

# Original Research Prevalence and Impact of Modifiable Risk Factors on Acute Coronary Syndrome: A Case Control Study

Anak Agung Ngurah Anindya Kusuma<sup>1\*</sup>, I Gede Bagus Gita Pranata Putra<sup>2,3</sup>, <sup>1</sup>Faculty of Medicine, Warmadewa University, Bali, Indonesia. <sup>2</sup>Department of Cardiology and Vascular Medicine, Sanjiwani Hospital, Bali, Indonesia. <sup>3</sup>Bali Branch of the Indonesian Association of Cardiovascular Doctors (PERKI BALI), Bali, Indonesia.

## ARTICLE INFO

Article history: Submitted February 19<sup>th</sup> 2024 Reviewed Mar 21<sup>st</sup> – 30<sup>th</sup> 2024 Accepted Mar 30<sup>th</sup> 2024 Available online March 31<sup>th</sup> 2024

\*Correspondence: turahanindya1818@gmail.com

Keywords:

Acute coronary syndrome Cardiovascular disease

## ABSTRACT

Background: Acute coronary syndrome (ACS) is defined by the abrupt reduction or total obstruction of blood flow to the myocardium. Recognized risk factors for ACS include conditions such as hypertension, dyslipidemia, smoking, obesity, diabetes mellitus, hyperuricemia, as well as variables like age, gender, and family history of the ailment. The objective of this research was to examine the prevalence and importance of modifiable risk factors associated with ACS. Material and Methods: The study is structured as a prospective case-control study. The research sample comprises 100 ACS patients, categorized into three groups: STEMI, NSTEMI, and UAP. The Chi-Square test and logistic regression were used to examine the samples. The threshold for statistical significance was set at p<0.05. Results: ACS occurred more frequently in male patients (54%) and those aged  $\geq$  40 years (85%). Several factors demonstrated significant associations with ACS, including smoking habits, dyslipidemia, hypertension, diabetes mellitus, obesity, and hyperuricemia. Among these, inpatient ACS was notably linked with obesity (OR: 7.42; 95% CI: 1.48-37.11; p=0.015) and hypertension (OR: 0.13; 95% CI: 0.03-0.53; p=0.005). The presence of ACS was also correlated with a notable increase in inpatient care, with obesity and hypertension emerging as risk factors for inpatient ACS. Conclusion: ACS was more common in males and individuals aged 40 or older, with significant associations identified between ACS and various factors, including smoking, dyslipidemia, diabetes, obesity, hyperuricemia, and hypertension, with obesity and hypertension specifically linked to inpatient ACS.

## **Highlights:**

- 1. Smoking duration, dyslipidemia, hypertension, diabetes mellitus, obesity, and hyperuricemia, are significantly associated with ACS.
- 2. Obesity and hypertension are identified as risk factors for inpatient ACS.

## Cite this as:

Kusuma, A. A. N. A., Putra, I G. B. G. P. (2024). Prevalence and Impact of Modifiable Risk Factors on Acute Coronary Syndrome: A Case Control Study. Cardiovascular and Cardiometabolic Journal (CCJ), 5(1), 23-34.

## Introduction

Acute coronary syndrome (ACS) is a potentially fatal illness that has a significant chance of mortality and subsequent cardiovascular events <sup>[1]</sup>. This syndrome encompasses ST-segment elevation myocardial infarction (STEMI), non-ST-segment elevation myocardial infarction (NSTEMI), and unstable angina (UA). The ramifications of STEMI can be extremely severe, especially when it strikes at a young age <sup>[2]</sup>. This can have a significant impact on the patient's psychological well-being, their ability to maintain employment, and can result in long-lasting socioeconomic and health burdens.<sup>[3]</sup>

Obesity, smoking, diabetes mellitus (DM), hypertension, and hypercholesterolemia are all risk factors for coronary artery disease (CAD) [4]. Notably, obesity is associated with an earlier onset of CAD <sup>[5]</sup>. No matter the patient's age, risk factors like obesity, hypertension, and smoking might affect how ACS manifests clinically obesity, hypertension, and smoking all have an impact on how clinically apparent ACS is in individuals of all ages <sup>[6]</sup>. Gender disparities have been noted in the symptoms reported by patients admitted for ACS. Women are more inclined to describe chest discomfort as opposed to the more typical chest pain experienced by men.<sup>[7]</sup>

Age is a significant risk factor for ACS, especially in individuals aged 65 years and older. Smoking, particularly over 60 pack-years, substantially

increases the risk of ACS mortality and incidence. Dyslipidemia is common in ACS patients and requires effective management for secondary prevention, yet many fail to achieve optimal lipid levels despite treatment efforts.<sup>[8]</sup>

Smoking is a substantial risk factor for ACS <sup>[9]</sup>. Over a 4-year period, continuing to smoke after developing ACS was linked to a 78% increased relative risk of death. Patients with over 60 packyears of smoking had a 57.8% higher ACS mortality rate and a 24.6% higher likelihood of experiencing any ACS event.<sup>[10]</sup>

Dyslipidemia is prevalent among ACS patients and requires effective management for secondary prevention, yet many fail to achieve optimal lipid levels despite treatment efforts. Hypertension, with its association with ACS, underscores the importance of effectively managing hypertension to reduce the risk of ACS and its related complications. Hyperglycemia is a metabolic disorder that is a hallmark of diabetes mellitus.<sup>[11]</sup>

Patients with diabetes who also have ACS have greater death rates than non-diabetic individuals. This is explained by the fact that diabetes accelerates the development of atherosclerosis and raises the risk of developing ACS. It's noteworthy that around 25-30% of ACS admissions involve patients with diabetes, and ACS tends to occur at an earlier age in individuals with diabetes.<sup>[12]</sup>

Obesity pertains to whether respondents have a history of obesity and its connection with ACS. Obesity is linked to an increased risk of ACS across various lifestyle behavior subgroups, including both healthy and less healthy ones <sup>[13]</sup>. Hyperuricemia, characterized by elevated uric acid levels in the blood, has demonstrated associations with ACS in numerous studies. It is a frequently observed condition in ACS patients, with a reported prevalence of 23%. In the general population, hyperuricemia seems to be associated with both fatal and non-fatal ACS episodes.<sup>[14]</sup>

Diverse studies have produced inconsistent results. While some have clearly linked a family history of CAD to ACS, especially in cases of early CAD, others have found that this correlation in patients experiencing chest discomfort is independent of age, gender, cardiovascular risk factors, or ECG findings.

The aim of this research is to explore and understand the prevalence and significance of modifiable risk factors associated with ACS. By investigating factors such as hypertension, dyslipidemia, smoking, obesity, diabetes mellitus, hyperuricemia, as well as demographic variables like age, gender, and family history of the condition, the research seeks to identify which of these factors are most closely linked to the occurrence of ACS. By doing so, the study aims to provide insights that can inform preventive strategies and interventions to reduce the incidence of ACS and its associated complications.

#### **Material and Methods**

This research represents an observational analytical study that utilized a prospective casecontrol approach. In a case-control study, the investigator distinguishes between a group of individuals who have the outcome of interest (the case group) and a group who do not (the control This study design is considered group). observational because the researcher does not actively decide which individuals go into each group, unlike in a pre-planned experimental study where the researcher has control over subject assignment.[15]

This research was carried out at RSUD Sanjiwani Gianyar in Kabupaten Gianyar, Provinsi Bali, over a four-month period, spanning from November 2022 to February 2023. The study population consisted of all inpatient individuals diagnosed with ACS in Gianyar, with a sample size of 100 patients selected via consecutive sampling and meeting the predefined inclusion criteria. These inclusion criteria entailed individuals diagnosed with ACS who were receiving treatment at RSUD Sanjiwani Gianyar and had provided their consent for participation. On the contrary, exclusion criteria encompassed patients who declined to participate and those with ACS who had passed away.

25

Data collection was carried out manually using a designated data collection sheet. Bivariate analysis employed the chi-square test to assess the significance of relationships between independent and dependent variables, while multivariate analysis utilized logistic regression to identify the most influential independent variables on the dependent variable. Risk factor analysis involved comparing these factors with the incidence of acute coronary syndrome, and the results were presented in tabular format, with the strength of associations quantified using the Odds Ratio (OR).

Statistical Package for the Social Sciences (SPSS) 25.00 was used to process and analyze the data <sup>[16]</sup>. A table with a variety of data that had been coded in accordance with the necessary analysis was made.<sup>[17]</sup>

## Result

In this method there is one step to get the result, namely all independent variables that have a p value <0.05, so that variables are obtained which are risk factors for ACS, the strength of the risk relationship from STEMI, namely obesity OR (7.42) and in NSTEMI namely hypertension (OR = 0.13). In the case of STEMI, the value of p was 0.414 with an odds ratio (OR) of 1.67 and a 95% confidence interval (CI) ranging from 0.489 to 5.68. For NSTEMI, the p-value was 0.732, the OR was 1.17, and the 95% CI spanned from 0.48 to 2.82.

It was observed that more men experienced ACS compared to women, and gender was not identified as a significant risk factor for ACS.Regarding age, those above 40 years had a higher incidence of ACS than those below 40 years. However, the age groups of less than 40 years and over 40 years were not statistically significant risk factors for ACS. For STEMI, the p-value was 0.363 with an OR of 2.23 and a 95% CI of 0.34 to 12.57, while NSTEMI had a p-value of 0.428 with an OR of 1.76 and a 95% CI ranging from 0.43 to 7.18.

Family history was not shown to be a significant risk factor for ACS. STEMI had a p-value of 0.041, an OR of 0.24, and a 95% CI between 0.06 and 0.94, while NSTEMI had a p-value of 0.045, an OR of 0.32, and a 95% CI of 0.11 to 0.98. In cases of both STEMI and NSTEMI, a smoking duration of more than 10 years was identified as a statistically significant risk factor for ACS. Also, the number of cigarettes smoked, exceeding 20, was a risk factor for ACS in both STEMI and NSTEMI and NSTEMI and NSTEMI, whereas those who smoked 10-20 cigarettes or less than 10 cigarettes were not statistically significant risk factors.

STEMI/UAP	Variable Independent	Р	OR (CI 95%)
	Smoking duration (> 10 years / not)	0,356	0,31(0,03-3,8)
	Number of cigarettes (>20 cigarettes)	0,476	0,42(0,04-4,55)
	10-20 sticks	0,771	1,45(0,12-17,65)
	Dyslipidemia (yes/no)	0,078	5,38(0,83-35,01)
	Hypertension (yes/no)	0,136	0,25(0,04-1,54)
	Obesity (yes/no)	0,015	7,42(1,48-37,11)
	DM	0,067	3,93(0,91-17,03)
	Hyperuricemia (yes/no)	0,208	0,2(0,02-2,45)
NSTEMI/UAP	Variable Independent	Р	OR (CI 95%)
NSTEMI/UAP	Variable Independent Smoking duration (> 10 years / not)	<b>P</b> 0,276	OR (Cl 95%) 0,37(0,06-2,24)
NSTEMI/UAP			. ,
NSTEMI/UAP	Smoking duration (> 10 years / not)	0,276	0,37(0,06-2,24)
NSTEMI/UAP	Smoking duration (> 10 years / not) Number of cigarettes (>20 cigarettes)	0,276 0,461	0,37(0,06-2,24) 0,54(0,1-2,8)
NSTEMI/UAP	Smoking duration (> 10 years / not) Number of cigarettes (>20 cigarettes) 10-20 sticks	0,276 0,461 0,939	0,37(0,06-2,24) 0,54(0,1-2,8) 1,07(0,2-5,74)
NSTEMI/UAP	Smoking duration (> 10 years / not) Number of cigarettes (>20 cigarettes) 10-20 sticks Dyslipidemia (yes/no)	0,276 0,461 0,939 0,926	0,37(0,06-2,24) 0,54(0,1-2,8) 1,07(0,2-5,74) 0,95(0,34-2,7)
NSTEMI/UAP	Smoking duration (> 10 years / not) Number of cigarettes (>20 cigarettes) 10-20 sticks Dyslipidemia (yes/no) Hypertension (yes/no)	0,276 0,461 0,939 0,926 0.005	0,37(0,06-2,24) 0,54(0,1-2,8) 1,07(0,2-5,74) 0,95(0,34-2,7) 0,13(0,03-0,53)

Table 1	. Ris	sk fac	tors
---------	-------	--------	------

Source: Research Data, Processed

Furthermore, for dyslipidemia, STEMI was found to be a significant risk factor with a p-value of 0.030, an OR of 0.23, and a 95% CI ranging from 0.06 to 0.87, while NSTEMI was not a significant risk factor with a p-value of 0.020, an OR of 0.29, and a 95% CI of 0.1 to 0.83. The presence of hypertension was associated with a higher incidence of ACS, and this was statistically significant in the cases of both STEMI (p-value = 0.029, OR = 4.2, 95% CI = 1.16-15.17) and NSTEMI (p-value = 0.470, OR = 1.4, 95% CI = 0.56-3.49). On the other hand, diabetes mellitus (DM) was found to be a significant risk factor for STEMI with a p-value of 0.011, an OR of 5.57, and a 95% CI ranging from 1.48 to 21.02, while it was not a risk factor for NSTEMI with a pvalue of 0.395, an OR of 1.6, and a 95% CI of 0.54-4.7.

Lastly, in the case of obesity, it was identified as a significant risk factor for STEMI with a p-value of 0.147, an OR of 0.2, and a 95% CI ranging from 0.02 to 1.76. However, for NSTEMI, obesity was not a significant risk factor, with a p-value of 0.683, an OR of 0.81, and a 95% CI of 0.28 to 2.28. It was also noted that hyperuricemia was not a significant risk factor for ACS, both in the context of STEMI and NSTEMI.

#### Discussion

From the analysis results in Table 1 Research findings suggest that gender is associated with the occurrence of ACS. Male respondents comprised the majority (80%), and another study reported higher death rates from CHD in men (24%) compared to women (11%). The susceptibility to coronary atherosclerosis rises with advancing age, reaching its highest incidence between the ages of 50 to 60 for men and 60 to 70 for women. There is a common male predominance in ACS registries <sup>[18]</sup>. Men tend to present with ACS about a decade earlier than women.<sup>[18]</sup>

Women with ACS may have atypical chest pain and heart symptoms compared to men. Women may have a greater probability of encountering microvascular angina, a condition linked to an elevated risk of ACS incidents and cardiac failure while keeping the ejection fraction intact <sup>[19]</sup>. Women admitted with non-ST segment elevation ACS generally exhibit more unfavorable clinical outcomes when compared to their male counterparts.<sup>[20]</sup>

From the data analysis based on age, it is evident that most ACS patients are above 40 years old, totaling 85 individuals, compared to 15 individuals below 40 years old. Within the youngest age group (those under 55), 44% of women and 56% of men presented with ST-elevation ACS; this percentage declined with age, especially for men. The results indicate that family history does not emerge as a significant risk factor for ACS and lacks statistical significance in this study. However, it's worth noting that individuals with a family history of ACS are generally at an increased risk of developing atherosclerosis, thrombosis, and proinflammatory responses, often linked to elevated levels of CRP. Other research has found a strong association between a family history of CAD and the onset of cardiovascular disease, independent of other risk factors.<sup>[21]</sup>

The study delved into the relationship between the duration of smoking and ACS. The results showed that patients with over 60 pack-years of smoking had a 57.8% higher ACS mortality rate and a 24.6% higher likelihood of experiencing any ACS event. Smoking is a substantial risk factor for ACS [22]. Moreover, the ACS risk increased by 13% for every 30 pack-years of smoking that was added to the tobacco habit. Continuing to smoke after an ACS episode was linked to a 78% greater relative risk of mortality over a 4-year period. Smokers, in general, carried a 75% higher risk of ACS compared to nonsmokers <sup>[23]</sup> Importantly, whether patients were current or former smokers, there was no survival benefit for those who were hospitalized with ACS, irrespective of the clinical presentation. Smoking cessation rates among ACS patients ranged from 31% without intervention to 60% when sustained intervention was provided post-hospitalization, as noted during a one-year surveillance.<sup>[24]</sup>

The study investigated the quantity of cigarettes smoked in relation to ACS. Individuals who have smoked for more than 60 pack years in the past faced a 24.6% increased risk of experiencing any ACS event and a 57.8% higher risk of ACS-related mortality. For every additional 30 pack-years of smoking, there was a 13% increase in the associated risk of ACS. In general, ACS risk was 75% higher in smokers than in non-smokers <sup>[23]</sup>. Regardless of the clinical presentation, there was no survival advantage seen in patients admitted with ACS, regardless of whether they were current or past smokers.

The term "dyslipidemia" pertains to whether respondents have a history of lipid disorders and its connection to ACS. Dyslipidemia, characterized by abnormal levels of lipids like cholesterol and triglycerides in the blood, is indeed linked to ACS. Among ACS patients, dyslipidemia was strikingly widespread; the highest prevalence was observed in those with unstable angina, at 64.3%, and NSTEMI was the next highest (48.1%) and STEM) (45.3%).<sup>[25]</sup>

Hypertension refers to whether respondents have a history of hypertension and its association with ACS. In women, hypertension may be especially important as a risk factor for ACS <sup>[26]</sup>. This association may be attributed to mechanical factors,

such as heightened mechanical stress on blood vessels. These insights highlight the role of hypertension in both the onset and prognosis of ACS, underscoring the importance of effectively managing hypertension to mitigate the risk of ACS and its related complications.<sup>[27]</sup>

The term "diabetes mellitus" pertains to whether respondents have a history of diabetes mellitus and its correlation with ACS. ACS patients with diabetes have greater death rates than non-diabetic individuals. Throughout the whole process, there is a segmental distribution of many vascular branches, with clear AS, indicative of DM coupled with coronary atherosclerotic heart disease.<sup>[28]</sup>

This is explained by the fact that diabetes accelerates the development of atherosclerosis, leading to an elevated risk of ACS development <sup>[29]</sup>. It's noteworthy that around 25-30% of ACS admissions involve patients with diabetes, and ACS tends to occur at an earlier age in individuals with diabetes <sup>[12]</sup>. The poorer outcomes among diabetic ACS patients are linked to an increased proinflammatory and prothrombotic state <sup>[29]</sup>. This condition is prevalent among ACS patients in China, where diabetic ACS patients are considerably greater risk of unfavorable hospital outcomes than people without diabetes.[12]

Obesity in this context pertains to whether respondents have a history of obesity and its connection with ACS <sup>[13]</sup>. Obesity is linked to an increased risk of ACS across various lifestyle behavior subgroups, including both healthy and less healthy ones. It's interesting to note that some research suggests a connection between obesity and a lower risk of mortality following ACS when compared to individuals with normal weight, a phenomenon referred to as the "obesity paradox" <sup>[30]</sup>. It's important to note that other studies have found that more severe levels of obesity are linked to an earlier onset of ACS. Furthermore, there seems to be a correlation between a high body mass index (BMI) and an increased risk of coronary artery disease.<sup>[31]</sup>

Hyperuricemia refers to whether respondents have a high level of uric acid in their blood and its association with ACS. Hyperuricemia, characterized by elevated uric acid levels in the blood, has demonstrated associations with ACS in numerous studies <sup>[32]</sup>. It is a frequently observed condition in ACS patients, with a reported prevalence of 23% <sup>[14]</sup>. In the general population, hyperuricemia seems to be associated with both fatal and non-fatal ACS episodes <sup>[14]</sup>. Metabolic syndrome—a cluster of risk factors that increases the risk of cardiovascular disease—and hyperuricemia are linked.<sup>[33]</sup>

The study employed a prospective case-control design to investigate the connection between risk variables and ACS in patients treated at RSUD Sanjiwani Gianyar. Data collection was done manually, and statistical analyses involved chisquare and logistic regression. However, the study's limitations include its exclusive focus on one hospital, potentially limiting the generalizability of the results. The study also noted the possibility of recall bias in elderly participants and interviewer bias due to communication challenges during interviews. These biases were addressed by assisting participants in recalling events and conducting unhurried interviews.

#### Conclusion

The study revealed that individuals with STEMI and obesity exhibited a significantly higher likelihood of developing ACS, while those with NSTEMI and hypertension displayed a notably reduced risk. This implies that hypertension may confer a protective effect against STEMI. However, factors such as gender, age, family history, smoking habits, dyslipidemia, diabetes mellitus, and hyperuricemia did not demonstrate a significant association with ACS. To further advance research in this field, it is advisable to conduct multicenter studies to validate obesity's role as a risk factor for ACS in STEMI patients and to explore the relationship between hypertension and NSTEMI in larger sample populations.

#### Acknowledgement

We would especially like to thank RSUD Sanjiwani Gianyar's Department of Internal Medicine, Cardiology, and Vascular Division for their support in this study.

## References

- Kristin E, Dinarti LK, Febrinasari RP, Pratiwi WR, Yasmina A, Jaya SI. Persistence to antihypertensive and clinical outcomes in acute coronary syndrome patients after percutaneous coronary intervention. Indones J Pharm. 2023;34(3):482–90. DOI: https://doi.org/10.22146/ijp.5499.
- Andhi N, Desham P, Madavi C, Bhavana S, Naresh D. Assessment of quality of life and drug prescription pattern in acute coronary syndrome. J Indian Coll Cardiol. 2022;12(3):111. DOI:

https://doi.org/10.4103/jicc.jicc\_50\_21.

 Samir A, Almahjori M, Zarif B, Elshinawi M, Yehia H, Elhafy M, et al. Characterization of features and outcomes of young patients (< 45 years) presenting with ST - segment elevation myocardial infarction. Egypt Hear J [Internet].
 2023;75(32):1–8. Available from: https://doi.org/10.1186/s43044-023-00357-2

- Mirza AJ, Taha AY, Khdhir BR. Risk factors for acute coronary syndrome in patients below the age of 40 years. Egypt Hear J [Internet].
   2018;70(4):233–5. Available from: https://doi.org/10.1016/j.ehj.2018.05.005
- Stătescu C, Anghel L, Benchea LC, Tudurachi BS, Leonte A, Zăvoi A, et al. A Systematic Review on the Risk Modulators of Myocardial Infarction in the "Young"—Implications of Lipoprotein (a). Int J Mol Sci. 2023;24(6). DOI: https://doi.org/10.3390/ijms24065927
- Balaha MF, Alamer AA, Kabel AM, Aldosari SA, Fatani S. A Prospective cross-sectional study of acute coronary syndrome patients' quality of life and drug prescription patterns at riyadh region hospitals, Saudi Arabia. Healthc. 2023;11(13). DOI:

https://doi.org/10.3390/ healthcare11131973

 Mahendiran T, Hoepli A, Foster-Witassek F, Rickli H, Roffi M, Eberli F, et al. Twenty-year trends in the prevalence of modifiable cardiovascular risk factors in young acute coronary syndrome patients hospitalized in Switzerland. Eur J Prev Cardiol [Internet]. 2023;30(14):1504–12. DOI:

https://doi.org/10.1093/eurjpc/zwad077

 Cowie MR, Linz D, Redline S, Somers VK, Simonds AK. Sleep Disordered Breathing and Cardiovascular Disease: JACC State-of-the-Art Review. J Am Coll Cardiol. 2021;78(6):608–24. DOI: https://doi.org/10.1016/j.jacc.2021.05.048

- Aminuddin A, Cheong SS, Roos NAC, Ugusman A. Smoking and unstable plaque in acute coronary syndrome: a systematic review of the role of matrix metalloproteinases. Int J Med Sci. 2023;20(4):482–92. DOI: https://doi.org/10.7150/ijms.79889.
- 10. Yudi MB, Farouque O, Andrianopoulos N, Ajani AE, Kalten K, Brennan AL, et al. The prognostic significance of smoking cessation after acute coronary syndromes: An observational, multicentre study from the Melbourne interventional group registry. BMJ Open. 2017;7(10):1–7. DOI:

https://doi.org/10.1136/bmjopen-2017-016874

- Ong C. Characteristic of Chronic Complications in Type 2 Diabetic Patient Based on Asian Perspective. Curr Intern Med Res Pract Surabaya J. 2022;3(1):13. DOI: https://doi.org/10. 20473/cimrj.v3i1.31412
- Zhou M, Liu J, Hao Y, Liu J, Huo Y, Smith SC, et al. Prevalence and in-hospital outcomes of diabetes among patients with acute coronary syndrome in China: Findings from the Improving Care for Cardiovascular Disease in China-Acute Coronary Syndrome Project. Cardiovasc Diabetol [Internet]. 2018;17(1):1– 14. DOI: https://doi.org/10.1186/s12933-018-0793-x

- Hao W, Wang X, Fan J, Guo R, Gong W, Yan Y, et al. Prognostic Implications of OSA in Acute Coronary Syndrome by Obesity Status. Chest [Internet]. 2023;164(1):219–30. DOI: https://doi.org/10.1016/j.chest.2023.02.001.
- Maloberti A, Biolcati M, Ruzzenenti G, Giani V, Leidi F, Monticelli M, et al. The role of uric acid in acute and chronic coronary syndromes. J Clin Med. 2021;10(20). DOI: https://doi.org/ 10.3390/jcm10204750
- Dey T, Mukherjee A, Chakraborty S. A Practical Overview of Case-Control Studies in Clinical Practice. Chest. 2020;s57–63. DOI: https://doi.org/https://doi.org/10.1016/j.chest. 2020.03.009.
- Melati KBDS, Hardaetha A, Kusuma W. The Effectiveness of Meloxicam Adjuvant Therapy against Negative Symptoms and Neutrophil Lymphocyte Ratio (NLR) in Schizophrenic Patients. JUXTA J IIm Mhs Kedokt Univ Airlangga. 2023;14(2):57–62. DOI: https://doi.org/10.20473/juxta.v14i22023.57-62.
- Faradiba AR, Athiyyah AF, Hariastawa IGBA.
  Evaluation of Bowel Function on Patient Post
  Operative Hirschsprung Disease. JUXTA J IIm
  Mhs Kedokt Univ Airlangga. 2023;14(2):105–
  10. DOI:

https://doi.org/10.20473/juxta.v14i22023.105-110.  Cader FA, Banerjee S, Gulati M. Sex Differences in Acute Coronary Syndromes: A Global Perspective. J Cardiovasc Dev Dis. 2022;9(239):1–20. DOI:

https://doi.org/10.3390/jcdd9080 239.

- Haider A, Bengs S, Luu J, Osto E, Siller-Matula JM, Muka T, et al. Sex and gender in cardiovascular medicine: Presentation and outcomes of acute coronary syndrome. Eur Heart J. 2020;41(13):1328–36. https://doi.org/10.1093/eurheartj/ehz898.
- Imbalzano E, Russo GT, Giandalia A, Sciacqua A, Orlando L, Russo V, et al. Sex-Specific Impact of Different Obesity/Metabolic Phenotypes on Long-Term Cardiovascular Outcomes in Acute Coronary Syndrome Patients. Biomedicines. 2022;10(2):1–18. DOI: https://doi.org/10.3390/biomedicines10020424.
- Agarwal MA, Garg L, Lavie CJ, Reed GL, Khouzam RN. Impact of family history of coronary artery disease on in-hospital clinical outcomes in ST-segment myocardial infarction. Ann Transl Med. 2018;6(1):3–3. DOI: https://doi.org/10.21037/atm.2017.09.27.
- Kondo T, Nakano Y, Adachi S, Murohara T. Effects of tobacco smoking on cardiovascular disease. Circ J. 2019;83(10):1980–5. DOI: https://doi.org/10.1253/circj.CJ-19-0323.

- 23. Hu G, Zhou M, Liu J, Jr SCS, Ma C, Ge J, et al. Smoking and provision of smoking cessation interventions among inpatients with acute coronary syndrome in china: findings from the improving care for cardiovascular disease in China acute coronary syndrome project. Glob Heart. 2020;15(1):1–11. DOI: https://doi.org/10.5334/gh.784.
- Abroug H, Hraiech A El, Mehrez O, Fredj M Ben, Zemni I, Salah A Ben, et al. Acute coronary syndrome: factors predicting smoking cessation. EMHJ. 2020;26(3):315–22. DOI: https://doi:10.26719/emhj.19.034.
- Muneeb M, Khan AH, Niazi AK, Khan MU, Zanib J. Patterns of Dyslipidemia Among Acute Coronary Syndrome (ACS) Patients at a Tertiary Care Hospital in Lahore, Pakistan. Cureus. 2022;14(12):10–4. DOI: https://doi.org/10.7759/cureus.32378.
- 26. Kringeland E, Tell GS, Midtbø H, Igland J, Haugsgjerd TR, Gerdts Ε. Stage 1 hypertension, sex, and acute coronary syndromes during midlife: The Hordaland Health Study. Eur J Prev Cardiol. 2022;29(1):147-54. DOI:

https://doi.org/10.1093/eurjpc/zwab068.

 Konstantinou K, Tsioufis C, Koumelli A, Mantzouranis M, Kasiakogias A, Doumas M, et al. Hypertension and patients with acute coronary syndrome: Putting blood pressure levels into perspective. J Clin Hypertens. 2019;21(8):1135–43. DOI:

https://doi.org/10.1111/ jch.13622.

- Li Y, Liu Y, Liu S, Gao M, Wang W, Chen K, et al. Diabetic vascular diseases: molecular mechanisms and therapeutic strategies. Signal Transduct Target Ther. 2023;8(1). DOI: https://doi.org/10.1038/s41392-023-01400-z.
- Babes EE, Bustea C, Behl T, Abdel-Daim MM, Nechifor AC, Stoicescu M, et al. Acute coronary syndromes in diabetic patients, outcome, revascularization, and antithrombotic therapy. Biomed Pharmacother [Internet].
   2022;148(February):112772. Available from: https://doi.org/10.1016/j.biopha.2022.112772.
- Demirci D, Demirci DE, Chi G. Association between obesity grade and the age of the first acute coronary syndrome: Prospective observational study. Int J Cardiol. 2022;351(15):93–9. DOI: https://doi.org/https://doi.org/10.1016/j.ijcard.20

21.11.080.

 Moniruzzaman M, Koli A, Malik F, Islam S. Association between body mass index (BMI) and severity of coronary artery disease in young onset acute coronary syndrome (ACS). Natl Hear Found Hosp Res Institute, Cardiol. 2019;779. DOI:

https://doi.org/10.1093/eurheartj/ ehac779.058.

- 32. Prasetyo D. Correlation between serum uric acid level and severity of coronary artery stenosis in patients with acute coronary syndrome. Bandung Med J. 2021;52(132):1–6. https://doi.org/10.15395/mkb.v53n1.2221.
- Nawaz I, Javed T, Zahra SR, Majeed U, Noeman A, Hanif S. Hyperuricemia in acute coronary syndrome and its relation with metabolic syndrome. J Cardiovasc Dis. 2023;9(1). DOI:

https://doi.org/10.55958/jcvd.v19i1.121.