Bukti Korespondensi dengan Jurnal Berkala Epidemiologi-Universitas Airlangga

"HYPERLIPIDEMIA IS A DOMINANT RISK FACTOR FOR CORONARY HEART DISEASE"

14:44

← Re: PEMBERITAHUAN JURNAL BERKALA EPIDEMIOLOGI

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Terima kasih, semoga sehat selalu

Salam

On Wed, 16 Mar 2022 at 10:11, I Made Sudarma Adiputra <adiputradharma@gmail.com> wrote:

> Dear Pengelola Jurnal JEB
>
>
> Sebelumnya kami mengucapkan banyak terima kasih atas feedback pada manuscript yang kami submit pada jurnal yang Bapak/Ibu kelola, ijin menginformasikan untuk revisi manuscript sudah kami submit kembali melalui OJS JEB dan bersama ini juga kami kirimkan manuscript yang sudah coba kami revisi, Terima kasih, salam sejahtera.
>
>
> Salam hormat
>
> Adiputra
>
> Departemen Informasi Kesehatan &
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> Kesehatan Komunitas
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>
> **From:** Jurnal Berkala Epidemiologi
> **Sent:** Monday, March 14, 2022 1:25 PM
> **To:** adiputradharma@gmail.com
> **Subject:** PEMBERITAHUAN JURNAL BERKALA EPIDEMIOLOGI
>
> Dear Author,

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to Me
23/03/2022, 11:58

Dear Author,

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Terima kasih,

Salam

On Mon, 21 Mar 2022 at 15:12, I Made Sudarma Adiputra <adiputradharma@gmail.com> wrote:

> Dear Pengelola Jurnal JBE
>
>
> Bersama ini kami kirimkan revisi ke 2 pada manuscript yang kami submit di JBE, file revisi juga kami upload di OJS JBE, mohon petunjuk dan arahan selanjtnya. Terima kasih, semoga sehat dan bahagia selalu.
>
>
> Salam hormat
>
> Adiputra
>
> Departemen Informasi Kesehatan &
>
> Kesehatan Komunitas
>
> _____
>
> **From:** Jurnal Berkala Epidemiologi
> **Sent:** Saturday, March 19, 2022 9:01 AM
> **To:** I Made Sudarma Adiputra
> **Subject:** Re: PEMBERITAHUAN JURNAL BERKALA EPIDEMIOLOGI
>
>
> Dear Author,
>
> Berikut kami kirimkan komentar terkait gaya selingkung ke 2, naskah yang berisi komentar juga kami upload di OJS. Mohon segera diperbaiki sesuai komentar yang ada dan dikembalikan ke redaksi. Mohon konfirmasinya juga melalui email ini apabila sudah melakukan perbaikan naskah.
> Terima kasih, semoga sehat selalu

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to Jurnal Berkala Epidemiologi
19/05/2022, 16:35

Dear Pengelola Jurnal JBE

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Salam hormat
Adiputra

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to Me
12/09/2022, 09:00

Dear Author,

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Terima kasih,
Salam.

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Salam hormat

Adiputra

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Salam

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Dear Pengelola Jurnal JEB

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Salam hormat

Adiputra

Departemen Informasi Kesehatan &

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From: Jurnal Berkala Epidemiologi
Sent: Monday, September 12, 2022 9:00 AM
To: Adi Putra
Subject: Re: PEMBERITAHUAN JURNAL BERKALA EPIDEMIOLOGI

Dear Author,

Berikut kami kirimkan naskah yang sudah diberi komentar oleh reviewer 2. Silahkan dijadikan satu dengan perbaikan naskah dari reviewer 1, dan naskah dapat dikembalikan lagi ke redaksi.

Terima kasih,

Salam.

On Thu, 19 May 2022 at 15:35, Adi Putra <adiputradharma@gmail.com> wrote:

Dear Pengelola Jurnal JBE

Selamat sore pengelola jurnal JBE, manuscript sudah coba kami perbaiki dan bersama ini kami kirimkan kembali, mohon petunjuk dan arahan selanjutnya. terima kasih.

Salam hormat

Adiputra

Pada Kamis, 19 Mei 2022 09.00.07 GMT+8, Jurnal Berkala Epidemiologi <jbepid@gmail.com> menulis:

Dear Author,

Berikut kami kirimkan naskah yang sudah direview oleh reviewer 1 (file terlampir). Silahkan perbaiki sesuai komentar yang ada, dan naskah dikembalikan ke redaksi melalui email ini.

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Salam hormat

Adiputra

Departemen Informasi Kesehatan &

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From: Jurnal Berkala Epidemiologi
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Dear Author,

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Terima kasih, semoga sehat selalu

Salam

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Jurnal Berkala Epidemiologi
to Me
19/05/2022, 09:00

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Terima kasih dan sehat selalu,
Salam.

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Salam.

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> Salam hormat
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> Adiputra
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Salam hormat

Adiputra

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Terima kasih, semoga sehat selalu

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Dear Author,

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Terima kasih,
Salam.

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Salam

Adiputra

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From: Jurnal Berkala Epidemiologi
Sent: Thursday, September 15, 2022 2:52 PM
To: I Made Sudarma Adiputra
Subject: Re: PEMBERITAHUAN JURNAL BERKALA EPIDEMIOLOGI

Dear author,

Mohon untuk menambahkan 1 kata kunci lagi pada naskah. Kata kunci tersebut harus sesuai dengan yang terdaftar pada SDGs (sesuaikan dengan tema naskah, naskah

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Subject: Re: PEMBERITAHUAN JURNAL BERKALA EPIDEMIOLOGI

Dear author,

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Terima kasih,
Salam

On Mon, 12 Sept 2022 at 10:14, I Made Sudarma Adiputra <adiputradharma@gmail.com> wrote:

> Dear Pengelola Jurnal JBE
>
> Selamat siang Bapak/Ibu Pengelola Jurnal JBE, manuscript sudah coba kami revisi untuk dua reviewer dan hasilnya sudah kami gabungkan, mohon petunjuk untuk tahap selanjutnya.
>
> Salam
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> Adiputra
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> Departemen Informasi Kesehatan &
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Dear Author,

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Kemudian kami menghimbau juga untuk author agar menambahkan 1-2 artikel dari artikel yang terbit di jurnal (tahun terbitan 2021 atau 2022) kami dengan menyesuaikan isi naskah. Hasil penambahan keyword SDGs dan sitasi artikel JBE kami harap dapat kami terima paling lambat 10 Januari 2023. Apabila setelah tanggal tersebut kami tidak menerima hasil perbaikan, maka penambahan akan dilakukan oleh redaksi kami.

Terima kasih,
Salam.

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Jurnal Berkala Epidemiologi
to Me
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Dear Author,

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Terima kasih

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Dear Author,

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HYPERLIPIDEMIA IS A DOMINANT RISK FACTOR OF CORONARY HEART DISEASE IN INDONESIA

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I Made Sudarma Adiputra[1], Ni Wayan Trisnadewi[2], Ni Putu Wiwik Oktaviani[3], Dewa Putu Dwita[4]

[1] Public Health, STIKES Wira Medika Bali, Indonesia, adiputra@stikeswiramedika.ac.id
[2] Doctoral Study Program of Medicine, Udayana University, Indonesia, trisnawika09@gmail.com
[3] Nursing program, STIKES Wira Medika Bali, Indonesia, oktaviani.wiwik@yahoo.com
[4] Cardiac Centre Care, Sanglah Hospital, Bali, Indonesia, dwita608@gmail.com
Correspondence Author: I Made Sudarma Adiputra, e-mail: adiputra@stikeswiramedika.ac.id, STIKES Wira Medika, Bali, 80113, Indonesia

ARTICLE INFO

ABSTRACT

Background: Coronary heart disease (CHD) is a major health problem in developed and developing countries. Until now, the death rate due to CHD is the highest in the world. Risk factors for CHD consist of modifiable major risk factors and non-modifiable risk factors. Modifiable risk factors include: Hyperlipidemia, hypertension, diabetes mellitus, obesity, and smoking. **AIMS:** This study aims to determine the major risk factors that can be modified by the incidence of coronary heart disease (CHD). **Methods:** The study design was unmatched case-control, the number of samples was 43 cases and 86 controls, which were similar in the variables of age, sex, and address. Cases and controls were taken at the integrated heart center of Sanglah Hospital Denpasar. Cases were patients diagnosed with CHD which were taken from the medical record data of the integrated heart center of Sanglah Hospital, while controls were non-CHD patients who were taken from medical record data at the same hospital. Data analysis was performed by using Chi-Square test and logistic regression. **Results:** The results showed that there were three risk factors that statistically significantly increased the incidence of CHD, namely history of total cholesterol $\geq$ 240mg/dl adjusted OR = 4.64 (95% CI: 1.60-13.49), Diabetes mellitus Type II adjusted OR = 2.85 (95% CI: 1.16- 6.99) and Smoke adjusted OR 2.54 (95% CI: 1.01-6.46). **Conclusion**: History of high cholesterol is statistically the most dominant risk factor for the incidence of CHD.

Keyword: CHD, Hiperlipidemia, Case Control

ABSTRAK

Latar belakang : Penyakit jantung koroner (PJK) merupakan masalah kesehatan utama di Negara maju dan Negara berkembang, sampai saat ini angka kematian akibat PJK menduduki urutan tertinggi didunia. Faktor risiko PJK terdiri dari faktor risiko mayor yang dapat dimodifikasi dan

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faktor risiko yang tidak dapat dimodifikasi. Faktor risiko yang dapat dimodifikasi seperti : Hiperlipidemia, hipertensi, diabetes mellitus, obesitas dan merokok. Penelitian ini bertujuan untuk mengetahui faktor risiko mayor yang dapat dimodifikasi kejadian penyakit jantung coroner (PJK).

Metode : Rancangan penelitian adalah unmatched case-control, jumlah sampel 43 kasus dan 86 kontrol, yang dimiripkan dalam variabel umur, jenis kelamin dan alamat. Kasus dan kontrol diambil di pusat jantung terpadu RSUP Sanglah Denpasar. Kasus adalah pasien yang didiagnosis PJK yang diambil dari data rekam medis pusat jantung terpadu RSUP Sanglah, sedangkan **k**ontrol adalah pasien Non PJK yang diambil dari data rekam medis pada rumah sakit yang sama. Analisis data dilakukan dengan uji Chi-Square dan Regresi logistic.

Hasil: Hasil penelitian menunjukkan bahwa terdapat tiga faktor risiko yang secara statistik signifikan meningkatkan kejadian PJK, yaitu riwayat kolesterol total 240mg/dl AOR = 4,64 (95% CI: 1,60-13,49), Diabetes mellitus Tipe II AOR = 2,85 (95% CI: 1,16-6,99) dan merokok AOR 2,54 (95% CI: 1,01-6,46).

Simpulan : Riwayat Cholesterol tinggi secara statistik merupakan faktor risiko paling dominan terhadap kejadian PJK.

Kata Kunci : PJK, Kolesterol, Faktor Risiko

INTRODUCTION

Heart disease is a degenerative disease related to lifestyle and socioeconomic conditions in society. Heart disease is a major health problem in developed and developing countries and causes one third of deaths in the world (Mozaffarian et al., 2016) (Malakar et al., 2019). Coronary heart disease (CHD) is the most common heart disease compared to other types of heart disease (Roth et al., 2017). CHD is a real threat to sustainable development in this century (Prabhakaran et al., 2018). Data from the World Health Organization (WHO) in 2008 stated that more than 17 million people in the world died from heart and blood vessel disease, around 7.3 million deaths were caused by coronary heart disease (World Health Organization, 2017).

In Indonesia, there has been a shift in the incidence of heart and blood vessel disease from 10th in 1980 to 8th in 1986. Meanwhile, the cause of death is still in the 3rd position. Although there is no definite epidemiological data, the morbidity/ mortality rate seems to be increasing. The results of the 2001 National Health Survey show that three out of 1,000 Indonesians suffer from CHD (Iskandar, Hadi, & Alfridsyah, 2017). The results of the Basic Health Research (Riskesdas) in 2018 showed that 1.5 percent or 15 out of 1,000 Indonesians suffer from coronary heart disease (Harigustian, Dewi, & Khoiriyati, 2016).

At the Sanglah General Hospital (RSUP) Denpasar, based on the annual activity report of the Integrated Heart Services at Sanglah Hospital Denpasar, the number of CHD patient visits to the PJT polyclinic at Sanglah Hospital Denpasar in the last three years was still relatively high. In 2017 there were 12,356 CHD patients, in 2018 there were 29,181 visits, there were 559 (1.9%) cases of new CHD patients and in 2019 there were 20,840 visits, there were 569 (2.7%) new CHD patients.

The cause of CHD is not yet known with certainty, however, there are several risk factors that are thought to have contributed to the incidence of CHD. according to Malakar et al. (2019) lifestyle, environmental factors, and genetic factors play a role as risk factors for the development of cardiovascular disease (Malakar et al., 2019). Risk factors for CHD can be divided into two, namely risk factors that can be changed or modified, and biological risk factors that cannot be changed. Biological risk factors that cannot be changed include age, sex, and family history. Modifiable risk factors include hyperlipidemia, hypertension, diabetes mellitus, smoking habits, poor diet, lack of movement, stress, obesity, and alcohol consumption (Herman & Syukri, 2015).

Smoking history has a role in the occurrence of CHD, active smoking has a strong relationship with the incidence of CHD (Grubb et al., 2020). Smoking is a major risk factor for cardiovascular disease (CVD) and a leading avoidable cause of death worldwide (Kondo, Nakano, Adachi, &

Murohara, 2019). According to Messner & Bernhard (2014) smoking is one of the most important preventable risk factors for the development of atherosclerosis (Messner & Bernhard, 2014).

Hypertension is thought to increase the risk of CHD events, according to Li et al (2020), people who have a history of hypertension and obesity are closely related to the incidence of CHD in the future (Li et al., 2020). A history of suffering from type 2 diabetes is also associated with the incidence of CHD. According to Naito & Miyauchi, (2017) diabetes mellitus type 2 (T2DM) is a major risk factor for coronary artery disease (CAD) (Naito & Miyauchi, 2017). Increased levels of glucose triglyceride index (TyG) are an independent risk factor for coronary artery disease (CAD) in patients with type 2 diabetes mellitus (Si et al., 2021) (Park et al., 2020), high triglyceride levels are a predictor of post percutaneous coronary intervention (PCI) CHD incidence (Ma et al., 2020) (Jin et al., 2018). A history of hyperlipidemia is also thought to increase the risk of CHD events, according to Nava-Boggan et al. (2015) a history of hyperlipidemia in young adulthood increases the risk of coronary heart disease in the future (Navar-Boggan et al., 2015) (Stewart, McCallin, Martinez, Chacko, & Yusuf, 2020).

Aging, family history and gender are risk factors for CHD that cannot be modified so that the handling is done more to control risk factors that can be modified. Modernization and changes in people's lifestyles can be considered as causes of CHD. Seeing the phenomenon that occurs in society today, generally people of productive age enjoy unhealthy lifestyles in their daily life such as poor food consumption, smoking habits, and lack of physical activity (Indonesian Heart Association, 2019).

The disease burden of CHD tends to increase due to the tendency of an increasing number of cases. The burden on CHD patients or their families is very heavy, both from a medical, psychological, social, and financial perspective. Comprehensive efforts are needed to prevent CHD and for that, more research is needed to determine the risk factors for CHD that can be changed or modified. This study aims to determine the dominant risk factors that increase the incidence of CHD

METHODS

This study used an unmatched case control design in which the case group and the control group were similar in terms of age, sex, and place of residence. The study was conducted in November 2020, February-April 2020. Case samples were patients diagnosed with CHD by doctors who came to the integrated cardiac service clinic at Sanglah Hospital Denpasar, while the control sample was patients with non-CHD who came to integrated cardiac polyclinic, based on clinical diagnosis, electrocardiography, and cardiac catheterization. The number of samples was determined using the Lemeshow formula and calculated using the WHO sample size calculator 2.0, and the number of case samples was 43 and control samples were 83.

All variables in this study were used as categorical variables as presented in Table 2, namely variables of history of hyperlipidemia, history of smoking, history of hypertension and history of diabetes mellitus.

Data analysis was performed using IBM SPSS software univariate (Table 1), bivariate (Table 2) and multivariate (Table 3). Univariate analysis is to determine the frequency distribution of each variable. Bivariate analysis to determine crude OR with Chi-Square. Multivariate analysis to calculate adjusted OR with logistic regression method. Crude OR and adjusted OR significance levels were set with 95% CI.

Research has been declared ethical by the Research Ethics Commission of the Faculty of Medicine, Udayana University/Sanglah Hospital, with no: 2412 / UN14.2.2.VII.14 / LT / 2020. Prior to the research, the potential subjects were informed with verbal and written description about procedures and that they could withdraw from the study. Subjects who agreed to participate in the study provided consent before measurement.

RESULTS

In Table 1, the characteristics of the case and control groups based on gender, age, address, education, and occupation are presented. Respondents who participated in this study were predominantly male, the case group 27 (62.8%) and the control group 47 (54.7%). Respondents' age was dominated > 50 years as many as 28 (65.1%) in the case group and 55 (64.0%) in the control group. For the case group living in urban areas 23 (53.5%) while the control group lived more in rural areas 49 (57%). For the level of education, both cases and controls are dominated by high school graduates. Respondents' occupations are predominantly self-employed

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Table 1.

Baseline Characteristics of Subjects

Baseline Characteristics	Case	Control	p-value
Gender			
Male	27 (62.8)	47 (54.7)	0.380
Female	16 (37.2)	38 (42.6	
Age			
≥ 55	25 (34,9)	31 (36,0)	0.897
< 55	28 (65,1)	55 (64,0)	
Residence			
Rural	20 (46,5)	49 (57,0)	0.263
Urban	23 (53,5)	37 (43,0)	
Education			
None	0	2 (2,3)	0.727
Elementary	3 (7,0)	13 (11,6)	
Junior High School	5 (11,6)	11 (12,8)	
Senior High School	29 (67,4)	39 (45,3)	
University	6 (24,0)	24 (27,9)	
Occupation			
None	4 (9,3)	6 (7,0)	0.233
Employe	8 (18,6)	9 (10,5)	
Self-Employed	23 (53,5)	51 (59,3)	
Public Servant	8 (18,6)	20 (23,3)	
Family history of CHD			
CHD	5 (11,6)	2(2,3)	0.029
None	38 (88,4)	84(97,7)	

Tabel 2

Bivariate analysis results (Crude Odds Ratio) for CHD

Risk Factor	Cases	Control	Crude OR	95% CI
Total Cholesterol				
≥ 240mg/dl	13	7	4,89	1,78-13,43
< 240mg/dl	30	79		
Triglyceride Levels				
≥ 200mg/dl	6	3	4,48	1,06-18,91
< 200mg/dl	37	83		
Diabetes mellitu sType II				

Risk Factor	Cases	Control	Crude OR	95% CI
Yes	17	14	3,36	1,46-7,77
None	26	72		
Hypertension stage I				
Yes	12	10	2,94	1,15-7,51
None	31	76		
Hypertension stage II-IV				
Yes	10	7	3,42	1,20-9,75
None	33	78		
Smoke				
Yes	15	13	3,01	1,27-7,17
None	28	73		
Body Mass Indek ≥ 25				
≥ 25	17	16	2,86	1,26-6,48
< 25	26	70		

Tabel 3

Multivariable-Adjusted odds ratio (AOR) for CHD

Risk Factor	Adjusted OR	95%CI		p-value
		Lower	Uper	
Total Cholesterol ≥ 240mg/dl	4.64	1.6	13.49	0.005
Diabetes mellitusType II	2.85	1.16	6.99	0.022
Smoke	2.54	1.01	6.46	0.049

In Table 2, the results of the bivariate analysis between cases and controls show that the risk factors that significantly increase the incidence of CHD are: Total Cholesterol Crude OR = 4,89 (95% CI: 1.78-13,43), Triglyceride Levels crude OR = 4.48 (95% CI: 1.06-18.92), Diabetes mellitus Type II crude OR = 3,36 (95%CI: 1.46-7.77), Hypertension stage I crude OR = 2,94 (95% CI: 1.15-7.51), Hypertension stage II-IV crude OR = 3.42 (95% CI: 1.20-9.75), Smoke crude OR = 3.01 (95% CI: 1.27-7,17) and Body Mass Index ≥ 25 Crude OR = 2.86 (95% CI: 1.26-6.48)

In Table 3, the results of the multivariate analysis using the logistic regression method of seven variables were found to be significant in the

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bivariate analysis, namely: Total Cholesterol, Triglyceride Levels, Diabetes mellitus Type II, Hypertension stage I, Hypertension stage II-IV, Smoke and Body Mass Index ≥ 25. The results of multivariate analysis showed three risk factors associated with the incidence of CHD. Total Cholesterol AOR = 4.64 (95% CI: 1.60-13.49), Diabetes mellitus Type II AOR = 2.85 (95% CI: 1.16- 6.99) and Smoke 2.54 (95% CI: 1.01-6.46).

DISCUSSION

The results of this study indicate that a history of hyperlipidemia has a significant relationship with the incidence of CHD with an AOR 4.64 (95% CI: 1.60-13.49), people with a history of hyperlipidemia have a 4.64 times greater risk of suffering from CHD than people those with normal lipid levels. This result is supported by the study of Verschuren (1995) that high lipid levels are a risk factor for CHD in almost all countries in the world OR = 2.74 (95% CI: 2.07-3.63) (Verschuren, 1995). According to Wilson et al. (1998) people who have cholesterol levels ≥240 have an increased risk of CHD events RR = 1.90 (95% CI: 1.47–2.47). According to Nava-Boggan et al. (2015) a history of hyperlipidemia in young adulthood increases the risk of coronary heart disease in the future (Navar-Boggan et al., 2015) (Stewart et al., 2020). CHD is a cardiovascular disorder that occurs due to arteriosclerosis in the coronary blood vessels, arteriosclerosis in the coronary arteries is usually caused by plaque or lipids depositing in the intima of the coronary arteries (Libby & Plutzky, 2000). Malfunctioning of the arterial walls begins with arteriosclerosis, which is caused by a buildup of lipoproteins in the intima lining of the coronary arteries (Badimon, Padró, & Vilahur, 2012). In the circulatory system, water-insoluble lipids circulate by attaching to water-soluble lipoproteins (apoliproteins). High concentrations of low-density lipoprotein (LDL) can penetrate the affected and oxidized endothelium (Ibanez, Vilahur, & Badimon, 2007). Oxidation of LDL will attract leukocytes into the intima tunica of the coronary arteries, which will then be taken up by macrophages and there is the formation of foamy cells. The foamy cells will replicate and form lesions, this lesion will be called arteriosclerosis in the early stages, this repeated process of lipids will cause a buildup or lesions gradually in the lining of the coronary blood and eventually arteriosclerosis which can block blood circulation in the coronary arteries and resulting in CAD (Ross, 1999) (Malakar et al., 2019).

History of type 2 diabetes mellitus obtained statistically significant results with the incidence of CHD AOR = 2.85 (95% CI: 1.16- 6.99), this result is supported by the study of Si et al. (2021) increased levels of glucose triglyceride index (TyG) in patients with type 2 diabetes are an independent risk factor for coronary artery disease (CAD), TyG index ≥8.2 OR = 5.732 (95% CI: 1.722–19.075) (Si et al., 2021). High TyG in patients with type 2 diabetes increases the risk of CHD events OR = 2,200 (95% CI: 1,555–3,113) (Park et al., 2020). High triglyceride level is a predictor of post percutaneous coronary intervention (PCI) CHD incidence (Ma et al., 2020) (Jin et al., 2018). According to Bhatia (2010) type 2 diabetes is associated with a marked increase in the risk of coronary artery disease, dyslipidemia is believed to be the main source of increased risk of CHD in type 2 DM patients.Several studies on diabetes patients have shown a decreased incidence of coronary artery disease with the use of drugs that are lowering low-density lipoprotein levels in diabetic patients, but another form of dyslipidemia (hypertriglyceridemia) is believed to play a role in the etiology of coronary artery disease in diabetes (Bhatia, 2010).

In this study, smoking history was a risk factor for CHD AOR 2.54 (95% CI: 1.01-6.46), people who had a history of smoking had a 2.54 times greater risk of developing CHD. These results are in line with research conducted by Grubb et al. (2020) smoking history has a role in the occurrence of CHD, active smokers have a strong relationship with the incidence of CHD (Grubb et al., 2020). Smoking is a major risk factor for cardiovascular disease (CVD) and a leading avoidable cause of death worldwide (Kondo et al., 2019). According to Messner & Bernhard (2014) smoking is one of the most important preventable risk factors for the development of atherosclerosis (Messner & Bernhard, 2014). Smoking can cause decreased oxygen levels to the heart, increased blood pressure and pulse, decreased HDL (High Density Lipoprotein) levels and increased LDL (Low Density Lipoprotein) levels, increased thrombogenesis and vasoconstriction. The risk of CHD from cigarettes is strongly influenced by the duration and depth of smoking, the more cigarettes smoked in a day, the more CHD risk increases and the deeper the cigarette smoke is smoked increases

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the risk of CHD. Smoking also increases coronary artery obstruction because it produces endothelial denudation and platelet adhesion to the tunica intima layer, this increases lipid infiltration and decreases platelet growth factor (Malakar et al., 2019).

The results of this study indicate that a history of hypertension increases the risk of CHD events in the future, Hypertension stage I crude OR = 2.94 (95% CI: 1.15-7.51), Hypertension stage II-IV crude OR = 3.42 (95% CI: 1.20-9.75), people suffering from stage II-IV hypertension had a 3.42 times greater risk of suffering from CAD than people without hypertension. The results of this study are supported by research by Li et al (2020) that people who have a history of hypertension and obesity are closely related to the incidence of CHD in the future (Li et al., 2020). The results of the research are in line with Kokubo & Matsumoto (2017) that hypertension is closely related to the incidence of CHD and other heart disorders, in which men have a greater tendency (Kokubo & Matsumoto, 2017). Stage 1 hypertension is a risk factor for CAD incidence in both men and women with RR = 1.67 (95% CI: 1.28–2.18) RR = 1.73 (95% CI: 1.19–2.52), while the higher CHD risk was found in stage II- IV RR = 1.84 (95% CI: 1.37–2.49) RR = 2.12 (95% CI: 1.42–3.17) (Wilson et al., 1998). According to Kokubo et al., (2008) stage 1 hypertension increased the incidence of CAD in both men RR = 3.35 (95% CI: 1.64–6.80) and women RR: 2.97 (95% CI: 1.11–7.91) (Kokubo et al., 2008). Continuously high blood pressure can cause damage to the artery walls. The lining of the blood vessels will thicken so that it can increase the resistance to blood flow. Structural changes in the small arteries and arterioles will cause progressive blockage of blood flow. When the blood vessels are narrowed, arterial blood flow will be interrupted and can cause tissue infarction.

Research Limitations

The weakness of this study is the wide AOR range in the analysis of risk factors for total cholesterol (95% CI: 1.60-13.49), possibly due to the small sample size. Based on the results of this study, the recommendation that can be put forward is the need for structured education to the public regarding risk factors that can still be changed to reduce or prevent the risk of CHD. Another recommendation is to conduct a study of modifiable risk factors in CHD with a larger sample size.

CONCLUSION

CHD is also known as CAD or arteriosclerosis; CHD is one of the main causes of death and morbidity in the world in both developed and developing countries. The exact cause of CHD is not known with certainty, in this study there were four risk factors that statistically increased the risk of CHD events, including a history of hyperlipidemia, a history of type 2 diabetes, a history of hypertension and smoking, among the four risk factors obtained, from multivariate analysis obtained a history of Hyperlipidemia is the dominant risk factor for CHD events.

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AUTHOR CONTRIBUTIONS

All persons who have made substantial contributions to the work reported in the manuscript, I Made Sudarma Adiputra (concepts, design, definition of intellectual content, clinical studies, data analysis, statistical analysis, manuscript preparation, manuscript editing and manuscript review), Ni Wayan Trisnadewi (literature search, data analysis and statistical analysis), Ni Putu Wiwik Oktaviani literature search, data acquisition, data analysis and statistical analysis) and Dewa Putu Dwita (Clinical Studies).

CONFLIC OF INTEREST

The authors declare that they have no conflicts of interests.

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ORIGINAL ARTICLE

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HYPERLIPIDEMIA IS A DOMINANT RISK FACTOR OF CORONARY HEART DISEASE

Hiperlid Merupakan Faktor Risiko Dominan Kejadian Penyakit Jantung Kororner

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ABSTRACT

Background: Coronary heart disease (CHD) is a major health problem in developed and developing countries. Until now, the death rate due to CHD is the highest in the world. Risk factors for CHD consist of modifiable major risk factors and non-modifiable risk factors, modifiable risk factors include: Hyperlipidemia, hypertension, diabetes mellitus, obesity, and smoking. **Purpose:** This study aims to determine the major risk factors that can be modified by the incidence of coronary heart disease (CHD). **Methods:** The study design was unmatched case-control, the number of samples was 43 cases and 86 controls taken by purposive sampling technique, case samples were CHD patients who had been diagnosed by a cardiologist and controls were non-CHD patients who visited the cardiac polyclinic, which were similar in the variables of age, sex, and address. Cases and controls were taken at the integrated heart center of Sanglah Hospital Denpasar. Cases were patients diagnosed with CHD which were taken from the medical record data of the integrated heart center of Sanglah Hospital, while controls were non-CHD patients who were taken from medical record data at the same hospital. Data analysis was performed by using Chi-Square test and logistic regression. **Results:** The results showed that there were three risk factors that statistically significantly increased the incidence of CHD, namely history of total cholesterol $\geq$ 240mg/dl adjusted OR = 4.64 (95% CI: 1.60-13.49), Diabetes mellitus Type II adjusted OR = 2.85 (95% CI: 1.16-6.99) and Smoke adjusted OR 2.54 (95% CI: 1.01-6.46). **Conclusion**: History of high cholesterol is statistically the most dominant risk factor for the incidence of CHD.

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ABSTRAK

Latar belakang : Penyakit jantung koroner (PJK) merupakan masalah kesehatan utama di Negara maju dan Negara berkembang, sampai saat ini angka kematian akibat PJK menduduki urutan tertinggi didunia. Faktor risiko PJK terdiri dari faktor risiko mayor yang dapat dimodifikasi dan faktor risiko yang tidak dapat dimodifikasi, faktor risiko yang dapat

dimodifikasi seperti : Hiperlipidemia, hipertensi, diabetes mellitus, obesitas dan merokok. Penelitian ini bertujuan untuk mengetahui faktor risiko mayor yang dapat dimodifikasi kejadian penyakit jantung coroner (PJK). **Metode** : Rancangan penelitian adalah unmatched case-control, jumlah sampel 43 kasus dan 86 kontrol diambil dengan Teknik *purposive sampling*, sampel kasus adalah pasien PJK yang sudah didiagnosis oleh dokter jantung dan kontrol adalah pasien non PJK yang berkunjung ke poli jantung, yang dimiripkan dalam variabel umur, jenis kelamin dan alamat. Kasus dan kontrol diambil di pusat jantung terpadu RSUP Sanglah Denpasar. Kasus adalah pasien yang didiagnosis PJK yang diambil dari data rekam medis pusat jantung terpadu RSUP Sanglah, sedangkan **k**ontrol adalah pasien Non PJK yang diambil dari data rekam medis pada rumah sakit yang sama. Analisis data dilakukan dengan uji Chi-Square dan Regresi logistic. **Hasil:** Hasil penelitian menunjukkan bahwa terdapat tiga faktor risiko yang secara statistik signifikan meningkatkan kejadian PJK, yaitu riwayat kolesterol total 240mg/dl AOR = 4,64 (95% CI: 1,60-13,49), Diabetes mellitus Tipe II AOR = 2,85 (95% CI: 1,16-6,99) dan merokok AOR 2,54 (95% CI: 1,01-6,46). **Simpulan :** Riwayat Cholesterol tinggi secara statistik merupakan faktor risiko paling dominan terhadap kejadian PJK.

INTRODUCTION

Heart disease is a degenerative disease related to lifestyle and socioeconomic conditions in society. Heart disease is a major health problem in developed and developing countries and causes one third of deaths in the world (Malakar et al., 2019). Coronary heart disease (CHD) is the most common heart disease compared to other types of heart disease (Roth et al., 2017). CHD is a real threat to sustainable development in this century (Prabhakaran et al., 2018). Data from the World Health Organization (WHO) in 2008 stated that more than 17 million people in the world died from heart and blood vessel disease, around 7.3 million deaths were caused by coronary heart disease (World Health Organization, 2017).

In Indonesia, there has been a shift in the incidence of heart and blood vessel disease from 10th in 1980 to 8th in 1986. Meanwhile, the cause of death is still in the 3rd position. Although there is no definite epidemiological data, the morbidity/ mortality rate seems to be increasing. The results of the 2001 National Health Survey show that three out of 1,000 Indonesians suffer from CHD (Iskandar, Hadi, & Alfridsyah, 2017).

At the Sanglah Central General Hospital Denpasar, based on the annual activity report of the Integrated Heart Services at Sanglah Central General Hospital Denpasar, the number of CHD patient visits to the *Pelayanan Jantung Terpadu (PJT)* polyclinic at Sanglah Hospital Denpasar in the last three years was still relatively high. In 2017 there were 12,356 CHD patients, in 2018 there were 29,181 visits, there were 559 (1.91%) cases of new CHD patients and in 2019 there were 20,840 visits, there were 569 (2.73%) new CHD patients.

The cause of CHD is not yet known with certainty, however, there are several risk factors that are thought to have contributed to the incidence of CHD. according to Malakar et al. (2019) lifestyle, environmental factors, and genetic factors play a role as risk factors for the development of cardiovascular disease (Malakar et al., 2019). Risk factors for CHD can be divided into two, namely risk factors that can be changed or modified, and biological risk factors that cannot be changed. Biological risk factors that cannot be changed include age, sex, and family history. Modifiable risk factors include hyperlipidemia, hypertension, diabetes mellitus, smoking habits, poor diet, lack of movement, stress, obesity, and alcohol consumption (Sarini & Suharyo, 2018).

Smoking history has a role in the occurrence of CHD, active smoking has a strong relationship with the incidence of CHD (Grubb et al., 2020). Smoking is a major risk factor for cardiovascular disease (CVD) and a leading avoidable cause of death worldwide (Kondo, Nakano, Adachi, & Murohara, 2019). More than a quarter of adults with CVD have a lifetime history of smoking (Reynolds et al., 2021).

Hypertension is thought to increase the risk of CHD events, according to Li et al (2020), people who have a history of hypertension and obesity are

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closely related to the incidence of CHD in the future. A history of suffering from type 2 diabetes is also associated with the incidence of CHD. Diabetes mellitus type 2 (T2DM) is a major risk factor for coronary artery disease (CAD) (Naito & Miyauchi, 2017). Increased levels of glucose triglyceride index (TyG) are an independent risk factor for coronary artery disease (CAD) in patients with type 2 diabetes mellitus (Si et al., 2021) (Park et al., 2020), high triglyceride levels are a predictor of post percutaneous coronary intervention (PCI) CHD incidence (Ma et al., 2020) (Jin et al., 2018). A history of hyperlipidemia is also thought to increase the risk of CHD events, according to Stewart et al. (2020) a history of hyperlipidemia in young adulthood increases the risk of coronary heart disease in the future.

Aging, family history and gender are risk factors for CHD that cannot be modified so that the handling is done more to control risk factors that can be modified. Modernization and changes in people's lifestyles can be considered as causes of CHD. Seeing the phenomenon that occurs in society today, generally people of productive age enjoy unhealthy lifestyles in their daily life such as poor food consumption, smoking habits, and lack of physical activity (Indonesian Heart Association, 2019).

The disease burden of CHD tends to increase due to the tendency of an increasing number of cases. The burden on CHD patients or their families is very heavy, both from a medical, psychological, social, and financial perspective. Comprehensive efforts are needed to prevent CHD and for that, more research is needed to determine the risk factors for CHD that can be changed or modified. This study aims to determine the dominant risk factors that increase the incidence of CHD.

METHODS

This study used an unmatched case control design in which the case group and the control group were similar in terms of age, sex, and place of residence. The study was conducted in November 2020, February-April 2020. Case samples were patients diagnosed with CHD by doctors who came to the integrated cardiac service clinic at Sanglah Hospital Denpasar, while the control sample was patients with non-CHD who came to integrated cardiac polyclinic, based on clinical diagnosis, electrocardiography, and cardiac catheterization. The number of samples was determined using the Lemeshow formula and calculated using the WHO sample size calculator 2.0, and the number of case samples was 43 and control samples were 83. The sample was taken using purposive sampling technique, the inclusion criteria for the case sample were patients who had been diagnosed with CHD by a cardiologist, while the control sample was non-CHD patients (extrasystolic, hypertension and non-CHD/CHF patients) who underwent an examination at the cardiac polyclinic.

All variables in this study were used as categorical variables as presented in Table 2, namely variables of history of hyperlipidemia, history of smoking, history of hypertension and history of diabetes mellitus. Data analysis was performed using IBM SPSS software univariate (Table 1), bivariate (Table 2) and multivariate (Table 3). Univariate analysis is to determine the frequency distribution of each variable. Bivariate analysis to determine crude OR with Chi-Square. Multivariate analysis to calculate adjusted OR with logistic regression method. Crude OR and adjusted OR significance levels were set with 95% CI.

Research has been declared ethical by the Research Ethics Commission of the Faculty of Medicine, Udayana University/Sanglah Hospital, with no: 2412 / UN14.2.2.VII.14 / LT / 2020. Prior to the research, the potential subjects were informed with verbal and written description about procedures and that they could withdraw from the study. Subjects who agreed to participate in the study provided consent before measurement.

RESULTS

In Table 1, the characteristics of the case and control groups based on gender, age, address, education, and occupation are presented. Respondents who participated in this study were predominantly male, the case group 27 (62.79%) and the control group 47 (54.65%). Respondents' age was dominated > 50 years as many as 28 (65.11%) in the case group and 55 (64%) in the control group. For the case group living in urban areas 23 (53.49%) while the control group lived more in rural areas 49 (57%). For the level of education, both cases and controls are dominated by high school graduates. Respondents' occupations are predominantly self-employed.

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Table 1.

Baseline Characteristics of Subjects

Baseline Characteristics	Case	Control	p-value
Gender			
Male	27 (62.79)	47 (54.65)	0.380
Female	16 (37.21)	39 (43.35)	
Age			
≥ 55	15 (34.88)	31 (36.04)	0.897
< 55	28 (65.11)	55 (63.96)	
Residence			
Rural	20 (46.51)	49 (56.97)	0.263
Urban	23 (53.49)	37 (43.03)	
Education			
None	0	2 (2.32)	0.727
Elementary	3 (6.97)	13 (15.11)	
Junior High School	5 (11.62)	11 (12.79)	
Senior High School	29 (67.44)	39 (45.34)	
University	6 (13.95)	24 (27.90)	
Occupation			
None	4 (9.30)	6 (6.97)	0.233
Employe	8 (18.60)	9 (10.46)	
Self-Employed	23 (50)	51 (59.30)	
Public Servant	8 (18.60)	20 (23.25)	
Family history of CHD			
CHD	5 (11.62)	2(2.32)	0.029
None	38 (88.38)	84(97.68)	

In Table 2, the results of the bivariate analysis between cases and controls show that the risk factors that significantly increase the incidence of CHD are: Total Cholesterol Crude OR = 4.89 (95% CI: 1.78-13.43), Triglyceride Levels crude OR = 4.48 (95% CI: 1.06-18.92), Diabetes mellitus Type II crude OR = 3.36 (95%CI: 1.46-7.77), Hypertension stage I crude OR = 2.94 (95% CI: 1.15-7.51), Hypertension stage II-IV crude OR = 3.42 (95% CI: 1.20-9.75), Smoke crude OR = 3.01 (95% CI: 1.27-7.17) and Body Mass Index ≥ 25 Crude OR = 2.86 (95% CI: 1.26-6.48).

Tabel 2

Bivariate analysis results (Crude Odds Ratio) for CHD

Risk Factor	Cases	Control	Crude OR	95% CI
Total Cholesterol				
≥ 240mg/dl	13	7	4.89	1.78-13.43
< 240mg/dl	30	79		
Triglyceride Levels				
≥ 200mg/dl	6	3	4.48	1.06-18.91
< 200mg/dl	37	83		
Diabetes mellitu sType II				
Yes	17	14	3.36	1.46-7.77
None	26	72		
Hypertension stage I				
Yes	12	10	2.94	1.15-7.51
None	31	76		
Hypertension stage II-IV				
Yes	10	7	3.42	1.20-9.75
None	33	78		
Smoke				
Yes	15	13	3.01	1.27-7.17
None	28	73		
Body Mass Indek ≥ 25				
≥ 25	17	16	2.86	1.26-6.48
< 25	26	70		

In Table 3, the results of the multivariate analysis using the logistic regression method of seven variables were found to be significant in the bivariate analysis, namely: Total Cholesterol, Triglyceride Levels, Diabetes mellitus Type II, Hypertension stage I, Hypertension stage II-IV, Smoke and Body Mass Index ≥ 25. The results of multivariate analysis showed three risk factors associated with the incidence of CHD. Total Cholesterol AOR = 4.64 (95% CI: 1.60-13.49), Diabetes mellitus Type II AOR = 2.85 (95% CI: 1.16- 6.99) and Smoke 2.54 (95% CI: 1.01-6.46).

Tabel 3

Multivariable-Adjusted odds ratio (AOR) for CHD

Risk Factor	Adjusted OR	95%CI Lower	95%CI Uper	*p-value*
Total Cholesterol ≥ 240mg/dl	4.64	1.60	13.49	0.005
Diabetes mellitusType II	2.85	1.16	6.99	0.022
Smoke	2.54	1.01	6.46	0.049

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DISCUSSION

The results of this study indicate that a history of hyperlipidemia has a significant relationship with the incidence of CHD, people with a history of hyperlipidemia have greater risk of suffering from CHD than people those with normal lipid levels. This result is supported by the study of Liu et al. (2018) showed that hyperlipidemia, hypertension and diabetes were independent risk factors for coronary heart disease, and the difference was statistically significant (P<0.05). High total cholesterol in pregnant women is positively related to the incidence of coronary heart disease in future offspring OR 2.10 (95% CI: 1.07-4.13) (Cao et al., 2021). Although they are a basic source of energy and are required for many biological functions, foods high in cholesterol can cause detrimental effects on cardiovascular health (Reynolds et al., 2021). Oxidation of LDL will attract leukocytes into the intima tunica of the coronary arteries, which will then be taken up by macrophages and there is the formation of foamy cells. The foamy cells will replicate and form lesions, this lesion will be called arteriosclerosis in the early stages, this repeated process of lipids will cause a buildup or lesions gradually in the lining of the coronary blood and eventually arteriosclerosis which can block blood circulation in the coronary arteries and resulting in CAD (Malakar et al., 2019).

History of type 2 diabetes mellitus obtained statistically significant results with the incidence of CHD, this result is supported by the study of Si et al. (2021) increased levels of glucose triglyceride index (TyG) in patients with type 2 diabetes are an independent risk factor for coronary artery disease (CAD), TyG index ≥8.2 OR = 5.73 (95% CI: 1.72–19.07 (Si et al., 2021). High TyG in patients with type 2 diabetes increases the risk of CHD events OR = 2.20 (95%

CI: 1.55–3.11) (Park et al., 2020). High triglyceride level is a predictor of post percutaneous coronary intervention (PCI) CHD incidence (Ma et al., 2020) (Jin et al., 2018). History of hypertension was statistically proven to be an independent risk factor for coronary heart disease (P<0.05) (Liu, Wang, Sun, & Zhou, 2018).

In this study, smoking history was a risk factor for CHD. These results are in line with research conducted by Grubb et al. (2020) smoking history has a role in the occurrence of CHD, active smokers have a strong relationship with the incidence of CHD (Grubb et al., 2020). Smoking is a major risk factor for cardiovascular disease (CVD) and a leading avoidable cause of death worldwide (Kondo et al., 2019). Smoking can cause decreased oxygen levels to the heart, increased blood pressure and pulse, decreased HDL (High Density Lipoprotein) levels and increased LDL (Low Density Lipoprotein) levels, increased thrombogenesis and vasoconstriction. The risk of CHD from cigarettes is strongly influenced by the duration and depth of smoking, the more cigarettes smoked in a day, the more CHD risk increases and the deeper the cigarette smoke is smoked increases the risk of CHD. Smoking also increases coronary artery obstruction because it produces endothelial denudation and platelet adhesion to the tunica intima layer, this increases lipid infiltration and decreases platelet growth factor (Malakar et al., 2019).

The results of this study indicate that a history of hypertension increases the risk of CHD events in the future, Hypertension stage I crude OR = 2.94 (95% CI: 1.15-7.51), Hypertension stage II-IV crude OR = 3.42 (95% CI: 1.20-9.75), people suffering from stage II-IV hypertension had a 3.42 times greater risk of suffering from CAD than people without hypertension. The results of this study are supported by research by Li et al (2020) that people who have a history of hypertension and obesity are closely related to the incidence of CHD in the future (Li et al., 2020). Hypertension is closely related to the incidence of CHD and other heart disorders, in which men have a greater tendency. Continuously high blood pressure can cause damage to the artery walls. The lining of the blood vessels will thicken so that it can increase the resistance to blood flow. Structural changes in the small arteries and arterioles will cause progressive blockage of blood flow. When the blood vessels are narrowed, arterial blood flow will be interrupted and can

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cause tissue infarction (Kokubo & Matsumoto, 2017).

Research Limitations

The weakness of this study is the wide AOR range in the analysis of risk factors for total cholesterol (95% CI: 1.60-13.49), possibly due to the small sample size. Based on the results of this study, the recommendation that can be put forward is the need for structured education to the public regarding risk factors that can still be changed to reduce or prevent the risk of CHD. Another recommendation is to conduct a study of modifiable risk factors in CHD with a larger sample size.

CONCLUSION

CHD is one of the main causes of death and morbidity in the world in both developed and developing countries. The exact cause of CHD is not known with certainty, in this study there were four risk factors that statistically increased the risk of CHD events, including a history of hyperlipidemia, a history of type 2 diabetes, a history of hypertension and smoking, among the four risk factors obtained, from multivariate analysis obtained a history of Hyperlipidemia is the dominant risk factor for CHD events.

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AUTHOR CONTRIBUTIONS

All persons who have made substantial contributions to the work reported in the manuscript, IMSA (concepts, design, definition of intellectual content, clinical studies, data analysis, statistical analysis, manuscript preparation, manuscript editing and manuscript review), NWT (literature search, data analysis and statistical analysis), NPWO (literature search, data acquisition, data analysis and statistical analysis) and DPD (Clinical Studies).

CONFLIC OF INTEREST

The authors declare that they have no conflicts of interests.

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ORIGINAL ARTICLE

HYPERLIPIDEMIA IS A DOMINANT RISK FACTOR OF CORONARY HEART DISEASE

Hiperlid Merupakan Faktor Risiko Dominan Kejadian Penyakit Jantung Kororner

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ABSTRACT

Background: Coronary heart disease (CHD) is a major health problem in developed and developing countries. Until now, the death rate due to CHD is the highest in the world. Its factors consist of modifiable major risk factors and non-modifiable risk factors, including: hyperlipidemia, hypertension, diabetes mellitus, obesity, and smoking. **Purpose:** This study aims to determine the major risk factors that can be modified by the incidence of coronary heart disease (CHD). **Methods:** The study design was unmatched case-control, total samples were 43 cases and 86 controls taken by purposive sampling technique, case samples were CHD patients who had been diagnosed by a cardiologist and controls were non-CHD patients who visited the cardiac polyclinic, which were similar in the variables of age, sex, and address. These were taken at the integrated heart center of Sanglah Hospital. The diagnosed patients were taken from the medical record data of the integrated heart center of Sanglah Hospital, while controls were non-CHD patients who were taken from medical record data at the same hospital. Data analysis was performed by using Chi-Square test and logistic regression. **Results:** The results showed that there were three risk factors that statistically significantly increased the incidence of CHD, namely history of total cholesterol $\geq$ 240mg/dl adjusted OR = 4.64 (95% CI: 1.60-13.49), Diabetes mellitus Type II adjusted OR = 2.85 (95% CI: 1.16- 6.99) and Smoke adjusted OR 2.54 (95% CI: 1.01-6.46). **Conclusion**: History of high cholesterol is statistically the most dominant risk factor for the incidence of CHD

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ABSTRAK

Latar belakang : Penyakit jantung koroner (PJK) merupakan masalah kesehatan utama di Negara maju dan Negara berkembang, sampai saat ini angka kematian akibat PJK menduduki urutan tertinggi didunia. Faktor risiko PJK terdiri dari faktor risiko mayor yang dapat dimodifikasi dan faktor risiko yang tidak dapat dimodifikasi, faktor risiko yang dapat dimodifikasi seperti : Hiperlipidemia, hipertensi, diabetes mellitus, obesitas dan merokok. Penelitian ini bertujuan untuk mengetahui faktor risiko mayor yang dapat dimodifikasi kejadian penyakit jantung coroner (PJK). **Metode** : Rancangan penelitian adalah unmatched case-control, jumlah

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sampel 43 kasus dan 86 kontrol diambil dengan Teknik *purposive sampling*, sampel kasus adalah pasien PJK yang sudah didiagnosis oleh dokter jantung dan kontrol adalah pasien non PJK yang berkunjung ke poli jantung, yang dimiripkan dalam variabel umur, jenis kelamin dan alamat. Kasus dan kontrol diambil di pusat jantung terpadu RSUP Sanglah Denpasar. Kasus adalah pasien yang didiagnosis PJK yang diambil dari data rekam medis pusat jantung terpadu RSUP Sanglah, sedangkan kontrol adalah pasien Non PJK yang diambil dari data rekam medis pada rumah sakit yang sama. Analisis data dilakukan dengan uji Chi-Square dan Regresi logistic. **Hasil:** Hasil penelitian menunjukkan bahwa terdapat tiga faktor risiko yang secara statistik signifikan meningkatkan kejadian PJK, yaitu riwayat kolesterol total 240mg/dl AOR = 4,64 (95% CI: 1,60-13,49), Diabetes mellitus Tipe II AOR = 2,85 (95% CI: 1,16-6,99) dan merokok AOR 2,54 (95% CI: 1,01-6,46). **Simpulan :** Riwayat Cholesterol tinggi secara statistik merupakan faktor risiko paling dominan terhadap kejadian PJK.

INTRODUCTION

Heart disease is a degenerative disease related to lifestyle and socioeconomic conditions in society. Heart disease is a major health problem in developed and developing countries and causes one third of deaths in the world (Malakar et al., 2019). Coronary heart disease (CHD) is the most common heart disease compared to other types of heart disease (Roth et al., 2017). CHD is a real threat to sustainable development in this century (Prabhakaran et al., 2018). Data from the World Health Organization (WHO) in 2008 stated that more than 17 million people in the world died from heart and blood vessel disease, around 7.3 million deaths were caused by coronary heart disease (World Health Organization, 2017).

In Indonesia, there has been a shift in the incidence of heart and blood vessel disease from 10th in 1980 to 8th in 1986. Meanwhile, the cause of death is still in the 3rd position. Although there is no definite epidemiological data, the morbidity/mortality rate seems to be increasing. The results of the 2001 National Health Survey show that three out of 1,000 Indonesians suffer from CHD (Iskandar, Alfridsyah, & Hadi, 2017). The results of the Basic Health Research (Riskesdas) in 2018 showed that 1.5 percent or 15 out of 1,000 Indonesians suffer from coronary heart disease (Kemenkes, 2019)

At the Sanglah Central General Hospital Denpasar, based on the annual activity report of the Integrated Heart Services at Sanglah Central General Hospital Denpasar, the number of CHD patient visits to the *Pelayanan Jantung Terpadu (PJT)* polyclinic at Sanglah Hospital Denpasar in the last three years was still relatively high. In 2017 there were 12,356 CHD patients, in 2018 there were 29,181 visits, there were 559 (1.91%) cases of new CHD patients and in 2019 there were 20,840 visits, there were 569 (2.73%) new CHD patients.

The cause of CHD is not yet known with certainty, however, there are several risk factors that are thought to have contributed to the incidence of CHD. according to Malakar et al. (2019) lifestyle, environmental factors, and genetic factors play a role as risk factors for the development of cardiovascular disease (Malakar et al., 2019). Risk factors for CHD can be divided into two, namely risk factors that can be changed or modified, and biological risk factors that cannot be changed. Biological risk factors that cannot be changed include age, sex, and family history. Modifiable risk factors include hyperlipidemia, hypertension, diabetes mellitus, smoking habits, poor diet, lack of movement, stress, obesity, and alcohol consumption (Sarini & Suharyo, 2018).

Smoking history has a role in the occurrence of CHD, active smoking has a strong relationship with the incidence of CHD (Grubb et al., 2020). Smoking is a major risk factor for cardiovascular disease (CVD) and a leading avoidable cause of death worldwide (Kondo, Nakano, Adachi, & Murohara, 2019). More than a quarter of adults

with CVD have a lifetime history of smoking (Reynolds et al., 2021).

Hypertension is thought to increase the risk of CHD events, according to Li et al., (2020), people who have a history of hypertension and obesity are closely related to the incidence of CHD in the future. A history of suffering from type 2 diabetes is also associated with the incidence of CHD. Diabetes mellitus type 2 (T2DM) is a major risk factor for coronary artery disease (CAD) (Naito & Miyauchi, 2017). Increased levels of glucose triglyceride index (TyG) are an independent risk factor for coronary artery disease (CAD) in patients with type 2 diabetes mellitus (Si et al., 2021) (Park et al., 2020), high triglyceride levels are a predictor of post percutaneous coronary intervention (PCI) CHD incidence (Ma et al., 2020) (Jin et al., 2018). A history of hyperlipidemia is also thought to increase the risk of CHD events, according to Stewart et al., (2020) a history of hyperlipidemia in young adulthood increases the risk of coronary heart disease in the future.

Aging, family history and gender are risk factors for CHD that cannot be modified so that the handling is done more to control risk factors that can be modified. Modernization and changes in people's lifestyles can be considered as causes of CHD. Seeing the phenomenon that occurs in society today, generally people of productive age enjoy unhealthy lifestyles in their daily life such as poor food consumption, smoking habits, and lack of physical activity (Indonesian Heart Association, 2019).

The disease burden of CHD tends to increase due to the tendency of an increasing number of cases. The burden on CHD patients or their families is very heavy, both from a medical, psychological, social, and financial perspective. Comprehensive efforts are needed to prevent CHD and for that, more research is needed to determine the risk factors for CHD that can be changed or modified. This study aims to determine the dominant risk factors that increase the incidence of CHD.

METHODS

This study used an unmatched case control design in which the case group and the control group were similar in terms of age, sex, and place of residence. The study was conducted in November 2020, February-April 2020. Case samples were patients diagnosed with CHD by

doctors who came to the integrated cardiac service clinic at Sanglah Hospital Denpasar, while the control sample was patients with non-CHD who came to integrated cardiac polyclinic, based on clinical diagnosis, electrocardiography, and cardiac catheterization. The number of samples was determined using the Lemeshow formula and calculated using the WHO sample size calculator 2.0, and the number of case samples was 43 and control samples were 83. The sample was taken using purposive sampling technique, the inclusion criteria for the case sample were patients who had been diagnosed with CHD by a cardiologist, while the control sample was non-CHD patients (extrasystolic, hypertension and non-CHD/CHF patients) who underwent an examination at the cardiac polyclinic.

All variables in this study were used as categorical variables as presented in Table 2, namely variables of history of hyperlipidemia, history of smoking, history of hypertension and history of diabetes mellitus. Data analysis was performed using IBM SPSS software univariate (Table 1), bivariate (Table 2) and multivariate (Table 3). Univariate analysis is to determine the frequency distribution of each variable. Bivariate analysis to determine crude OR with Chi-Square. Multivariate analysis to calculate adjusted OR with logistic regression method. Crude OR and adjusted OR significance levels were set with 95% CI.

Research has been declared ethical by the Research Ethics Commission of the Faculty of Medicine, Udayana University/Sanglah Hospital, with no: 2412 / UN14.2.2.VII.14 / LT / 2020. Prior to the research, the potential subjects were informed with verbal and written description about procedures and that they could withdraw from the study. Subjects who agreed to participate in the study provided consent before measurement.

RESULTS

In Table 1, the characteristics of the case and control groups based on gender, age, address, education, and occupation are presented. Respondents who participated in this study were predominantly male, the case group 27 (62.79%) and the control group 47 (54.65%). Respondents' age was dominated > 50 years as many as 28 (65.11%) in the case group and 55 (64%) in the control group. For the case group living in urban areas 23 (53.49%) while the control group lived more in rural areas 49 (57%). For the level of education, both cases and controls are dominated by high school graduates. Respondents'

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occupations are predominantly self-employed. Family history of CHD, both cases and controls, showed that the dominant result was no history of CHD in the family.

Table 1.

Baseline Characteristics of Subjects

Baseline Characteristics	Case	Control	p-value
Gender			
Male	27 (62.79)	47 (54.65)	0.380
Female	16 (37.21)	39 (43.35)	
Age			
$\geq$ 55	15 (34.88)	31 (36.04)	0.897
$<$ 55	28 (65.11)	55 (63.96)	
Residence			
Rural	20 (46.51)	49 (56.97)	0.263
Urban	23 (53.49)	37 (43.03)	
Education			
None	0	2 (2.32)	0.727
Elementary	3 (6.97)	13 (15.11)	
Junior High School	5 (11.62)	11 (12.79)	
Senior High School	29 (67.44)	39 (45.34)	
University	6 (13.95)	24 (27.90)	
Occupation			
None	4 (9.30)	6 (6.97)	0.233
Employe	8 (18.60)	9 (10.46)	
Self-Employed	23 (50)	51 (59.30)	
Public Servant	8 (18.60)	20 (23.25)	
Family history of CHD			
CHD	5 (11.62)	2(2.32)	0.029
None	38 (88.38)	84(97.68)	

In Table 2, the results of the bivariate analysis between cases and controls show that the risk factors that significantly increase the incidence of CHD are: Total Cholesterol Crude OR = 4.89 (95% CI: 1.78-13.43), Triglyceride Levels crude OR = 4.48 (95% CI: 1.06-18.92), Diabetes mellitus Type II crude OR = 3.36 (95%CI: 1.46-7.77), Hypertension stage I crude OR = 2.94 (95% CI: 1.15-7.51), Hypertension stage II-IV crude OR = 3.42 (95% CI: 1.20-9.75), Smoke crude OR = 3.01 (95% CI: 1.27-7.17) and Body Mass Index $\geq$ 25 Crude OR = 2.86 (95% CI: 1.26-6.48).

Table 2

Bivariate analysis results (Crude Odds Ratio) for CHD

Risk Factor	Cases	Control	Crude OR	95% CI
Total Cholesterol				
$\geq$ 240mg/dl	13	7	4.89	1.78-13.43
$<$ 240mg/dl	30	79		
Triglyceride Levels				
$\geq$ 200mg/dl	6	3	4.48	1.06-18.91
$<$ 200mg/dl	37	83		
Diabetes mellitu sType II				
Yes	17	14	3.36	1.46-7.77
None	26	72		
Hypertension stage I				
Yes	12	10	2.94	1.15-7.51
None	31	76		
Hypertension stage II-IV				
Yes	10	7	3.42	1.20-9.75
None	33	78		
Smoke				
Yes	15	13	3.01	1.27-7.17
None	28	73		
Body Mass Indek $\geq$ 25				
$\geq$ 25	17	16	2.86	1.26-6.48
$<$ 25	26	70		

In Table 3, the results of the multivariate analysis using the logistic regression method of seven variables were found to be significant in the bivariate analysis, namely: Total Cholesterol, Triglyceride Levels, Diabetes mellitus Type II, Hypertension stage I, Hypertension stage II-IV, Smoke and Body Mass Index $\geq$ 25. The results of multivariate analysis showed three risk factors associated with the incidence of CHD. Total Cholesterol AOR = 4.64 (95% CI: 1.60-13.49), Diabetes mellitus Type II AOR = 2.85 (95% CI: 1.16- 6.99) and Smoke 2.54 (95% CI: 1.01-6.46).

Table 3

Multivariable-Adjusted odds ratio (AOR) for CHD

Risk Factor	Adjusted OR	95%CI		p-value
		Lower	Uper	
Total Cholesterol ≥ 240mg/dl	4.64	1.60	13.49	0.005
Diabetes mellitusType II	2.85	1.16	6.99	0.022
Smoke	2.54	1.01	6.46	0.049

DISCUSSION

The results of this study indicate that a history of hyperlipidemia has a significant relationship with the incidence of CHD, people with a history of hyperlipidemia have greater risk of suffering from CHD than people those with normal lipid levels. This result is supported by the study of Liu et al., (2018) showed that hyperlipidemia, hypertension and diabetes were independent risk factors for coronary heart disease, and the difference was statistically significant (P<0.05). High total cholesterol in pregnant women is positively related to the incidence of coronary heart disease in future offspring OR 2.10 (95% CI: 1.07-4.13) (Cao et al., 2021). Although they are a basic source of energy and are required for many biological functions, foods high in cholesterol can cause detrimental effects on cardiovascular health (Reynolds et al., 2021). Oxidation of LDL will attract leukocytes into the intima tunica of the coronary arteries, which will then be taken up by macrophages and there is the formation of foamy cells. The foamy cells will replicate and form lesions, this lesion will be called arteriosclerosis in the early stages, this repeated process of lipids will cause a buildup or lesions gradually in the lining of the coronary blood and eventually arteriosclerosis which can block blood circulation in the coronary arteries and resulting in CAD (Malakar et al., 2019). People with a history of high total cholesterol and high-density lipoprotein cholesterol levels were at risk for myocardial infarction and other cardiac disorders with adjusted hazard ratios of 1.39 (95% CI, 1.10-1.76; P = 0.006) (Chen et al., 2017). According to Y. H. Li et al., (2017) low density lipoprotein cholesterol (LDL-C) and low density lipoprotein cholesterol (non-HDL-C) were significant predictors of coronary artery disease in Taiwan. The risk of CHD events depends on the cumulative exposure and duration of previous exposure to LDL cholesterol, exposure to cholesterol that occurs from a young age has a greater risk of developing CHD later in life when compared to exposure to LDL cholesterol in old age (Domanski et al., 2020).

History of type 2 diabetes mellitus obtained statistically significant results with the incidence of CHD, this result is supported by the study of Si et al. (2021) increased levels of glucose triglyceride index (TyG) in patients with type 2 diabetes are an independent risk factor for coronary artery disease (CAD), TyG index ≥8.2 OR = 5.73 (95% CI: 1.72–19.07 (Si et al., 2021). High TyG in patients with type 2 diabetes increases the risk of CHD events OR = 2.20 (95% CI: 1.55–3.11) (Park et al., 2020). High triglyceride level is a predictor of post percutaneous coronary intervention (PCI) CHD incidence (Ma et al., 2020) (Jin et al., 2018). History of hypertension was statistically proven to be an independent risk factor for coronary heart disease (P<0.05) (Liu et al., 2018).

In this study, smoking history was a risk factor for CHD. These results are in line with research conducted by Grubb et al. (2020) smoking history has a role in the occurrence of CHD, active smokers have a strong relationship with the incidence of CHD (Grubb et al., 2020). Smoking is a major risk factor for cardiovascular disease (CVD) and a leading avoidable cause of death worldwide (Kondo et al., 2019). Smoking can cause decreased oxygen levels to the heart, increased blood pressure and pulse, decreased HDL (High Density Lipoprotein) levels and increased LDL (Low Density Lipoprotein) levels, increased thrombogenesis and vasoconstriction. The risk of CHD from cigarettes is strongly influenced by the duration and depth of smoking, the more cigarettes smoked in a day, the more CHD risk increases and the deeper the cigarette smoke is smoked increases the risk of CHD. Smoking also increases coronary artery obstruction because it produces endothelial denudation and platelet adhesion to the tunica intima layer, this increases lipid infiltration and decreases platelet growth factor (Malakar et al., 2019).

The results of this study indicate that a history of hypertension increases the risk of CHD events in the future, Hypertension stage I crude OR = 2.94 (95% CI: 1.15-7.51), Hypertension stage II-IV crude OR = 3.42 (95% CI: 1.20-9.75), people suffering from stage II-IV hypertension had a 3.42 times greater risk of suffering from CAD than people without hypertension. The results of

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this study are supported by research by Li et al., (2020) that people who have a history of hypertension and obesity are closely related to the incidence of CHD in the future (X. Li et al., 2020). Hypertension is closely related to the incidence of CHD and other heart disorders, in which men have a greater tendency. Continuously high blood pressure can cause damage to the artery walls. The lining of the blood vessels will thicken so that it can increase the resistance to blood flow. Structural changes in the small arteries and arterioles will cause progressive blockage of blood flow. When the blood vessels are narrowed, arterial blood flow will be interrupted and can cause tissue infarction (Kokubo & Matsumoto, 2017). According to Chen et al., (2017) age, gender, race, clinical location, education level, physical activity, total cholesterol level, high density lipoprotein cholesterol level, systolic blood pressure, use of antihypertensive medication, current smoking, diabetes status, body mass index, protein C level -reactive, hemoglobin A1c levels, phosphorus levels, troponin T levels, log levels of N-terminal pro-B-type natriuretic peptide, levels of fibroblast growth factor 23, estimated glomerular filtration rate, and proteinuria are associated with the incidence of myocardial infarction and other cardiac disorders with adjusted hazard ratios 1.39 (95% CI, 1.10-1.76; P = 0.006).

Research Limitations

The weakness of this study is the wide AOR range in the analysis of risk factors for total cholesterol (95% CI: 1.60-13.49), possibly due to the small sample size. Based on the results of this study, the recommendation that can be put forward is the need for structured education to the public regarding risk factors that can still be changed to reduce or prevent the risk of CHD. Another recommendation is to conduct a study of modifiable risk factors in CHD with a larger sample size.

CONCLUSION

CHD is one of the main causes of death and morbidity in the world in both developed and developing countries. The exact cause of CHD is not known with certainty, in this study there were four risk factors that statistically increased the risk of CHD events, including a history of hyperlipidemia, a history of type 2 diabetes, a history of hypertension and smoking, among the four risk factors obtained, from multivariate analysis obtained a history of Hyperlipidemia is the dominant risk factor for CHD events.

AUTHOR CONTRIBUTIONS

All persons who have made substantial contributions to the work reported in the manuscript, IMSA (concepts, design, definition of intellectual content, clinical studies, data analysis, statistical analysis, manuscript preparation, manuscript editing and manuscript review), NWT (literature search, data analysis and statistical analysis), NPWO literature search, data acquisition, data analysis and statistical analysis) and DPD (Clinical Studies).

CONFLIC OF INTEREST

The authors declare that they have no conflicts of interests.

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Si, Y., Fan, W., Shan, W., Zhang, Y., Liu, J., Han, C., & Sun, L. (2021). Association between triglyceride glucose index and coronary artery disease with type 2 diabetes mellitus in middle-aged and elderly people. *Medicine*, *100*(9), e25025. https://doi.org/10.1097/MD.00000000000250 25

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World Health Organization. (2017). Cardiovascular diseases (CVDs).

ORIGINAL ARTICLE

HYPERLIPIDEMIA IS A DOMINANT RISK FACTOR OF CORONARY HEART DISEASE

Hiperlid Merupakan Faktor Risiko Dominan Kejadian Penyakit Jantung Kororner

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ABSTRACT

Background: Coronary heart disease (CHD) is a major health problem in developed and developing countries. Until now, the death rate due to CHD is the highest in the world. Its factors consist of modifiable major risk factors and non-modifiable risk factors, including: hyperlipidemia, hypertension, diabetes mellitus, obesity, and smoking. **Purpose:** This study aims to determine the major risk factors that can be modified by the incidence of coronary heart disease (CHD). **Methods:** The study design was unmatched case-control, total samples were 43 cases and 86 controls taken by purposive sampling technique, case samples were CHD patients who had been diagnosed by a cardiologist and controls were non-CHD patients who visited the cardiac polyclinic, which were similar in the variables of age, sex, and address. These were taken at the integrated heart center of Sanglah Hospital. The diagnosed patients were taken from the medical record data of the integrated heart center of Sanglah Hospital, while controls were non-CHD patients who were taken from medical record data at the same hospital. Data analysis was performed by using Chi-Square test and logistic regression. **Results:** The results showed that there were three risk factors that statistically significantly increased the incidence of CHD, namely history of total cholesterol $\geq$ 240mg/dl adjusted OR = 4.64 (95% CI: 1.60-13.49), Diabetes mellitus Type II adjusted OR = 2.85 (95% CI: 1.16- 6.99) and Smoke adjusted OR 2.54 (95% CI: 1.01-6.46). **Conclusion**: History of high cholesterol is statistically the most dominant risk factor for the incidence of CHD

> **Commented [ASUS2]:** risk factors

ABSTRAK

Latar belakang : Penyakit jantung koroner (PJK) merupakan masalah kesehatan utama di Negara maju dan Negara berkembang, sampai saat ini angka kematian akibat PJK menduduki urutan tertinggi didunia. Faktor risiko PJK terdiri dari faktor risiko mayor yang dapat dimodifikasi dan faktor risiko yang tidak dapat dimodifikasi, faktor risiko yang dapat dimodifikasi seperti : Hiperlipidemia, hipertensi, diabetes mellitus, obesitas dan merokok. Penelitian ini bertujuan untuk mengetahui faktor risiko mayor yang dapat dimodifikasi kejadian penyakit jantung coroner (PJK). **Metode** : Rancangan penelitian adalah unmatched case-control, jumlah

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sampel 43 kasus dan 86 kontrol diambil dengan Teknik *purposive sampling*, sampel kasus adalah pasien PJK yang sudah didiagnosis oleh dokter jantung dan kontrol adalah pasien non PJK yang berkunjung ke poli jantung, yang dimiripkan dalam variabel umur, jenis kelamin dan alamat. Kasus dan kontrol diambil di pusat jantung terpadu RSUP Sanglah Denpasar. Kasus adalah pasien yang didiagnosis PJK yang diambil dari data rekam medis pusat jantung terpadu RSUP Sanglah, sedangkan kontrol adalah pasien Non PJK yang diambil dari data rekam medis pada rumah sakit yang sama. Analisis data dilakukan dengan uji Chi-Square dan Regresi logistic. **Hasil:** Hasil penelitian menunjukkan bahwa terdapat tiga faktor risiko yang secara statistik signifikan meningkatkan kejadian PJK, yaitu riwayat kolesterol total 240mg/dl AOR = 4,64 (95% CI: 1,60-13,49), Diabetes mellitus Tipe II AOR = 2,85 (95% CI: 1,16-6,99) dan merokok AOR 2,54 (95% CI: 1,01-6,46). **Simpulan :** Riwayat Cholesterol tinggi secara statistik merupakan faktor risiko paling dominan terhadap kejadian PJK.

INTRODUCTION

Heart disease is a degenerative disease related to lifestyle and socioeconomic conditions in society. Heart disease is a major health problem in developed and developing countries and causes one third of deaths in the world (Malakar et al., 2019). Coronary heart disease (CHD) is the most common heart disease compared to other types of heart disease (Roth et al., 2017). CHD is a real threat to sustainable development in this century (Prabhakaran et al., 2018). Data from the World Health Organization (WHO) in 2008 stated that more than 17 million people in the world died from heart and blood vessel disease, around 7.3 million deaths were caused by coronary heart disease (World Health Organization, 2017).

In Indonesia, there has been a shift in the incidence of heart and blood vessel disease from 10th in 1980 to 8th in 1986. Meanwhile, the cause of death is still in the 3rd position. Although there is no definite epidemiological data, the morbidity/ mortality rate seems to be increasing. The results of the 2001 National Health Survey show that three out of 1,000 Indonesians suffer from CHD (Iskandar, Alfridsyah, & Hadi, 2017). The results of the Basic Health Research (Riskesdas) in 2018 showed that 1.5 percent or 15 out of 1,000 Indonesians suffer from coronary heart disease (Kemenkes, 2019)

At the Sanglah Central General Hospital Denpasar, based on the annual activity report of the Integrated Heart Services at Sanglah Central General Hospital Denpasar, the number of CHD patient visits to the *Pelayanan Jantung Terpadu (PJT)* polyclinic at Sanglah Hospital Denpasar in the last three years was still relatively high. In 2017 there were 12,356 CHD patients, in 2018 there were 29,181 visits, there were 559 (1.91%) cases of new CHD patients and in 2019 there were 20,840 visits, there were 569 (2.73%) new CHD patients.

The cause of CHD is not yet known with certainty, however, there are several risk factors that are thought to have contributed to the incidence of CHD. according to Malakar et al. (2019) lifestyle, environmental factors, and genetic factors play a role as risk factors for the development of cardiovascular disease (Malakar et al., 2019). Risk factors for CHD can be divided into two, namely risk factors that can be changed or modified, and biological risk factors that cannot be changed. Biological risk factors that cannot be changed include age, sex, and family history. Modifiable risk factors include hyperlipidemia, hypertension, diabetes mellitus, smoking habits, poor diet, lack of movement, stress, obesity, and alcohol consumption (Sarini & Suharyo, 2018).

Smoking history has a role in the occurrence of CHD, active smoking has a strong relationship with the incidence of CHD (Grubb et al., 2020). Smoking is a major risk factor for cardiovascular disease (CVD) and a leading avoidable cause of death worldwide (Kondo, Nakano, Adachi, & Murohara, 2019). More than a quarter of adults

with CVD have a lifetime history of smoking (Reynolds et al., 2021).

Hypertension is thought to increase the risk of CHD events, according to Li et al., (2020), people who have a history of hypertension and obesity are closely related to the incidence of CHD in the future. A history of suffering from type 2 diabetes is also associated with the incidence of CHD. Diabetes mellitus type 2 (T2DM) is a major risk factor for coronary artery disease (CAD) (Naito & Miyauchi, 2017). Increased levels of glucose triglyceride index (TyG) are an independent risk factor for coronary artery disease (CAD) in patients with type 2 diabetes mellitus (Si et al., 2021) (Park et al., 2020), high triglyceride levels are a predictor of post percutaneous coronary intervention (PCI) CHD incidence (Ma et al., 2020) (Jin et al., 2018). A history of hyperlipidemia is also thought to increase the risk of CHD events, according to Stewart et al., (2020) a history of hyperlipidemia in young adulthood increases the risk of coronary heart disease in the future.

Aging, family history and gender are risk factors for CHD that cannot be modified so that the handling is done more to control risk factors that can be modified. Modernization and changes in people's lifestyles can be considered as causes of CHD. Seeing the phenomenon that occurs in society today, generally people of productive age enjoy unhealthy lifestyles in their daily life such as poor food consumption, smoking habits, and lack of physical activity (Indonesian Heart Association, 2019).

The disease burden of CHD tends to increase due to the tendency of an increasing number of cases. The burden on CHD patients or their families is very heavy, both from a medical, psychological, social, and financial perspective. Comprehensive efforts are needed to prevent CHD and for that, more research is needed to determine the risk factors for CHD that can be changed or modified. This study aims to determine the dominant risk factors that increase the incidence of CHD.

METHODS

This study used an unmatched case control design in which the case group and the control group were similar in terms of age, sex, and place of residence. The study was conducted in November 2020, February-April 2020. Case samples were patients diagnosed with CHD by

doctors who came to the integrated cardiac service clinic at Sanglah Hospital Denpasar, while the control sample was patients with non-CHD who came to integrated cardiac polyclinic, based on clinical diagnosis, electrocardiography, and cardiac catheterization. The number of samples was determined using the Lemeshow formula and calculated using the WHO sample size calculator 2.0, and the number of case samples was 43 and control samples were 83. The sample was taken using purposive sampling technique, the inclusion criteria for the case sample were patients who had been diagnosed with CHD by a cardiologist, while the control sample was non-CHD patients (extrasystolic, hypertension and non-CHD/CHF patients) who underwent an examination at the cardiac polyclinic.

All variables in this study were used as categorical variables as presented in Table 2, namely variables of history of hyperlipidemia, history of smoking, history of hypertension and history of diabetes mellitus. Data analysis was performed using IBM SPSS software univariate (Table 1), bivariate (Table 2) and multivariate (Table 3). Univariate analysis is to determine the frequency distribution of each variable. Bivariate analysis to determine crude OR with Chi-Square. Multivariate analysis to calculate adjusted OR with logistic regression method. Crude OR and adjusted OR significance levels were set with 95% CI.

Research has been declared ethical by the Research Ethics Commission of the Faculty of Medicine, Udayana University/Sanglah Hospital, with no: 2412 / UN14.2.2.VII.14 / LT / 2020. Prior to the research, the potential subjects were informed with verbal and written description about procedures and that they could withdraw from the study. Subjects who agreed to participate in the study provided consent before measurement.

RESULTS

In Table 1, the characteristics of the case and control groups based on gender, age, address, education, and occupation are presented. Respondents who participated in this study were predominantly male, the case group 27 (62.79%) and the control group 47 (54.65%). Respondents' age was dominated > 50 years as many as 28 (65.11%) in the case group and 55 (64%) in the control group. For the case group living in urban areas 23 (53.49%) while the control group lived more in rural areas 49 (57%). For the level of education, both cases and controls are dominated by high school graduates. Respondents'

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occupations are predominantly self-employed. Family history of CHD, both cases and controls, showed that the dominant result was no history of CHD in the family.

Table 1.

Baseline Characteristics of Subjects

Baseline Characteristics	Case	Control	p-value
Gender			
Male	27 (62.79)	47 (54.65)	0.380
Female	16 (37.21)	39 (43.35)	
Age			
≥ 55	15 (34.88)	31 (36.04)	0.897
< 55	28 (65.11)	55 (63.96)	
Residence			
Rural	20 (46.51)	49 (56.97)	0.263
Urban	23 (53.49)	37 (43.03)	
Education			
None	0	2 (2.32)	0.727
Elementary	3 (6.97)	13 (15.11)	
Junior High School	5 (11.62)	11 (12.79)	
Senior High School	29 (67.44)	39 (45.34)	
University	6 (13.95)	24 (27.90)	
Occupation			
None	4 (9.30)	6 (6.97)	0.233
Employe	8 (18.60)	9 (10.46)	
Self-Employed	23 (50)	51 (59.30)	
Public Servant	8 (18.60)	20 (23.25)	
Family history of CHD			
CHD	5 (11.62)	2(2.32)	0.029
None	38 (88.38)	84(97.68)	

In Table 2, the results of the bivariate analysis between cases and controls show that the risk factors that significantly increase the incidence of CHD are: Total Cholesterol Crude OR = 4.89 (95% CI: 1.78-13.43), Triglyceride Levels crude OR = 4.48 (95% CI: 1.06-18.92), Diabetes mellitus Type II crude OR = 3.36 (95%CI: 1.46-7.77), Hypertension stage I crude OR = 2.94 (95% CI: 1.15-7.51), Hypertension stage II-IV crude OR = 3.42 (95% CI: 1.20-9.75), Smoke crude OR = 3.01 (95% CI: 1.27-7.17) and Body Mass Index ≥ 25 Crude OR = 2.86 (95% CI: 1.26-6.48).

Table 2

Bivariate analysis results (Crude Odds Ratio) for CHD

Risk Factor	Cases	Control	Crude OR	95% CI
Total Cholesterol				
≥ 240mg/dl	13	7	4.89	1.78-13.43
< 240mg/dl	30	79		
Triglyceride Levels				
≥ 200mg/dl	6	3	4.48	1.06-18.91
< 200mg/dl	37	83		
Diabetes mellitu sType II				
Yes	17	14	3.36	1.46-7.77
None	26	72		
Hypertension stage I				
Yes	12	10	2.94	1.15-7.51
None	31	76		
Hypertension stage II-IV				
Yes	10	7	3.42	1.20-9.75
None	33	78		
Smoke				
Yes	15	13	3.01	1.27-7.17
None	28	73		
Body Mass Indek ≥ 25				
≥ 25	17	16	2.86	1.26-6.48
< 25	26	70		

In Table 3, the results of the multivariate analysis using the logistic regression method of seven variables were found to be significant in the bivariate analysis, namely: Total Cholesterol, Triglyceride Levels, Diabetes mellitus Type II, Hypertension stage I, Hypertension stage II-IV, Smoke and Body Mass Index ≥ 25. The results of multivariate analysis showed three risk factors associated with the incidence of CHD. Total Cholesterol AOR = 4.64 (95% CI: 1.60-13.49), Diabetes mellitus Type II AOR = 2.85 (95% CI: 1.16- 6.99) and Smoke 2.54 (95% CI: 1.01-6.46).

Table 3

Multivariable-Adjusted odds ratio (AOR) for CHD

Risk Factor	Adjusted OR	95%CI		p-value
		Lower	Uper	
Total Cholesterol ≥ 240mg/dl	4.64	1.60	13.49	0.005
Diabetes mellitusType II	2.85	1.16	6.99	0.022
Smoke	2.54	1.01	6.46	0.049

DISCUSSION

The results of this study indicate that a history of hyperlipidemia has a significant relationship with the incidence of CHD, people with a history of hyperlipidemia have greater risk of suffering from CHD than people those with normal lipid levels. This result is supported by the study of Liu et al., (2018) showed that hyperlipidemia, hypertension and diabetes were independent risk factors for coronary heart disease, and the difference was statistically significant (P<0.05). High total cholesterol in pregnant women is positively related to the incidence of coronary heart disease in future offspring OR 2.10 (95% CI: 1.07-4.13) (Cao et al., 2021). Although they are a basic source of energy and are required for many biological functions, foods high in cholesterol can cause detrimental effects on cardiovascular health (Reynolds et al., 2021). Oxidation of LDL will attract leukocytes into the intima tunica of the coronary arteries, which will then be taken up by macrophages and there is the formation of foamy cells. The foamy cells will replicate and form lesions, this lesion will be called arteriosclerosis in the early stages, this repeated process of lipids will cause a buildup or lesions gradually in the lining of the coronary blood and eventually arteriosclerosis which can block blood circulation in the coronary arteries and resulting in CAD (Malakar et al., 2019). People with a history of high total cholesterol and high-density lipoprotein cholesterol levels were at risk for myocardial infarction and other cardiac disorders with adjusted hazard ratios of 1.39 (95% CI, 1.10-1.76; P = 0.006) (Chen et al., 2017). According to Y. H. Li et al., (2017) low density lipoprotein cholesterol (LDL-C) and low density lipoprotein cholesterol (non-HDL-C) were significant predictors of coronary artery disease in Taiwan. The risk of CHD events depends on the cumulative exposure and duration of previous exposure to LDL cholesterol, exposure to cholesterol that occurs from a young age has a greater risk of developing CHD later in life when compared to exposure to LDL cholesterol in old age (Domanski et al., 2020).

History of type 2 diabetes mellitus obtained statistically significant results with the incidence of CHD, this result is supported by the study of Si et al. (2021) increased levels of glucose triglyceride index (TyG) in patients with type 2 diabetes are an independent risk factor for coronary artery disease (CAD), TyG index ≥8.2 OR = 5.73 (95% CI: 1.72–19.07 (Si et al., 2021). High TyG in patients with type 2 diabetes increases the risk of CHD events OR = 2.20 (95% CI: 1.55–3.11) (Park et al., 2020). High triglyceride level is a predictor of post percutaneous coronary intervention (PCI) CHD incidence (Ma et al., 2020) (Jin et al., 2018). History of hypertension was statistically proven to be an independent risk factor for coronary heart disease (P<0.05) (Liu et al., 2018).

In this study, smoking history was a risk factor for CHD. These results are in line with research conducted by Grubb et al. (2020) smoking history has a role in the occurrence of CHD, active smokers have a strong relationship with the incidence of CHD (Grubb et al., 2020). Smoking is a major risk factor for cardiovascular disease (CVD) and a leading avoidable cause of death worldwide (Kondo et al., 2019). Smoking can cause decreased oxygen levels to the heart, increased blood pressure and pulse, decreased HDL (High Density Lipoprotein) levels and increased LDL (Low Density Lipoprotein) levels, increased thrombogenesis and vasoconstriction. The risk of CHD from cigarettes is strongly influenced by the duration and depth of smoking, the more cigarettes smoked in a day, the more CHD risk increases and the deeper the cigarette smoke is smoked increases the risk of CHD. Smoking also increases coronary artery obstruction because it produces endothelial denudation and platelet adhesion to the tunica intima layer, this increases lipid infiltration and decreases platelet growth factor (Malakar et al., 2019).

The results of this study indicate that a history of hypertension increases the risk of CHD events in the future, Hypertension stage I crude OR = 2.94 (95% CI: 1.15-7.51), Hypertension stage II-IV crude OR = 3.42 (95% CI: 1.20-9.75), people suffering from stage II-IV hypertension had a 3.42 times greater risk of suffering from CAD than people without hypertension. The results of

this study are supported by research by Li et al., (2020) that people who have a history of hypertension and obesity are closely related to the incidence of CHD in the future (X. Li et al., 2020). Hypertension is closely related to the incidence of CHD and other heart disorders, in which men have a greater tendency. Continuously high blood pressure can cause damage to the artery walls. The lining of the blood vessels will thicken so that it can increase the resistance to blood flow. Structural changes in the small arteries and arterioles will cause progressive blockage of blood flow. When the blood vessels are narrowed, arterial blood flow will be interrupted and can cause tissue infarction (Kokubo & Matsumoto, 2017). According to Chen et al., (2017) age, gender, race, clinical location, education level, physical activity, total cholesterol level, high density lipoprotein cholesterol level, systolic blood pressure, use of antihypertensive medication, current smoking, diabetes status, body mass index, protein C level -reactive, hemoglobin A1c levels, phosphorus levels, troponin T levels, log levels of N-terminal pro-B-type natriuretic peptide, levels of fibroblast growth factor 23, estimated glomerular filtration rate, and proteinuria are associated with the incidence of myocardial infarction and other cardiac disorders with adjusted hazard ratios 1.39 (95% CI, 1.10-1.76; P = 0.006).

Research Limitations

The weakness of this study is the wide AOR range in the analysis of risk factors for total cholesterol (95% CI: 1.60-13.49), possibly due to the small sample size. Based on the results of this study, the recommendation that can be put forward is the need for structured education to the public regarding risk factors that can still be changed to reduce or prevent the risk of CHD. Another recommendation is to conduct a study of modifiable risk factors in CHD with a larger sample size.

CONCLUSION

CHD is one of the main causes of death and morbidity in the world in both developed and developing countries. The exact cause of CHD is not known with certainty, in this study there were four risk factors that statistically increased the risk of CHD events, including a history of hyperlipidemia, a history of type 2 diabetes, a history of hypertension and smoking, among the four risk factors obtained, from multivariate analysis obtained a history of Hyperlipidemia is the dominant risk factor for CHD events.

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AUTHOR CONTRIBUTIONS

All persons who have made substantial contributions to the work reported in the manuscript, IMSA (concepts, design, definition of intellectual content, clinical studies, data analysis, statistical analysis, manuscript preparation, manuscript editing and manuscript review), NWT (literature search, data analysis and statistical analysis), NPWO literature search, data acquisition, data analysis and statistical analysis) and DPD (Clinical Studies).

CONFLIC OF INTEREST

The authors declare that they have no conflicts of interests.

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Manuscript Title
Hyperlipidemia is a Dominant Risk Factor for Coronary Heart Disease

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