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IDENTIFYING THE ODD RATIOS OF HIGH BLOOD PRESSURE AND SMOKING AS RISK FACTORS IN CORONARY ARTERY DISEASE: A META-ANALYSIS AND SYSTEMATIC REVIEW

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Abstract

Objectives: *Smoking and High blood pressure have been found to be important contributors to the development of coronary artery disease (CAD). This study combined data from several epidemiological studies to quantitatively and qualitatively evaluate the likelihood that smoking and blood pressure are the risk factors for CAD.*

Methodology: *Following a database search in compliance with MOOSE guidelines, suitable studies were added based on predefined inclusion criteria. The measures of association were calculated using the MedCalc statistical program, version 18.11.3. Heterogeneity was taken into account while calculating the odds ratios.*

Results: *The odds of exposure of high blood pressure in coronary artery disease patients were found to be 2.511 (95% CI of 1.662 to 3.795) and for smoking the odds ratio of 1.649 (95% CI of 1.382 to 1.969) were found.*

Conclusions: *The results highlight how smoking and high blood pressure are significant risk factors for CAD, underscoring the need for focused preventative measures. These are the risk factors that can be modified. Therefore, the strategies that focus on risk factors management have the potential to significantly lower the prevalence of disease worldwide. It is recommended to investigate the effects of exposure duration as well as interactions with other risk factors.*

INTRODUCTION

The majority of deaths globally are caused by non-communicable diseases (NCDs). This comprises conditions like heart disease, diabetes, cancer, and lung diseases [1]. Cardiovascular Diseases (CVDs) aka heart diseases comprise a wide range of conditions that includes conditions affecting heart muscles and the vascular system that carries blood and nutrients to the brain, heart, and other essential organs [2]. The World Health Organization (WHO) has included coronary artery disease, congenital heart disease, peripheral arterial disease, rheumatic heart disease, cerebrovascular disease, pulmonary embolism and deep venous thrombosis in the classification of CVD [1]. The 2019 Global Burden Disease Study has highlighted the prevalence of CVDs that has risen almost two folds from 1990 to 2019 showing an increase from 271 million people in 1990 to 523 million in 2019 [3]. The WHO Mortality rate due to coronary heart disease shows the death toll in Pakistan has reported to be 16.49% of total deaths [4].

The World Health Federation has hinted at the causes of coronary artery disease (CAD) such as a combination of socio-economic, behavioral, and environmental risk factors. The modifiable risk factors have been proven to play a major role in the development of CAD [5,6]. One of the considerable causes is high blood pressure or hypertension (HTN) and has an association with development of CAD [7].

According to the American Heart Association (AHA), there are studies which have shown the relationship between insulin resistance (a finding of diabetes) and high blood pressure. When patients suffer from both, high blood pressure and diabetes, their risk for CAD increases even more [8]. NCDs and their risk factors mainly diabetes and hypertension are prevalent in the Pakistani population [9].

A risk factor that is attributable to the development of CAD has also been noted, smoking. The consequence of smoking is the fatal CVD event in comparison to those who did not smoke. Also, the onset of disease and longevity has been compromised in individuals who do smoking. This shows the hazardous outcomes of smoking on cardiovascular health of an individual [8].

Heart disease, more particularly coronary artery disease, has been a prominent cause of mortality globally because of lifestyle changes, limited health literacy, and these barriers often compound the disease risk. The results of previous studies will be combined in this meta-analysis to produce a comprehensive and extensive evaluation of the most significant risk factors. In addition to addressing important knowledge gaps, this meta-analysis will also strengthen the foundation for tailored, effective cardiovascular health strategies. Since, evidence based practices are used to guide reforming early detection, and preventive measures to overcome the occurrence of diseases.

METHODOLOGY

The two investigators performed the strategies for finding relevant literature, identifying and choosing studies, evaluating their quality, and extracting data. The MOOSE (Meta-analyses Of Observational Studies in Epidemiology) standards were adhered to all the design, execution, and reporting phases of this meta-analysis [10]. It is a reporting guideline that provides a guide for authors, editors, reviewers, and readers on how to report the findings of observational study meta-analyses. The steps for presenting background, search strategy, techniques, findings, conclusions, and discussion are outlined in the MOOSE recommendations.

Study identification

We had conducted a comprehensive search across several databases and search engines including PubMed, Cochrane Library, google scholar, PEDrO, and Web of Science between August 2024 to November 2024. The search aimed to identify publications from 2014 to 2024. We used specific search strategies, combining keywords (MeSH) with the Boolean operator (AND, OR, NOT) in the following combination: “Cardiovascular disease” OR “coronary artery disease” OR “coronary heart disease” AND “risk factors” OR “prevalence” AND “case-control study” OR “observational studies” AND “hypertension” OR “high blood pressure". We filtered the related articles according to the study's selection criteria and contained a thorough list of relevant research.

Study selection

The abstracts of all relevant articles were studied first according to the designed inclusion criteria: coronary artery disease patients, studies that assessed the odds ratio of coronary artery disease in a group with exposure of hypertension and/or smoking to a group with no exposure, studies that included patients more than 30 years of age.

The exclusion criteria were used for the study: population included non-coronary artery disease patients, case reports and case series, and the studies that included interventions.

Quality assessment: the Newcastle Ottawa scale

As suggested by the Cochrane Non-Randomized Studies Methods, the Newcastle Ottawa Scale (NOS) was used to assess the quality of the studies included in this meta-analysis. This tool was created to evaluate the caliber of non-randomized research, particularly case-control and cohort studies [11]. In accordance with NOS case-control studies were judged based on three broad perspectives through the star system: selection of study groups, comparability of study groups, and ascertainment of exposure (Table 1).

Table 1: Newcastle Ottawa Scale for quality assessment.

References	Year	Study design	NOS quality score (maximum 9)
Sudikno [10]	2023	Observational study	8
El hasan Mehmoud [15]	2023	Observational study	9
Fatima Ghaddar [13]	2022	Observational study	8
Yen ju chen [14]	2021	Observational study	8
MS Basher [12]	2015	Observational study	7

Data extraction

Data from individual research were extracted and recorded using standardized abstraction sheets. Important details that were taken from every study and then entered into a composite evidence table that included: author, year of publication, target population, sample size, study design, risk factors and results.

Outcomes

Our main outcome is the measure of association through odds ratio of coronary artery disease (event) with smoking and hypertension (exposure).

Statistical analysis

The MedCalc statistical software version 18.11.3 for this meta-analysis was employed. For dichotomous variables, the strength of link was estimated using the odds ratio (OR) with 95% confidence interval. Using Cochrane Q, the odds ratios of the included studies were evaluated for heterogeneity. For $P < 0.05$, between-study heterogeneity was deemed significant. A fixed effects model was applied if heterogeneity was absent. A random effect model was taken into consideration if heterogeneity was discovered.

RESULTS

Characteristics of studies included

Out of 82 eligible studies screened for retrieval, 77 articles, irrelevant studies were excluded. After detailed evaluation 5 articles that contain the desired outcome measures were included. Initially, 1,067,196 articles were obtained initially, without adding advanced filters, through digital search strategies that included PubMed (35,117), Web of Science (2,009), Google Scholar (1,030,000), Cochrane Library (15), and PEDro (55). After screening on the basis of publication year, identical records 18,309 studies were screened and after meeting the selection criteria, study design, the number of final studies that were investigating the exposure to desired risk factors in coronary artery disease patients was five. We did not include randomized controlled trials. Five studies, with a total of 33,299 patients, published between 2014 and 2024 met our search criteria (Figure 1). All studies were observational studies that reported odds ratio of high blood pressure and smoking in coronary artery disease. All the studies were reported in the English language (Table 2).

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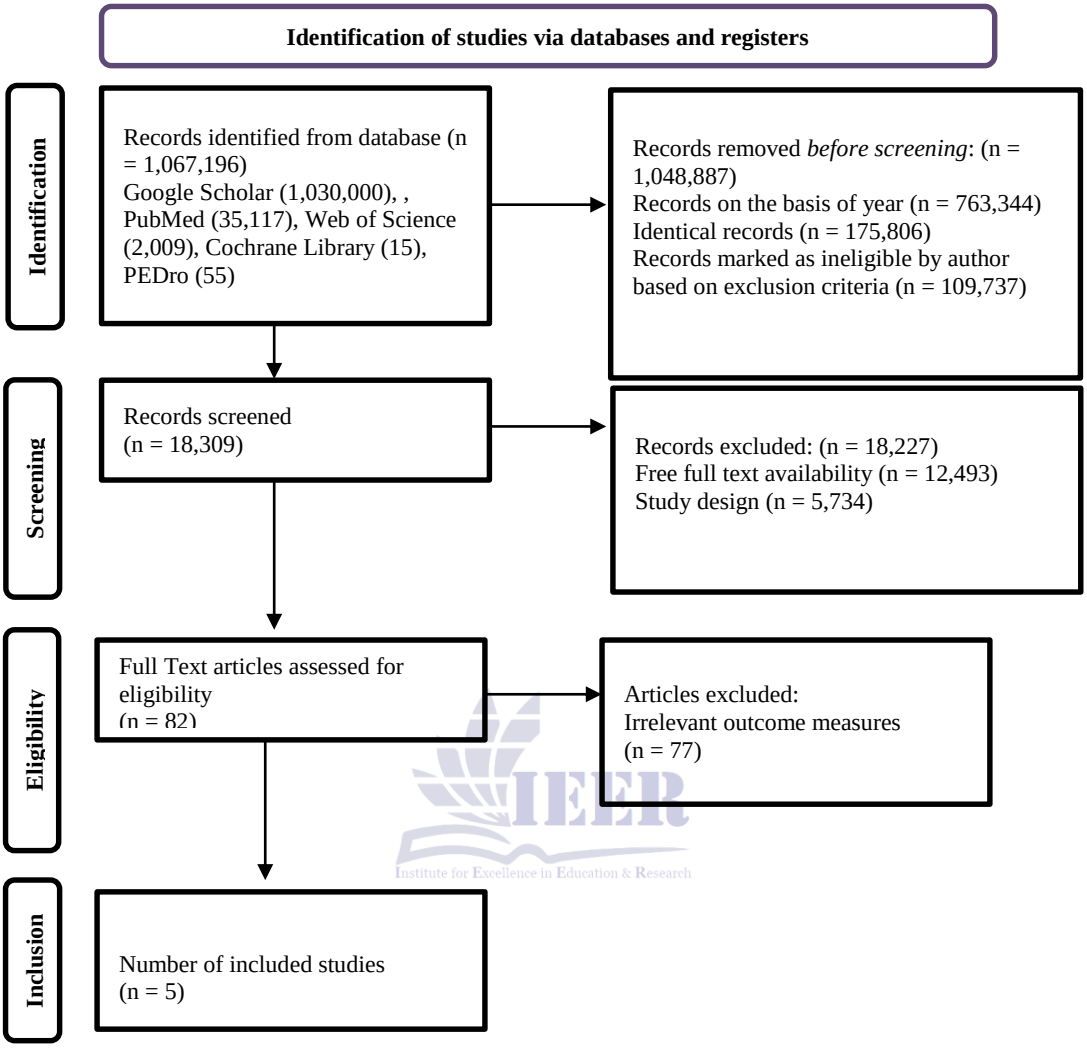


Figure 1: QUORUM diagram of literature search.

Table 2: Components of the studies included in the meta-analysis.

S. No.	Author (year)	Target Population	n	Study Design	Risk Factors	Results
1	Sudikno (2023) [10]	coronary artery disease	592 (444 controls and 148 cases)	observational study	Hypertension, Smoking	The case group showed higher blood pressure than control subjects
2	Elhassan Mahmoud (2023) [15]	cardiovascular disease	1045(836 control, 209 cases)	observational study	Hypertension, Smoking	Smokers had 1.47 times higher odds of reporting cardiovascular disease diagnoses compared to non-smokers.

3	Fatima Ghaddar (2022) [13]	coronary artery disease	1500 (1200 controls and 300 cases)	observational study	Hypertension, Smoking	Hypertension, cigarette smoking were strongly associated with CAD.
4	Yen-Ju Chen (2021) [14]	Major adverse cardiovascular events (MACEs) in RA	29,970 (23,976 controls and 5994 cases)	observational study	Hypertension	Hypertension is associated with an increased risk of MACE development in RA patients.
5	MS Basher (2015) [12]	Coronary artery disease	192 (96 controls and 96 cases)	observational study	Hypertension, Smoking	The association of smoking with the development of coronary artery disease disease was found positive.

Data of patients was studied for meta-analysis to identify the odds ratio of hypertension and smoking in patients with coronary artery disease (cases) with the individuals who do not have coronary artery disease (controls).

The findings of meta-analysis had shown, according to the Cohen's rule of thumb, for the exposure of hypertension shown an odds ratio of 2.511 (95% CI of 1.662 to 3.795) in a random effect model in the coronary artery disease patients as shown in Table 3.

Table 3: Demonstrating the findings of Hypertension meta-analysis.

Study	Intervention	Controls	Odds ratio	95% CI	z	P	Weight (%)	
							Fixed	Random
Sudikno (2023) [10]	94/148	203/444	2.067	1.409 to 3.032			2.03	19.88
El hasan Mehmoud (2023) [15]	104/209	259/836	2.207	1.621 to 3.003			3.14	21.16
Fatima Ghaddar (2022) [13]	274/300	821/1200	4.865	3.196 to 7.406			1.69	19.22
Yen ju chen (2021) [14]	3159/5994	9942/23976	1.573	1.486 to 1.665			92.32	23.89
MS Basher (2015) [12]	54/96	26/96	3.462	1.891 to 6.335			0.82	15.85

Total (fixed effects)	3685/6747	11251/26552	1.656	1.568 to 1.748	18.178	<0.001	100.00	100.00
Total (random effects)	3685/6747	11251/26552	2.511	1.662 to 3.795	4.372	<0.001	100.00	100.00

Additionally, as illustrated in Figure 2, this effect magnitude was further increased in the forest plot with 95% confidence interval in the random effect model. To calculate the percentage of heterogeneity, I2 was utilized. However, Cochrane Q was used to assess the percentages of discrepancies between the odds ratio of included studies, taking into account the value of I2 = 89.68% (95% CI of 78.73 to 94.99) with Q = 38.7420 as demonstrated in Table 4.

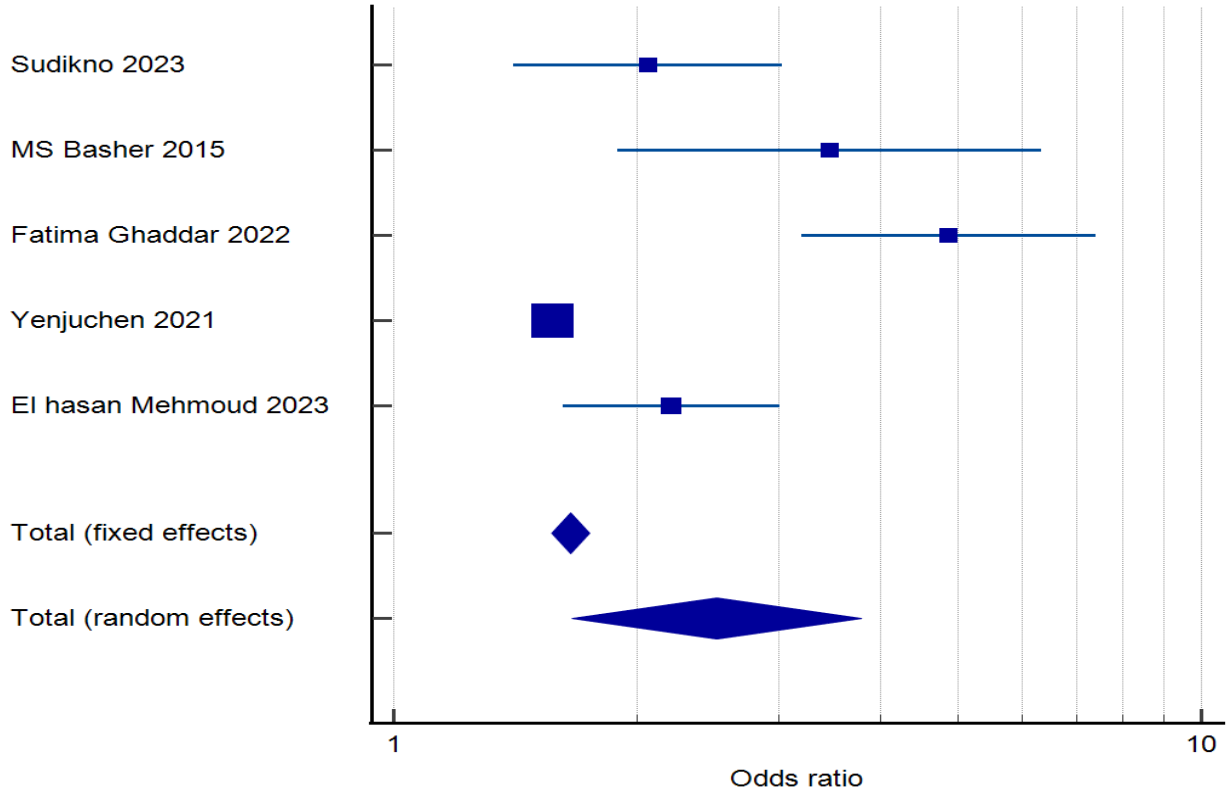


Figure 2: Forest plot showing fixed and random effect model for High blood pressure.

Table 4: Test for heterogeneity.

Q	38.7420
DF	4
Significance level	$p < 0.0001$

I^2 (inconsistency)	89.68%
95% CI for I^2	78.73 to 94.99

The exposure of smoking showed an odds ratio of 1.649 (95% CI of 1.382 to 1.969) in a fixed effect model among individuals with coronary artery disease, as seen in Table 5. Additionally, this effect size was further explained in the fixed effect model's forest plot with a 95% confidence interval (Figure 3). I2 was employed to calculate the heterogeneity %. But using Cochrane Q, percentages of inconsistencies in the odds ratio of included studies were computed, taking into account I2 = 45.67% (95% CI of 0.00 to 81.91) with Q = 5.5213 as demonstrated in Table 6.

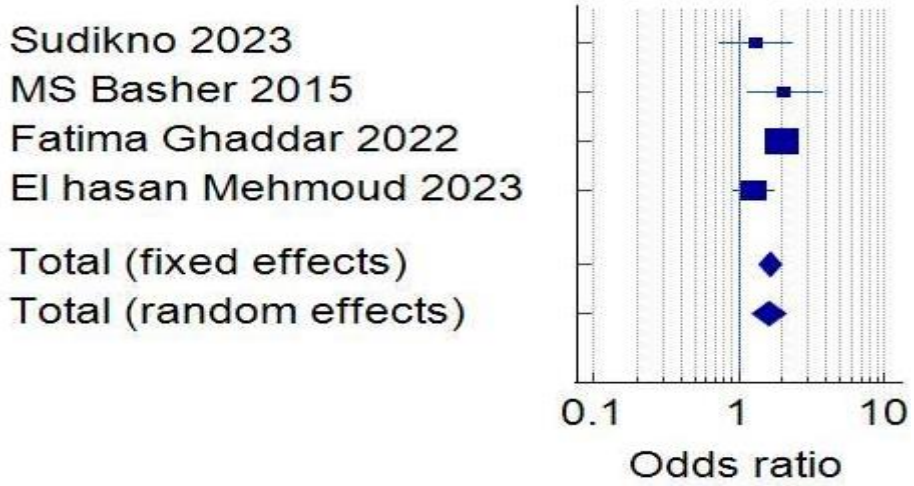


Figure 3: Forest plot showing fixed and random effect model for Smoking.

Table 5: Demonstrating the findings of Smoking meta-analysis.

Study	Intervention	Controls	Odds ratio	95% CI	z	P	Weight (%)	
							Fixed	Random
Sudikno (2023) [10]	19/148	45/444	1.306	0.737 to 2.313			9.73	15.79
El hasan Mehmoud (2023) [15]	83/209	284/836	1.280	0.937 to 1.749			32.71	32.06
Fatima Ghaddar (2022) [13]	155/300	423/1200	1.964	1.521 to 2.535			48.72	37.43
MS Basher (2015) [12]	69/96	53/96	2.073	1.138 to 3.777			8.84	14.72
Total (fixed effects)	326/753	805/2576	1.649	1.382 to 1.969	5.535	<0.001	100.00	100.00

Total (random effects)	326/753	805/2576	1.618	1.239 to 2.114	3.529	<0.001	100.00	100.00

Table 6: Test for heterogeneity for smoking.

Q	5.5213
DF	3
Significance level	p = 0.1374
I^2 (inconsistency)	45.67%
95% CI for I^2	0.00 to 81.91

Study case and control population

All five studies included coronary artery disease patients exposed to either risk factor high blood pressure or smoking (study/cases) and patients who are not exposed to these risk factor high blood pressure or smoking (control).

DISCUSSION

The study conducted by Huang et al. has reported that hypertension was significantly associated with an increased risk of coronary artery events (OR 1.28, 95% CI: 1.07–1.52, p = 0.006), also our study has shown similar findings that has shown association of hypertension with CVD (OR = 2.511 (95% CI of 1.662 to 3.795), this shows that patients who have exposure to risk factor (hypertension) are two and half times more prone to develop cardiovascular disease in comparison to the individuals who have no exposure to this risk factor [16]. Also, Nazarzadeh et al. have found the positive association of elevated blood pressure with the development of CAD (OR = 1.30 [95% CI 1.23 to 1.38]) but they only studied the association of systolic blood in comparison our study has considered the elevated values of both systolic and diastolic readings [17].

A cohort study in Japan also found the association of hypertension with incidence of cardiovascular events, regardless of the blood glucose levels [18]. The synergy index was calculated between hypertension and diabetes in relation to coronary artery disease 1.43 found, this indicates the individuals who have both conditions experience a greater risk of developing CAD greater than what would be predicted if each condition's effects were considered separately. In comparison, our study has taken into account solely the exposure of hypertension and their odds were calculated in the diseased individuals [19].

Another risk factor of coronary artery disease was studied in our meta-analysis, smoking. Exposure to smoking has been reported to increase the risk of cardiac disease (OR 3.2 [95% CI 1.7, 6.3]) in a study conducted by Attard et al. Our study findings have shown similar results OR = 1.649 (95% CI of 1.382 to 1.969) [20], the exposure of smoking in comparison to no smoking among the population doubled the possibility of occurrence of CAD [21].

This association of smoking was further discussed in another study that reported the odds of various disease outcomes in cigarette consumers, showing the odds range from 1.20 to 1.41 [22]. Chang et al. study has shown lower risk of cardiovascular disease in individuals who smoke from heavy to light smoking (RR = 0.78, 95% CI: 0.67, 0.89) but not in those who reduced by more than 50% and reduced smoking from heavy to moderate [23].

CONCLUSIONS

This meta-analysis has shown smoking and hypertension being positively related to cardiovascular disease development significantly to coronary artery disease. Therefore, further studies should be conducted with multiple outcome measures to clarify more about the other risk factors that are associated with coronary artery disease and other non-communicable diseases.

Limitations/Recommendation:
The analysis is limited to aggregated data from studies rather than individual-level data, which restricts more precise subgroup analyses. Future meta-analyses should ensure representation from different ethnicities and socioeconomic backgrounds for broader generalizability. Investigating dose-response relationships could provide more precise risk estimates.

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CONFLICT OF INTEREST:
The authors declare no conflict of interest.

ETHICAL APPROVAL:
This is a meta-analysis that does not involve human and animal subject or specimen; therefore, doesn't involve any related ethical issues. There is no breach of confidentiality or any unethical act in this study.

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