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Determinants of coronary heart disease among adults: a case-control study

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ABSTRACT

BACKGROUND
According to recent World Health Organization data, coronary heart disease (CHD) remains the leading cause of death worldwide. Although the risk factors of this disease are well known, the strength of these factors varies in different populations. The aim of the study was to assess the determinants of CHD in Indonesian adults aged 25 years and over.

METHODS
A case–control study was carried out involving 592 subjects aged 25 years and over (444 controls and 148 cases). Participants were interviewed using validated questionnaires. Physical examinations and supporting examinations were conducted. The Chi square test, Fisher's exact test, and independent t test were used to analyze the data. To determine independent predictors of CHD, the odds ratio (OR) was determined via the multiple logistic regressions test.

RESULTS
The CHD subjects (case group) showed higher blood sugar and systolic pressure than non-CHD subjects (controls), with mean fasting blood sugar of 92.53±27.05 mg/dL vs 88.29 ±23.43 mg/dL (p=0.038), 2-hour postprandial blood sugar of 133.15±65.09 mg/dL vs 120.87±44.60 mg/dL (p=0.000), and systolic blood pressure of 89±27.62 mmHg vs 129.98±10.58 mmHg (p=0.002). The logistic regression analysis in the case group showed that higher education (college) had a 2.32-fold greater effect (95% CI. 1.01-5.35) on CHD incidence compared to the control group.

CONCLUSIONS
This study has demonstrated that the most frequent risk factor for CVD in adults aged 25 years and over is higher education. Control and prevention of CHD need to be done with regular control of blood sugar levels and blood pressure to stabilize them within normal limits.

Keywords: Coronary heart disease, blood sugar, blood pressure, adults

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INTRODUCTION

About three-quarters of the proportion of deaths from non-communicable diseases (NCDs) occurs in low- and middle-income countries, with no difference in mortality between men and women.(1) The global prevalence of cardiovascular heart disease (CHD) has increased over the last 20 years and the disease is now recognized as a leading cause of death and disability worldwide.(2)

Data from the American Heart Association (AHA) statistics in 2016 reported that 15.5 million individuals aged 20 years had CHD. Its prevalence increases with age in women as well as in men. It is estimated that every 42 seconds there will be one more CHD sufferer in the US.(3) In addition to the reported increase in cases, the pattern of the ten main causes of death in 2017 is identical to that in 2016, namely heart disease, cancer, injury, chronic lower respiratory disease, stroke, Alzheimer's disease, diabetes mellitus (DM), influenza and pneumonia, kidney disease, and suicide.(4)

In Indonesia, from the 2013 Basic Health Research (Riskesdas) data it is apparent that heart disease sufferers increase with age, the highest number being in the 65-74 year age group, which is about 2 percent of the population aged 15 years and over.(5) Basic health research data (Riskesdas) for 2018 show that West Java ranks 5th highest in Indonesia (1.6%) with 186,809 individuals with heart disease from all age groups.(5)

There are various risk factors for heart disease. Population studies over the last 20 years have proven that overweight (overweight and obesity), hypertension, and hypercholesterolemia are the four risk factors that have the highest contribution to cardiovascular disease.(6) The results of further analysis of the 2011 non-communicable disease cohort study showed that hypertension, LDL cholesterol, HDL cholesterol, triglycerides, and obesity are also risks for CHD with a probability of 64.84 percent.(7) Diabetes mellitus (including hyperglycemia), abnormal lipid profile, changes in inflammatory mediators, and coagulation or thrombolytic parameters, as well as other risk factors that are closely related to insulin resistance, are reported to have a risk of CHD. Diabetes mellitus increases the risk of CHD 2 to 4 times.(8)

An unmatched case-control study that was conducted on 143 newly diagnosed patients with CVD and 286 controls demonstrated that the most frequent risk factors for CVD were older age, smoking history, low level of physical activity, and greater waist circumference.(9) However, this study is inconsistent with the finding from India with the same study design, demonstrating that no significant association was observed between physical inactivity and coronary artery disease (CAD) among females.(10) A matched case control study conducted on 1000 male military patients [250 with CAD and 750 without CAD] indicated that the risk factors, including diabetes, hyperlipidemia, smoking, hypertension, and positive family history of CAD, increase the probability of CAD.(11) Although these risk factors have been identified, CAD is still highly prevalent. Diabetes, smoking, hypertension, hyperlipidemia, and positive family history are well-known factors for cardiovascular disease, but it is unclear what their precise effects are in different populations.(11) Previous studies have shown that several factors are associated with coronary heart disease, such as coffee drinking habits, high carbohydrate diet, fasting blood sugar levels, systolic blood pressure, and education.(12–14) Considering these cases, the present study aimed to estimate the proportion of the determinants of CHD in adults aged 25 years and over.

METHODS

Research design

This study was a further analysis with a matched case-control design using sub-sample data from the "Cohort Study of NCD Risk Factors" which was conducted in five villages of Central Bogor District, Bogor City, in 2011-2018. The study was performed between January 2011 and December 2018 in the aforementioned five villages of Central Bogor District, Bogor City.

Research subjects

The sample determination for the case-control study used a 1:3 ratio of cases and controls, after conducting a pilot study on the percentage of exposed controls in the study setting considering hypertension as a risk factor. The proportion of CHD in subjects with and without hypertension was 33.1% and 16.5%, respectively;[12] using the following case-control formula with a power of 80% ($Z\beta$ = 0.84); 5% significance level ($Z\alpha/2$ = 1.96), and a ratio of controls to cases of 3, a minimum sample size of 133 per group was obtained.

The sample population was all individuals in the age group of 25 years and over. The study sample was individuals with CHD cumulatively from 2011-2018,[15] and the controls were individuals who did not suffer from CHD, during the 8 years of the study and did not suffer from other diseases such as diabetes mellitus. Individuals in the two selected groups were matched for age and gender. There were 148 CHD cases identified from 2011-2018, while the control group consisted of 444 individuals, which is 3 times the number of individuals with CHD in the cases group.[16] The chart of the CHD sample size can be seen below (Figure 1).

Selection of cases

Cases were adult patients who had a confirmed diagnosis of CHD. The criteria for CHD are individuals who are declared to have coronary heart disease based on the results of electrocardiography (ECG) examinations which are carried out at a follow-up examination every two years. The results of the ECG were evaluated by a consultant cardiologist (mentioned by his/her initials). In addition, deaths of individuals from CHD were confirmed through verbal autopsy by a trained Puskesmas medical doctor. Therefore the diagnosis of CHD is based on an electrocardiogram (ECG) for living persons or verbal autopsy result for deceased individuals.[5]

Selection of controls

Controls were defined as individuals who had not experienced CHD based on a doctor's diagnosis and were selected by simple random sampling, taking into account gender and age matching. In addition, we excluded outpatients with hypertension and diabetes mellitus because the risk factors for these diseases may be similar to those of cases.

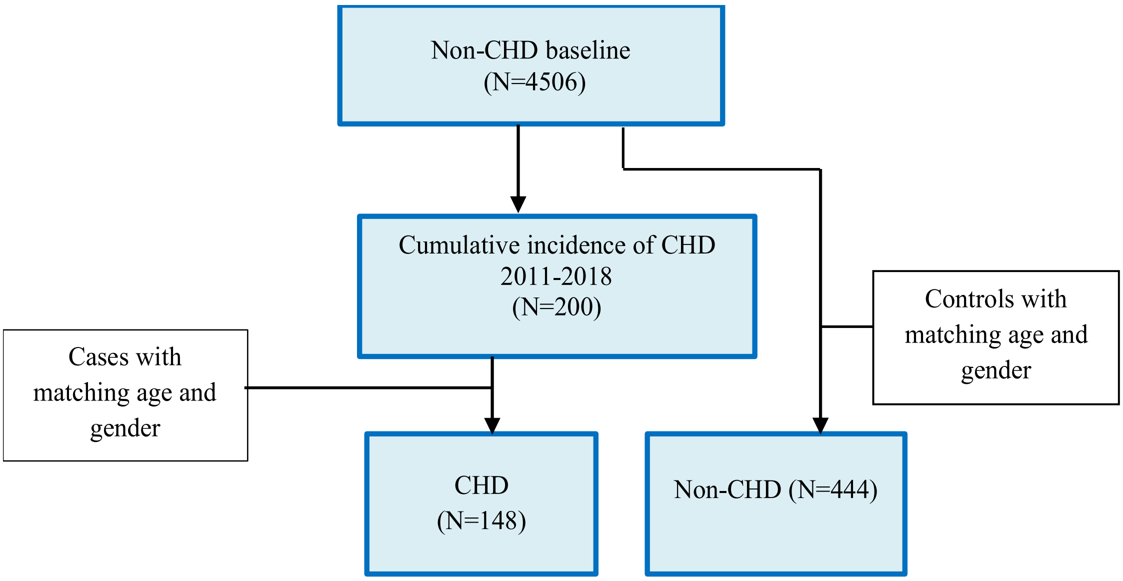

Figure 1. Individuals with and without CHD

Data sources and case handling

The data come from structured interviews, physical examinations, and supporting examinations that are carried out every two years. Interviews included socio-demographic data, past illnesses, diet, medication history, and behavior (physical activity, smoking, etc.). Physical examinations carried out were anthropometric measurements (weight, height, abdominal circumference, and blood pressure [systolic and diastolic pressure]). Investigations include clinical chemistry examination (lipid profile, blood sugar, kidney function, and HbA1c), and supporting electrocardiograms (ECG).

Individuals with abnormalities in the results of physical and supporting examinations are referred to health facilities, namely *Puskesmas* and referral hospitals for treatment and health control.(5) The laboratory results use the Third Report of the National Cholesterol Education Program (NCEP) or Adult Treatment Panel III as reference,(17) which has been adapted to Asian individual conditions. The risk limits used were waist circumference for men of >90 cm and for women of >80 cm, triglycerides >150 mg/dl, HDL cholesterol of <40 mg/dl and <50 mg/dl for men and women, respectively, fasting blood glucose of 110 mg/dl., and blood pressure of 130/85 mmHg.(18)

Data quality assurance

Before data collection, the questionnaire was pretested for feasibility in 10% of study subjects. Data recording quality was checked by the end of each day of data collection, for consistency, completeness, clarity, and accuracy; also during data processing, the information was checked for completeness and internal consistency. Data collection was done by four clinical nurses. A one-day training and practical demonstration session on interview techniques and measurement procedures was given to the data collectors by supervisors.

Data analysis

This further analysis uses SPSS software version 16, (serial number 5061284). The Kolmogorov–Smirnov test was used to determine the data distribution, which proved to be normal. Because of the normal data distribution ($p>0.05$), the Chi square test, Fisher's exact test, and independent t test were used. Bivariate and multiple logistic regression was used to determine the predictors of CHD within 8 years. Factors with p values of <0.25 in the bivariate analysis were selected and used in multiple logistic regression analysis to adjust the confounders. Statistical significance was set at a p value of < 0.05.

RESEARCH ETHICS

The study protocol was reviewed and approved by the Health Research Ethics Committee, Health Research and Development Agency, when collecting data from 2011 to 2018 under the following numbers: KE.01.08/EC/485/2011; KE.01.05/EC/394/2012; LB.02.01/5.2/KE.215/2013; LB.02.01/5.2/KE. 143/2014; LB.02.01/5.2/KE.135/2015; LB.02.01/5.2/KE.042/2016; LB.02.01/2/KE.108/2017; and LB.02.01/2/KE.076/2018. Informed consent was obtained from all participants.

RESULTS

In the initial data collected in 2011, there were 4,506 respondents who were not diagnosed with CHD. The cumulative incidence of CHD cases from the results of follow-up examinations from 2013 to 2018 was identified, but only 148 cases with and 444 cases without CHD could be further analyzed by case-control (Figure 1).

Characteristics of study subjects at baseline generally described case subjects as having higher mean lipid levels, blood sugar levels, body mass index, abdominal circumference, and blood pressure than control individuals (Table 1). However, only the mean fasting blood sugar, post-prandial blood glucose, and systolic blood pressure of case subjects were significantly higher than those of control subjects ($p<0.05$).

The education of individuals with and without CHD was mostly low and secondary education,

Table 1. Characteristics of study subjects at baseline

Characteristics	Case (n=148)	Control (n= 444)	p value
Gender			
Male	35 (23.6)	105 (23.6)	1.000 @
Female	113 (76.4)	339 (76.4)	
Age groups (years)			
40-49	67 (45.3)	201 (45.3)	1.000 @
50-59	64 (43.2)	192 (43.2)	
60 +	17 (11.5)	51 (11.5)	
Age (years)	50.37±6.49	50.37±6.47	1.000 #
Total cholesterol (mg/dL)	213.46±35.07	207.70±35.88	0.968 #
Triglycerides (mg/dL)	119.47±60.54	113.49±67.23	0.659 #
LDL-C (mg/dL)	135.81±31.02	131.97±31.01	0.733 #
HDL-C (mg/dL)	53.06±11.32	51.52 ±11.28	0.811#
Fasting blood glucose (mg/dL)	92.53±27.05	88.29±23.43	**0.038 #**
Post-prandial blood glucose (mg/dL)	133.15±65.09	120.87±44.60	**0.000 #**
BMI (kg/m^2)	25.58±4.16	25.08±4.46	0.461 #
Waist circumference (cm)	81.42±10.98	80.32±8.88	0.501#
Blood pressure			
Diastolic (mmHg)	85.64±13.11	80.74±12.23	0.418 #
Systolic (mmHg)	140.89±27.62	129.98±10.58	**0.002 #**

Note: Data presented as n (%) and mean ± SD, LDL-C = low density lipoprotein cholesterol, HDL-C = high density lipoprotein cholesterol, BMI = body mass index; @ Chi-square test; # Independent t-test

but higher education was two and a half times greater in the case group than in the control group. Most of the individuals in both groups had obesity, hypercholesterolemia, and high LDL levels. Although the majority of fasting and post-prandial blood glucose levels in the case and control groups were within normal limits, fasting and post-prandial blood glucose levels in the case group were 1.5 – 2 times higher than in the control group. Similarly, systolic blood pressures of 130 mmHg and diastolic blood pressures of 85 mmHg were more frequent in the case group than in the control group (Table 2).

From the results of logistic regression analysis after controlling for other risk factors, it appears that only higher education was a predictor of CHD. Subjects with higher education were 2.32 times more likely to suffer from CHD than those with low education. Other risk factors such as physical activity, smoking behavior, mental-emotional disorders, routine medications, consumption of sodium, fat, and sugar, central obesity, BMI, blood pressure, and lipid profile had no effect on the incidence of CHD in the analysis (Tables 2 and 3).

DISCUSSION

The results showed that a high level of education was a predictor of CHD. The results of this study did not show a relationship of blood pressure and lipid profile with CHD, although several previous studies have shown such a relationship. A study in China found a positive association between blood pressure and cardiovascular disease.[19] The results of our analysis show the same results as previous studies, in that systolic blood pressure is a predictor of CHD.[20] The same result was also reported by the study of Qi et al. [21] namely the higher the blood pressure, the greater the risk of CHD. A systolic pressure of 130–139 mmHg and/or a diastolic pressure of 80–89 mmHg has a 1.7 times risk, and a systolic pressure of 140–159 mmHg and/or a diastolic pressure of 90–99 mmHg has a 2.4 times risk of developing CHD. The study

Table 2. Relationship between risk factors and coronary heart disease

Risk factors	Case (n=148)	Control (n= 444)	OR (CI 95%)	p value
Education				
Low (elementary school and no schooling)	72 (48.6)	207 (46.6)	1	
Middle (Middle school and high school)	61 (41.2)	219 (49.3)	0.33 (0.15-0.70)	0.004
High	15 (10.1)	18 (4.1)	0.41 (0.20-0.87)	0.020
Physical activity				
Sufficiently	94 (63.5)	298 (67.3)	1	
Less	54 (36.5)	145 (32.7)	1.18 (0.80-1.74)	0.403
Smoking				
Never smoker	87 (65.9)	232 (62.4)	1	
Light smoker	16 (12.1)	75 (20.2)	0.56 (0.31-1.03)	0.062
Moderate smoker	19 (14.4)	45 (12.1)	1.12 (0.62-2.03)	0.694
Heavy smoker	10 (7.6)	20 (5.4)	1.33 (0.60-2.96)	0.480
Emotional mental disorder				
No	137 (92.6)	401 (90.5)	1	
Yes	11 (7.4)	42 (9.5)	0.76 (0.38-1.53)	0.451
Treatment*				
Regularly	65 (62.9)	118 (95.2)	1	
No regularly	5 (7.1)	6 (4.8)	1.51 (0.44-5.14)	0.508
Sodium				
< 2000 mg	69 (73.4)	208 (71.5)	1	
>= 2000 mg	25 (26.6)	83 (28.5)	0.90 (0.53-1.53)	0.718
Fat				
<67 g	84 (56.8)	250 (56.4)	1	
>= 67 g	64 (43.2)	193 (43.6)	0.98 (0.67-1.43)	0.945
Sugar				
<50 g	111 (92.5)	324 (90.0)	1	
>= 50 g	9 (7.5)	36 (10.0)	0.73 (0.34-1.56)	0.417
Central obesity				
Normal	46 (31.1)	142 (32.0)	1	
Obese	102 (68.9)	302 (68.0)	1.04 (0.69-1.55)	0.838
BMI				
Normal	35 (23.6)	112 (25.3)	1	
Underweight	4 (2.7)	17 (3.8)	0.75 (0.23-2.38)	0.630
Overweight	18 (12.2)	66 (14.9)	0.87 (0.45-1.66)	0.679
Obese	91 (61.5)	248 (56.0)	1.16 (0.74-1.83)	0.494
Total cholesterol				
Normal<200 mg/dL	38 (25.7)	142 (32.1)	1	
High >=200 mg/dL	110 (74.3)	301 (67.9)	1.36 (0.89-2.07)	0.145
Triglycerides				
Normal<150 mg/dL	97 (65.5)	320 (72.1)	1	
High >=150 mg/dL	51 (34.5)	124 (27.9)	1.35 (0.91-2.01)	0.132
LDL-C				
Normal	19 (12.8)	54 (12.2)	1	
High	129 (87.2)	390 (87.8)	0.94 (0.53-1.64)	0.829
HDL-C				
Normal	89 (60.1)	256 (57.7)	1	
Low	59 (39.9)	188 (42.3)	0.90 (0.61-1.31)	0.597
Fasting blood glucose				
<126 mg/dL	119 (80.4)	401 (90.3)	1	
>=126 mg/dL	29 (19.6)	43 (9.7)	2.27 (1.36-3.79)	**0.002**
Post-prandial blood glucose				
<200 mg/dL	119 (80.4)	389 (87.6)	1	
>=200 mg/dL	29 (19.6)	55 (12.4)	1.72 (1.05-2.82)	**0.031**
Systolic blood pressure				
<130 mmHg	54 (36.5)	241 (54.3)	1	
>=130 mmHg	94 (63.5)	203 (45.7)	2.06 (1.40-3.03)	**0.000**
Diastolic blood pressure				
<85 mmHg	62 (41.9)	260 (58.6)	1	
>=85 mmHg	86 (58.1)	184 (41.4)	1.96 (1.34-2.85)	**0.000**

Note : Data presented as n (%);OR : Odds Ratio; C.I, : Confidence interval; LDL-C = low density lipoprotein cholesterol; HDL-C = high density lipoprotein cholesterol; BMI = body mass index

Table 3. The results of multiple logistic regression analysis of CHD risk factors

Risk factors	OR	95%CI	p value
Education			
Low (elementary school and no schooling)	1		
Middle (Middle school and high school)	0.80	0.52-1.24	0.333
High	2.32	1.01-5.35	0.047
Smoking			
Never smoker	1		
Light smoker	0.66	0.36-1.22	0.193
Moderate smoker	1.26	0.68-2.32	0.459
Heavy smoker	1.05	0.44-2.50	0.898
Total cholesterol			
Normal<200 mg/dl	1		
High >=200 mg/dl	1.05	0.65-1.69	0.823
Triglycerides			
Normal<150 mg/dl	1		
High >=150 mg/dl	1.12	0.70-1.80	0.617
Fasting blood glucose			
<126 mg/dl	1		
>=126 mg/dl	1.96	0.97-3.95	0.060
Post-prandial blood glucose			
<200 mg/dl	1		
>=200 mg/dl	1.15	0.57-2.32	0.678
Systolic blood pressure			
<130 mmHg	1		
>=130 mmHg	1.35	0.76-2.41	0.298
Diastolic blood pressure			
<85 mmHg	1		
>=85 mmHg	1.69	0.95-3.00	0.073

Note: factors with $p < 0.25$ in the bivariate analysis were included in the multivariate models

by Turin et al.[22] showed that CHD was influenced by hypertension in both men and women, who had a 2-times higher risk of CHD than did normotensives. Similarly for blood sugar levels.

The result of this study did not show a relationship between lipid profile and CHD, and was therefore different from previous studies. The results of a meta-analysis of 32 articles in the Middle East, with a sample size of 191,979 individuals, reported that the highest risk factors for heart disease were dyslipidemia, hypertension and diabetes. The proportion of dyslipidemia (43.3%) in this region is higher than that of hypertension (26.2%) and diabetes mellitus (16%).[23] Research on CHD risk factors was also conducted in Shenzhen, China, on 3,395 hypertensive respondents aged between 30 and 79 years. It was found that 1,153 individuals had CHD within 3 years. The reported risk factors for coronary heart disease are age, body mass index, diabetes, dyslipidemia, and chronic kidney disease as predictors in individuals with hypertension. The Chinese study also found that the odds ratio of mental and emotional disorders is 1.54 times and sleep disturbance is 1.69 times (95%1CI. 1.21-2.34) with an Area Under Curve (AUC) of 0.839. This shows that individuals with hypertension need to maintain psychological health and good quality of sleep to help prevent coronary heart disease.[24]

Blood pressure has a consistent relationship with CHD, the higher the blood pressure, the higher the likelihood of CHD. Hypertension triggers atherosclerosis which can damage the endothelium through oxidative stress, resulting in increased endothelial cell synthesis of collagen and fibronectin, and its reduction is dependent on nitric oxide and increased permeability to lipoproteins.[25]

Meta-analysis studies show that a decrease in glycemic index and glycemic load is associated with the incidence of CHD in women. The pooled analysis showed increased CHD risk for the highest compared with the lowest glycemic index quintile.[26] Other studies have reported that type 1 and type 2 diabetes lead to an increased incidence of ischemic heart disease and congestive heart failure. Coronary heart disease accounts for up to 80 percent of mortality in type 2 diabetes patients, especially in women with diabetes.[27] The underlying factors for diabetic heart disease are coronary artery disease, hypertension, metabolic disorders such as hyperglycemia and dyslipidemia, microvascular disease, and autonomic neuropathy. The increase in diabetes-related sudden death may be due to autonomic neuropathy.[28]

Other studies have shown that CHD is more common in women. Stroke, hypertension, and hyperglycemia (fasting blood sugar level 100 mg/dl) are determinant factors for CHD.[29] Meanwhile, metabolic syndrome contributes to an increased risk of CHD and type 2 DM, which is twice the risk of CHD and five times the risk of DM in individuals without metabolic syndrome. Diabetes mellitus will also increase the risk of CHD up to three times that of non-DM disorders.[30]

A study by Jiang et al.[31] showed that postprandial hyperglycemia correlated with CHD, and suggested fasting blood sugar to be used to screen for CHD. Fasting sugar levels that are higher than normal are also associated with levels of arterial stiffness, coronary artery hypercalcemia, and risk of cardiovascular disease. Conversely, hypoglycemia or rapid changes in plasma glucose levels can cause an increase in counterregulatory hormones, such as epinephrine and norepinephrine. An increase in this hormone induces vasoconstriction and platelet aggregation.[32] Likewise, people with hypercholesterolemia and hyperlipidemia generally have abnormal carbohydrate metabolism with elevated insulin levels.[33] Insulin resistance predicts future cardiovascular risk.[34] Thus, any dietary factor that worsens glucose tolerance or increases insulin resistance is likely to increase the risk of death from CHD.

The result of this study showed that higher education had a 2.32-fold risk of getting CHD compared to low education. This finding is interesting and differs from the results of studies of genetic data with the hypothesis that low education is a causal risk factor in the development of CHD. Similarly, research by Maharani et al.[35] reported that individuals with lower education suffered from CHD. The higher the level of education, the fewer people suffer from CHD and from above-normal blood sugar. This finding is also similar to the research of Tillmann et al.[36], in that low education is a risk factor in the development of CHD. So it is possible that the cause of CHD is more complex in individuals with higher education than in those with low education because there are other factors that need to be investigated more deeply, including diet, life demands, work status, and environmental influences. Moreover, level of education is considered to affect the individual's ability to turn information into practical measures and behavior, affects access to recourses, employment-related problems and social exclusion if unemployed.

A limitation of this case-control study was that food consumption or eating patterns could not be accurately measured, due to difficulties in measuring food recall. As is well known, CHD is affected by the consumption of macronutrients such as carbohydrates, fats, protein, and fiber. It is also influenced by micronutrients such as sodium and vitamins. Khazanah's et al.[37] proves that excess sodium has an effect on blood pressure which will increase heart risk, and that consumption patterns of high carbohydrates, fat, cholesterol, and low fiber consumption.

Based on the results of this study, it is still necessary to control CHD risk factors, especially those related to increased blood glucose and blood pressure. Subjects with higher education need to get proper nutritional knowledge so that they are expected to have alternatives in choosing healthy foods. In addition, it is necessary to routinely monitor the health of respondents by health workers at Posyandu and primary health facilities.

CONCLUSION

Higher education is a predictor of CHD among adults. Suggested CHD prevention and control programs can be carried out by regular control of blood sugar levels and blood pressure. It is necessary to investigate further to find the reason why higher education is a predictor of CHD in this study.

CONFLICT OF INTEREST

None.

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AUTHOR'S CONTRIBUTION

S and SD contributed to literature search, data analysis and writing of the draft. JP contributed to literature search and analysis of participant characteristics. All authors have read and approved the final manuscript

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