as predictor for the outcome and the planning therapy.

## METHODS

### Sample

This study using a cross sectional method. All the population are patients with diabetic foot in Dr Wahidin Sudirohusodo general hospital from April until June 2018. Sample was patient with diabetic foot which match the inclusion criteria, all patient with diabetic foot without any treatment before and agreed to joined this study. This exclusion criterias are multiorgan failure, history of malignancy, smoking or history of smoking, severe infection or sepsis, already got treatment, and refuse to join this study. Total sample are 41 patients and all agreed to sign the inform consent.

### The classification of diabetic

The diagnosis of diabetic based on its pathogenesis which lead to hyperglycaemic condition in the vascular. Type 1 diabetic caused by destruction of *beta cells* in pancreas and type II diabetic may variate from insulin resistance, decrease of insulin secretion or hepatic glucose overproduction.<sup>6,7</sup>

### Diabetic foot ulcer classification

Wagner Classification for diabetic foot ulcer:<sup>8,9</sup>

- Grade 0: No ulcer in a high risk foot.
- Grade 1: Superficial ulcer involving the full skin thickness but not underlying tissues.
- Grade 2: Deep ulcer, penetrating down to ligaments and muscle, but no bone involvement or abscess formation.
- Grade 3: Deep ulcer with cellulitis or abscess formation, often with osteomyelitis.
- Grade 4: Localized gangrene
- Grade 5: Extensive gangrene involving the whole foot

### Data analysis

The data analysis using SPSS version 22. Authors perform Spearman's Correlation, Anova and Chi Square statistic analyzing with significant value  $p < 0.05$ .

### Ethical clearance

Ethical approval for this study was obtained from Research Ethics Committee, Faculty of Medicine,

Hasanuddin University, Makassar, Indonesia. Number; 581/H4.8.4.5.31/PP36-KOMETIK/2015.

## RESULTS

Total sample are 41 patients with diabetic foot with age 21 to 79 years old, Mean 57 years old. The HDL serum between 9-52 mg%, Mean 29.41 mg% (Table 1 and 2).

**Table 1: Sample characteristic (n=41).**

Variabel	n	%	
Gender	Man	25	61.0
	Woman	16	39.0
Age	<40 y.o	3	7.3
	40-49 y.o	5	12.2
	50-59 y.o	14	34.1
	60-69 y.o	14	34.1
	>=70 y.o	5	12.2
Wagner Classification	I	8	19.5
	II	9	22.0
	III	8	19.5
	IV	8	19.5
	V	8	19.5
HDL serum	Low	34	82.9
	High	7	17.1

**Table 2: Statistic deskriptif for age and HDL serum (n=41).**

Variables	Minimum	Maximum	Mean	SD
Age	21	79	57.05	12.89
HDL serum	9	52	29.41	12.33

**Table 3: Correlation of HDL serum and Wagner classification (Spearman's Correlation).**

Wagner classification	n	Mean	SD	p
I	8	46.1	4.2	<0.001
II	9	36.4	6.1	
III	8	28.8	2.5	
IV	8	17.2	2.8	
V	8	17.6	9.1	

From the Spearman's Correlation showing a significant negative correlation between HDL serum and Wagner Classification whereas the lower HDL serum followed by higher grade of diabetic foot ( $p < 0.001$ ). The highest HDL serum found in grade I diabetic foot (46.1%) with  $p < 0.001$  and the lowest HDL serum found in grade IV and V diabetic foot (17.2 and 17.6 mg%) (Table 3).

From the Chi Square analysis, HDL serum and Wagner Classification shown a significant correlation ( $p < 0.05$ ) as authors can found the diabetic foot grade III, IV and V (high grade) have a lower HDL serum and the diabetic

foot grade I and II (low grade) have a normal HDL serum (Table 4).

**Table 4: Correlation of HDL serum and Wagner Classification (Chi Square).**

Klasifikasi Wagner		HDL		Total
		Rendah	Normal	
I	n	4	4	8
	%	11.8%	57.1%	19.5%
II	n	6	3	9
	%	17.6%	42.9%	22.0%
II	n	8	0	8
	%	23.5%	0.0%	19.5%
I	n	8	0	8
	%	23.5%	0.0%	19.5%
V	n	8	0	8
	%	23.5%	0.0%	19.5%
V	n	8	0	8
	%	23.5%	0.0%	19.5%
Total	n	34	7	41
	%	100.0%	100.0%	100.0%

Chi Square test (p=0.013)

## DISCUSSION

The result of the study show a significant negative correlation between HDL serum and Wagner classification as authors found lower HDL serum in higher grade of diabetic foot. Diabetic is a metabolic disease characterized with a hyperglycemia due to insulin disorder.<sup>6</sup> Anamnesis was performed include diabetes duration, sign of peripheral vascular disorder, neuropathy, ulceration, history of treatment, and other complications like retinopathy or nephropathy.<sup>8</sup>

Authors perform physical examination including inspection of the foot to find any abnormality like deformity, dry skin, ulcer and also the temperature change of the foot, increasing temperature is a sign of inflammation and decreasing temperature is a sign of ischemic. Capillary refilling time and perifer pulse also important to be examined.<sup>8</sup> Ulcer is the most clinical complication finding in diabetic foot. Patient with diabetic foot ulcer more difficult to cured due to it's neuropathy and vasculopathy. In this study, authors have 51 sample with in 3 months and from it, authors exclude 10 samples due to smoking.

HDL particle consist of 50% apoprotein, 20% cholesterol, 15% phospholipid and 5% triglyceride. It will form a shape of hydrophobic cholesterol molecule. This molecule will take the lipid at surface of vascular endothelial as a protective agent. These molecule will prevent the atherosclerosis.<sup>10</sup>

This sample age between 21 to 79 years old with Mean age 57 years old, authors found the HDL serum level between 9-52mg% with Mean 29.41 mg%. Most of this samples are men (61.0%), range sample age 50-69 years

old (68.2%), most sample are Wagner classification grade II (22.0%) and most sample has low HDL serum (82.9%).

Spearman's Correlation shown a negative significant correlation of HDL serum and Wagner classification where authors found lower HDL serum with higher grade of diabetic foot (p<0.001). The correlation of HDL serum and Wagner classification are significant with p<0.001, as authors found the highest HDL serum found in grade I diabetic foot (46.1 mg%) and the lowest at grade IV, V (17.2 and 17.6 mg%)

Authors perform clinical analysis and authors found significant correlation between HDL serum and Wagner classification (p<0.05) with diabetic foot grade III, IV, V (high grade) has a low HDL serum and sample with diabetic foot grade I and II has a higher HDL serum level

## CONCLUSION

HDL (High Density Lipoprotein) serum has a significant negative correlation with Wagner classification. HDL serum can also be used to value the prognosis and planning therapy in diabetic foot. Authors suggest to do more study with more sample and more duration of study to exclude more variable, so authors can have a better and more precise correlation between HDL serum and the grade of the diabetic foot.

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