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CORONARY SLOW FLOW PHENOMENON AT RSUD SITI FATIMAH: PREVALENCE AND CHARACTERISTICS

Nyimas Afifah Nadhirah Olivia[1] , Yudhie Tanta[2] , Desi Oktariana[3], Erwin Azmar[2], Safyudin[4]

1. Medical Education Study Program, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia
2. Cardiovascular Division, Internal Medicine Department, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia
3. Clinical Pathology Department, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia
4. Biochemistry Department, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia

nanolivia02@gmail.com

ABSTRACT

Coronary Slow Flow Phenomenon (CSFP) is defined as an angiographic findings which shows delayed opacification of contrast in distal coronary vessel in the absence of obstructive coronary artery disease.The occurrence of CSFP are often underrecognized. Research on the prevalence and characteristics of CSFP patients is needed to determine the population at risk and can perfom early detection of CSFP. This observational descriptive study was conducted using secondary data from the medical records of CSFP patients at RSUD Siti Fatimah Palembang for the period of January 2020 - June 2023, with total sampling method. This study found that the prevalence of CSFP cases at RSUD Siti Fatimah was 3.92% with the common age group being 56-65 years (31.57%), and 57.89% of patients were female. CSFP patients have a high BMI and 68.42% suffer from hypertension. All patients (100%) complained of chest pain during exertion. The ECG results of 88.89% of patients showed abnormal results, and slow flow was mostly found in the LAD (94.73%).

Keywords: *Coronary Slow Flow Phenomenon* (CSFP), prevalence, characteristics

1. INTRODUCTION

Coronary Slow Flow Phenomenon (CSFP) is defined as an angiographic finding that shows delayed opacification of contrast in distal coronary vessels without a history of obstructive coronary artery disease, but with delayed blood flow perfusion.[1-3] Previous studies have stated that the prevalence of CSFP cases is 1 - 7% of patients who perform coronary angiograms with complaints of chest pain.[1] The risk factors and pathogenesis of CSFP are still unknown. Coronary Slow Flow Phenomenon is more common in male patients.[4] Coronary slow flow phenomenon is often found in young male patients who smoke and suffer from metabolic syndrome.[1] Based on the previous study, CSFP patients in Iran tend to be obese, hyperlipidemic, suffer from hypertension, and smoke.[5] Previous studies found some possible etiopathogenesis of CSFP, such as endothelial dysfunction, inflammatory response, abnormalities in microvascular reserve, subclinical atherosclerosis, abnormalities of blood and platelets, and genetic factors. In CSFP patients, it was found that there was a decrease in endothelial nitric oxide synthase (eNOS) expression and an increase in Endothelial-1, which resulted in an imbalance of vasoconstriction and vasodilation of the coronary arteries as a result of endothelial dysfunction.[6,7] In CSFP patients, it was found that there was an increase in Toll-like receptor 4 (TLR4), miR-155, TNF-α, IL-1, and IL-6 and a decrease in IL-10 levels. There was also an increase in plasma concentrations of CRP and IL-6 in CSFP patients. From these findings, the inflammatory response may have a role in the occurrence of CSFP.[8,9,10] If there is impaired

coronary microvessel flow reserve, perfusion of cardiac muscle microvessels will decrease, thus slowing coronary blood flow.[11] CSFP also may be an early form of atherosclerosis, referred to as subclinical atherosclerosis, which is not clinically evident and has a long latent period.[12] Subclinical atherosclerosis may fail to show evidence of significant stenosis, although blood vessels may show morphologic evidence, as well as changes in intima-media thickness due to cell proliferation during disease progression.[12] Blood cell composition and hemodynamics affect the flow and rate of blood flow in the coronary arteries, changes in the number and function of different types of blood cells may influence the development of CSFP.[13] Deformation and aggregation of red blood cells affect blood viscosity and change flow resistance, in some studies, it has been shown that the distribution of red blood cells is increased in patients with CSFP.[13] Another study of the population in South Sumatra found that ACE I/D (angiotensin converting enzyme insertion/deletion) gene polymorphism significantly increased the risk of CSFP. ACE I/D gene polymorphism is also involved in the pathogenesis of atherosclerosis and has an important role in endothelial function.[14]

Data on CSFP cases, such as prevalence and characteristics, are needed to determine the number of CSFP cases and the population at risk of complications from CSFP, so that these data can be used as additional data to determine further actions for these cases, namely management and prevention. Therefore, this study was conducted to know the prevalence of CSFP cases and patient characteristics related to CSFP risk factors at RSUD Siti Fatimah Palembang. The results of this study are expected to provide data on the prevalence and characteristics of CSFP at RSUD Siti Fatimah and can be used as educational material to increase public awareness and insight into CSFP so that specific examinations can be carried out and the diagnosis can be made earlier.

2. METHODS

This study is a descriptive observational type with a cross-sectional research design. The data used is secondary data from the medical records of CSFP patients at RSUD Siti Fatimah for the period January 1, 2020 - June 30, 2023, the data was taken using the total sampling method.

The inclusion criteria for this study were patients aged over 19 years, performed coronary angiograms with angiographic results of ≤40% stenosis[15], and patients diagnosed with CSFP. The exclusion criteria of this study are patients who experience secondary coronary slow flow or slow flow due to coronary artery obstruction, have a history of taking anticoagulant drugs, have blood hypercoagulation disease, and have a history of substance abuse.

The variables to be studied include age, gender, BMI, smoking history, history of comorbidities, symptoms, and clinical signs in the form of ECG and coronary angiography.

3. RESULT

Initial data was obtained as much as 485 patient data with complaints of chest pain. Samples that met the inclusion criteria were selected and 25 data met the inclusion criteria. Then, from 25 data, samples that met the exclusion criteria were excluded. Finally, 19 CSFP patient data were obtained that met the inclusion criteria and did not include the exclusion criteria.

The prevalence of CSFP cases at RSUD Siti Fatimah for the period January 1, 2020 - June 30, 2023 was calculated using the following formula.

$$\text{CSFP Prevalence} = \frac{a}{a + b}\ 100\%$$

a : Number of CSFP patients in the Cardiovascular Clinic of RSUD Siti Fatimah
b : Number of non-CSFP patients in the Cardiovascular Clinic of RSUD Siti Fatimah

$$\text{CSFP Prevalence} = \frac{19}{485}\ 100\%$$

$$\text{CSFP Prevalence} = 3{,}917\% = 3{,}92\%$$

Based on the prevalence formula, the prevalence of CSFP cases at RSUD Siti Fatimah for the period January 1, 2020 - June 30, 2023 is 3.92%.

Sociodemographic analysis data, including age and gender can be seen in table 1.

Table 1. Sociodemographic Characteristics

No.	Characteristics	n	%
1.	Age (N = 19)		
	a) 19-25 years old	0	0%
	b) 26-35 years old	0	0%
	c) 36-45 years old	4	21,05%
	d) 46-55 years	5	26,31%
	e) 56-65 years	6	31,57%
	f) >65 years old	4	21,05%
2.	Gender (N = 19)		
	a) Male	8	42,10%
	b) Female	11	57,89%

Based on the results of sociodemographic analysis, it was found that the largest age group was 56 - 65 years (31.57%). Based on gender analysis, CSFP patients at RSUD Siti Fatimah Palembang were mostly female (57.89%).

Analysis of risk factors for CSFP patients in this study was assessed from body mass index (BMI), smoking history, and comorbidities. Risk factor data can be seen in table 2 below.

Table 2. Risk Factor Characteristics

No.	Risk Factors	n	%
1.	Body mass index (BMI) (N = 10)		
	a) Underweight: <18.5 kg/m^2	0	0%
	b) Normal: 18.5 - 22.9 kg/m^2	2	20%
	c) Overweight with risk: 23 - 24.9 kg/m^2	3	30%
	d) Obesity I: 25 - 29.9 kg/m^2	2	20%
	e) Obesity II: ≥ 30 kg/m^2	3	30%
2.	Smoking history (N = 2)		
	a) Yes	0	0%
	b) No	2	100%
3.	Comorbidities (N = 19)		
	a) Hypertension	13	68,42%
	b) Dyslipidemia	12	63,15%
	c) Heart Disease	10	52,63%
	d) Diabetes mellitus	5	26,31%

From the results of the analysis of risk factors for CSFP patients above, it was found that CSFP was mostly suffered by patients with a body mass index of more than normal or more than 23 kg/m^2 (80%). The average body mass index value of CSFP patients in this study was 26.6 kg/m^2.

The smoking history of CSFP patients only obtained 2 data and found that the patient did not smoke (100%).

Based on comorbid analysis, the most common comorbidity suffered by CSFP patients was hypertension (63.15%), while the least common was diabetes mellitus (26.31%). From the data of 19 CSFP patients, there were several patients who had more than one comorbid. 47.36% of patients had hypertension and dyslipidemia. In addition, 15.78% of patients had all of the comorbidities that became variables in this study (hypertension, dyslipidemia, heart disease, and diabetes mellitus).

The description of chest pain symptoms complained of by CSFP patients is contained in the following table 3.

Table 3. Symptomatic Overview of Patients

No.	Symptoms	n	%
1.	Chest pain (N = 17)		
	a) Chest pain on exertion	15	88,23%
	b) Chest pain on exertion and at rest	2	11,76%

From the data obtained, patients who only felt chest pain symptoms during activity were 88.23% and patients who felt chest pain symptoms during activity and rest were 11.76%.

Clinical signs of CSFP patients were assessed based on the results of ECG and coronary angiography. The results of ECG and coronary angiography of CSFP patients are in the following tables 4 and 5.

Table 4. ECG Clinical Signs

No.	ECG Result	n	%
1.	ECG (N = 9)		
	a) Normal	1	11,11%
	b) Abnormal	8	88,89%

Based on the results of the analysis of ECG in CSFP patients at RSUD Siti Fatimah Palembang, 8 patients (88.89%) had abnormal ECGs, while 1 patient (11.11%) had a normal ECG.

Table 5. Clinical Signs of Coronary Angiography

No.	Coronary Angiography Results	n	%
1.	CSFP angiography (N=19)		
	a) Slow flow in Left Main Coronary Artery (LM)	8	42,10%
	b) Slow flow in the Left Anterior Descending Artery (LAD)	18	94,73%
	c) Slow flow in Left Circumflex Artery (LCX)	17	89,47%
	d) Slow flow in the Right Coronary Artery (RCA)	14	73,68%

Based on the analysis results in Table 5, it was found that most patients had slow flow in the Left Anterior Descending Artery/LAD (94.73%) and Left Circumflex Artery/LCX (89.47%). Meanwhile, the least slow flow was found in the Left Main Coronary Artery/LM (42.10%), this is due to the length of the LM which is too short so that slow flow cannot be assessed in the LM.The angiographic results of CSFP patients contained several patients who experienced slow flow in more than 1 coronary artery. The grouping of affected arteries can be seen in table 6 below

Table 6. Clinical Signs of Coronary Angiography by Affected Artery Group

No.	Coronary Angiography Results	n	%
1.	CSFP angiography (N=19)		
	a) Slow flow in LAD	1	5,26%
	b) Slow flow at LAD and LCX	2	10,52%
	c) Slow flow in LM and RCA	1	5,26%
	d) Slow flow at LM, LAD, and LCX	2	10,52%
	e) Slow flow at LAD, LCX, and RCA	8	42,10%
	f) Slow flow at LM, LAD, LCX, RCA	5	26,31%

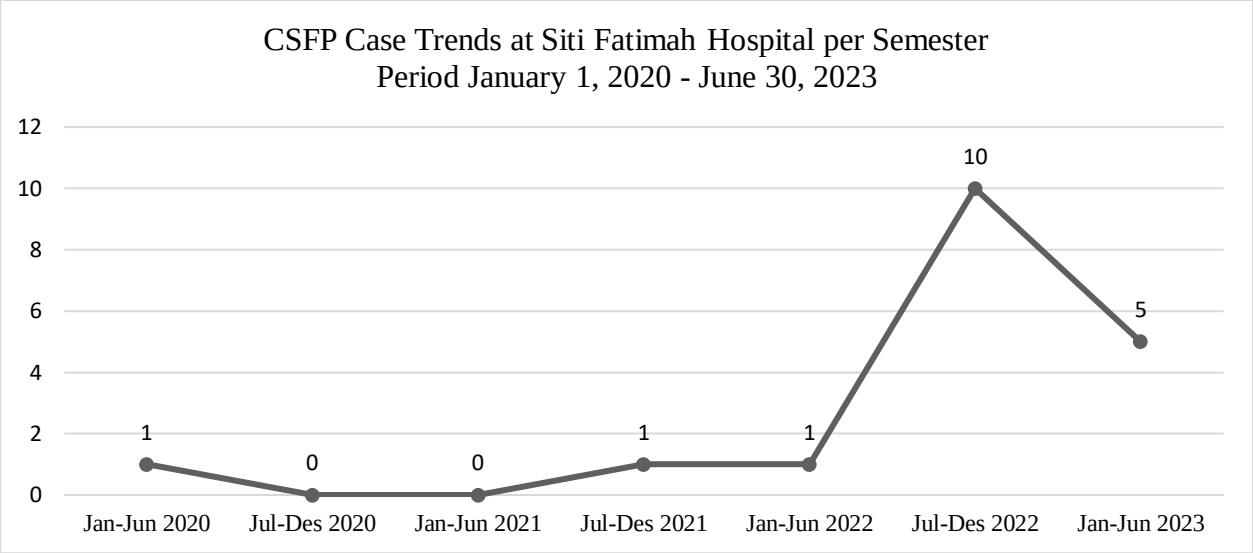
Based on the results of the analysis in Table 6 regarding the coronary artery groups affected by slow flow, it was found that the coronary artery groups that were more frequently affected were the LAD, LCX, and RCA coronary artery groups (42.10%). In addition, patients who experienced slow flow in all coronary arteries were also quite numerous (26.31%).

4. DISCUSSION

This study found that the prevalence of CSFP cases at RSUD Siti Fatimah for the period January 1, 2020 - June 30, 2023 was 3.92%. This finding is in line with research conducted by Aparicio et al. and Alvarez et al. which states that the prevalence of CSFP cases ranges from 1-5%.[1,2]

The trend of CSFP cases at RSUD Siti Fatimah per semester can be seen in the following graph.

Figure 1. CSFP Case Trends at RSUD Siti Fatimah per Semester



Based on the trend graph, it can be concluded that CSFP cases at RSUD Siti Fatimah are increasing every year.

The average age of CSFP patients in this study was 56 years. This finding is in line with research by Finley et al. and Sadr-Ameli et al., that the average age of CSFP patients is 52 years.[16,17] The youngest patient in this study was 36 years old and the oldest patient age was 78 years old. Zhu et al. stated that CSFP can occur in all ages, but patients over 50 years old with comorbid hypertension and dyslipidemia need more attention.[18]

From this study, it was found that 57.89% of CSFP patients were female. This is different from studies by Rouzbahani et al., Sanghvi et al., and Zhu et al.[4,5,18] These studies stated that most CSFP patients were male. The large number of female patients is thought to be related to the age of patients who are over 50 years old. Ryczkowska et al. mentioned that menopause increases the risk of coronary artery disease; this is related to the decrease in estrogen hormones in menopausal women.[19] Estrogen hormone is cardioprotective. Fineschi et al. stated that gender has no effect on CSFP disease, because the risk of suffering from CSFP is equal for men and women.[20]

Most CSFP patients in this study had a BMI of more than normal and the average BMI in this study was 26.6 kg/m^2. This is in accordance with research from Rouzbahani et al. and Mukhopadhyay et al. which states that most CSFP patients have a high BMI.[5,21] High BMI values are associated with the risk of endothelial dysfunction that can trigger coronary slow flow. The mean BMI value of this study was 26.6 kg/m^2, similar to previous research from Zhu et al. that the mean BMI of CSFP patients was 26 kg/m^2 .[18]

Smoking history data from this study was only obtained for 2 patients and the patients did not smoke. The lack of data causes the analysis to be less representative. Nevertheless, in another study previously conducted by Finley et al. on CSFP patients, that patients who smoke have a greater likelihood of endothelial dysfunction than patients who do not smoke.[16] In the study also mentioned that smoking can increase microvascular resistance which will trigger coronary slow flow.[16]

Hypertension was the most common comorbidity in this study. A total of 68.42% of CSFP patients at RSUD Siti Fatimah suffered from hypertension. Based on research from Climie et al., it was found that hypertension

affects nitric oxide production in the endothelium which causes the availability of nitric oxide to decrease and trigger endothelial dysfunction.[22]

Dyslipidemia is the second most common comorbidity after hypertension from this study. As many as 63.15% of CSFP patients at RSUD Siti Fatimah experienced dyslipidemia. Research conducted by Addisu et al. states that increased LDL cholesterol, decreased HDL cholesterol, and increased triglyceride levels are factors in cardiovascular disease.[23] Lipid buildup can also cause smooth muscle cell proliferation and activation of inflammatory cells, which will play a role in the formation of atherosclerosis.[23]

From the results of data analysis of CSFP patients, it was found that 52.63% of CSFP patients also had heart disease. The most common heart disease suffered by CSFP patients at RSUD Siti Fatimah is hypertensive heart disease (HHD). Based on medical record data, all patients with HHD in this study had a history of hypertension. There are no publications that explain the direct link between HHD and CSFP, but from this study it can be concluded that HHD is a complication of chronic hypertension suffered by CSFP patients.

CSFP patients who also had diabetes mellitus in this study were 26.31%. Based on the findings from Elsanan et al.'s study of the Egyptian population, it was stated that patients with diabetes mellitus have poor glycemic control, which will ultimately increase the risk of microvascular endothelial dysfunction due to inflammation.[24] Endothelial dysfunction plays a role in the occurrence of CSFP. Gupta et al. mentioned that the process of atherosclerosis formation can occur earlier and develop faster in diabetics.[25]

All CSFP patients in this study complained of chest pain during activities that occurred repeatedly. This is in line with statements from previous studies which state that 80-90% of CSFP patients complain of recurrent chest pain and interfere with daily life.[26] Based on Tambe et al. research, the exact cause of chest pain that occurs in CSFP patients is still unknown.[15] Chest pain that occurs in CSFP patients is thought to be due to decreased perfusion to the heart muscle due to slowed blood flow.

The ECG results of CSFP patients in this study were found to be mostly abnormal. The abnormal ECG results found mostly showed the presence of LVH or left ventricle hypertrophy. Left ventricular hypertrophy is an early compensatory response to hemodynamic overload and can be found in patients with hypertensive heart disease/HHD.[27]

Coronary angiography at RSUD Siti Fatimah uses the corrected TIMI frame count method, declared slow flow if CTFC >27 frames.[15] From the results of coronary angiography analysis, it was found that slow flow mostly occurred in the left anterior descending artery (LAD) as much as 73.68% and left circumflex artery (LCX) as much as 73.68%. This finding is in line with previous studies which found that slow flow was found more in the LAD, followed by the LCX and RCA (right coronary artery).[4,5,28] From this study, the least slow flow was found in the left main coronary artery (LM) which amounted to 26.31%.

Based on the results of research conducted by Shui et al. it is stated that slow flow is most commonly found in the LAD, followed by the RCA and LCX in order. These findings are slightly different from the results obtained from this study. Shui et al. also added that most patients (49.5%) experienced slow flow in three coronary arteries, namely the LAD, LCX, and RCA. This finding is in line with the results of this study which found that 42.10% of patients experienced slow flow in the LAD, LCX, and RCA. Thus, it can be concluded that the artery groups most involved in slow flow are the LAD, LCX, and RCA coronary artery groups.[29]

5. CONCLUSION

CSFP cases are mostly found in patients above 50 years, most patients have BMI above normal, hypertension is the most common comorbidity suffered, the most common symptom complained of is chest pain on exertion, most patients have an abnormal ECG, and the most common affected coronary artery is the left anterior descending artery/LAD.

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