

Prevalence, Mortality, and Risk Factors of Acute Myocardial Infarction in Patients with Schizophrenia: A Systematic Review and Meta-Analysis

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Background: Acute myocardial infarction (AMI) is a life-threatening condition, especially for patients with schizophrenia (SCZ). Given their increased vulnerability to cardiovascular events, this study aimed to systematically review and meta-analyze the available literature on the prevalence, mortality, and risk factors of acute myocardial infarction in patients with schizophrenia.

Methods: The study followed the PRISMA guidelines. A systematic search was conducted across international databases to identify relevant studies. Study selection and data extraction adhered to PRISMA standards. Results were reported using Garrard's approach, and the meta-analysis was performed with CMA software.

Results: Ten studies were included in the quantitative analysis, and thirteen in the qualitative review. The prevalence of AMI in SCZ patients was 0.9%, with a mortality rate of 14.9%. Risk factors included low socioeconomic status, rural living, male gender, age under 65, and antipsychotic medication use. Smoking, diabetes, dyslipidemia, hypertension, and the nature of schizophrenia along with its symptoms contributed to higher AMI incidence and mortality in SCZ patients.

Conclusion: SCZ patients face a significantly higher risk of mortality from AMI compared to the general population. The primary contributors to this increased risk are lifestyle factors. Targeted treatment and lifestyle intervention programs could reduce the burden of AMI in this vulnerable group.

Keywords: acute myocardial infarction, schizophrenia, prevalence, mortality, risk factor

Introduction

Because of the rapidly increasing number of deaths from non-communicable diseases, especially in low- and middle-income countries, the World Health Organization (WHO) has identified non-communicable diseases, including cardiovascular diseases (CVDs), as health priorities for the next two decades.¹ One of the important cause of the death from CVDs is acute myocardial infarction (AMI).² Acute myocardial infarction, commonly introduces as acute heart attack, is often caused by a reduction of blood flow to the muscle of the heart and is usually caused by a blood clot in the coronary artery that leads to necrosis of the heart muscle.³ In the United States, 720,000 peoples have MI each year and about 122,000 peoples dead, and also the cost of health care and treatment in the first year of MI was estimated between \$ 22,000 and \$ 87,000 per patient.⁴ The potential risk factors for AMI included hypertension, diabetes, physical activity, alcohol use, smoking, diet, dyslipidemia, abdominal obesity, psychological and social stressors.⁵⁻¹⁰ Stress is one of the risk factors for AMI.¹¹ Also the studies reported the social isolation as a main risk factor for AMI. Social isolation and loneliness are associated with an approximately 30% increase in the risk of AMI.¹² In addition, it is reported that the depression and anxiety are relation with myocardial infarction.¹³ We can see these symptoms in mental disorders like schizophrenia.^{14,15} Mental disorders such as schizophrenia (SCZ) are one of the risk factors to AMI and other cardiovascular diseases (CVDs).^{16,17} Schizophrenia is a severe, chronic, and debilitating mental disorder.¹⁸ On average,

15.2 of every 100,000 people have the disease.¹⁹ Death from cardiovascular disease is a major cause of a 2 to 3 rate increase in mortality and a 20% reduction in life expectancy for patients with schizophrenia compared to the general population and a wide range of factors, from genes to the environment, play roles as risk factors for cardiovascular disease in SCZ patients.^{18,20} It is important to note that the studies were conducted in different countries, which may contribute to variability in reported mortality rates. Studies have shown that MI is less commonly diagnosed in people with schizophrenia, so, AMI is associated with higher mortality in these individuals due to less treatment.²¹ Because acute myocardial infarction is associated with mortality and patients with schizophrenia are at risk for AMI, the present study is conducted with the aim to determine the prevalence and mortality of AMI in schizophrenic patients. The reported risk factors for AMI and mortality were also investigated in this study.

Materials and Methods

Registration and Objective

The Protocol of this systematic review study was approved in Kurdistan University of Medical Sciences with ID: IR.MUK.REC.1403.235. This study explores the prevalence, mortality, and risk factors of acute myocardial infarction (AMI) in schizophrenia patients through a systematic review and meta-analysis.

Search Strategy

In this study, we used the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) protocol in design, searching, study selection, and data extraction and reporting findings. This protocol is considered a valid method to review past studies comprehensively, following the conceptual and structural framework of review studies.²² A comprehensive search was conducted in international database to November 5th, 2024. The searched databases were included Web of Sciences, Scopus, PubMed, and Google Scholar. The strategy of the search was performed by keywords related to the study aims, and similar keywords in published studies and also via PubMed standard MeSH terms. We searched databases with keywords included Acute Myocardial Infarction/AMI, Schizophrenia/SCZ, Myocardial Infarction/MI, Cardiovascular death, Sudden death, Mental Disorders, Mental Illness, and Prevalence, Mortality, Death, and Risk Factor. Also, we checked the reference lists of the articles for other eligible papers.

Inclusion and Exclusion Criteria

We included the observational studies that reported the results in prevalence, mortality, or risk factors. In addition, the studies that had more than one data, we included all of them. The studies with review and meta-analysis design, letters, commentaries, and other similar papers were excluded from further process. The list of eligible studies was included in reference manager software for more screening.

Search Validation and Study Selection

All eligible papers were obtained by a comprehensive search and use of different keywords by November 5th, 2024. The study selection protocol is based on PRISMA.²² The references list of all studies was entered into the Endnote X9 software and screened to identify and remove the duplicate titles. The titles of all remaining papers were then reviewed independently by two of the authors (MK, MJ) to identify eligible titles. In the next step, the abstract of the remaining articles was screened, and finally the full text of the eligible studies was reviewed in detail by the research team to select the studies. After study selection, their full text was carefully read several times to select and extract the required data. Any differences between the authors in the process of searching and selecting studies and data extraction were resolved through group discussions.

Meta-Analysis and Assessment of Publication Bias

We conducted a meta-analysis to estimate the prevalence and mortality rates of acute myocardial infarction (AMI) in patients with schizophrenia using Comprehensive Meta-Analysis (CMA) software. Given the substantial heterogeneity

among studies (prevalence: $I^2 = 93.68\%$, $P < 0.001$; mortality: $I^2 = 99.37\%$, $P < 0.001$), a random-effects model was employed to calculate pooled estimates, in accordance with standard meta-analytic practice.

Assessment of heterogeneity was performed using the I^2 statistic, and potential sources of variability were explored qualitatively, including differences in study design, population characteristics, and geographic regions.

Publication bias was evaluated visually using funnel plots and statistically using Egger's test. A P-value < 0.05 in Egger's test was considered indicative of significant asymmetry. This approach follows the PRISMA guidelines for systematic reviews and meta-analyses, ensuring transparency and reproducibility in reporting the results.

Data Extraction and Report

The data were extracted after a detailed screening of the full text of the studies. The data were reported using the Garrard table, and the information for prevalence, mortality, and risk factors were reported in other tables. The Garrard table is a framed method for reporting the results of review studies that introduced by Judith Garrard and we used the 2020 edition of this table.²³ Studies characteristics were reported including author, design, publish year, country, and participants. In studies that reported more than one data, we have included all of them.

Results

Study Selection

All articles were searched until November 5th, 2024. Six hundred and ninety-one papers were found in the initial search. All papers were extracted into the Endnote X9 software and similar titles were removed. After removing the similar papers, 623 articles remained, and the titles of these articles and abstracts were reviewed independently by two of the authors (MJ, MK). At this stage, 547 papers based on the design, title and abstract were eliminated and 76 papers remained. The full text of the 76 studies was screened in detail and finally 14 studies were eligible for data extraction. Ten studies were included in the quantitative review and 13 studies were included in the qualitative screening. Some studies had more than 1 data. Four articles reported the prevalence of AMI in SCZ patients, five articles reported the mortality rate, and 13 articles reported the risk factors. The selection process was based on the PRISMA statement (Figure 1).

Characteristics of Articles

Fourteen studies were included in the review. These studies were published from 2008 to 2021 and all had a cross-sectional design. Four of them conducted in Taiwan and 4 in Denmark. There are also 2 studies in Canada and 2 in Sweden. In addition, 1 article was conducted in Lebanon and 1 article in Scotland. A total of 86507 schizophrenic patients and 1039361 non-schizophrenic peoples were participated in these studies (Table 1).

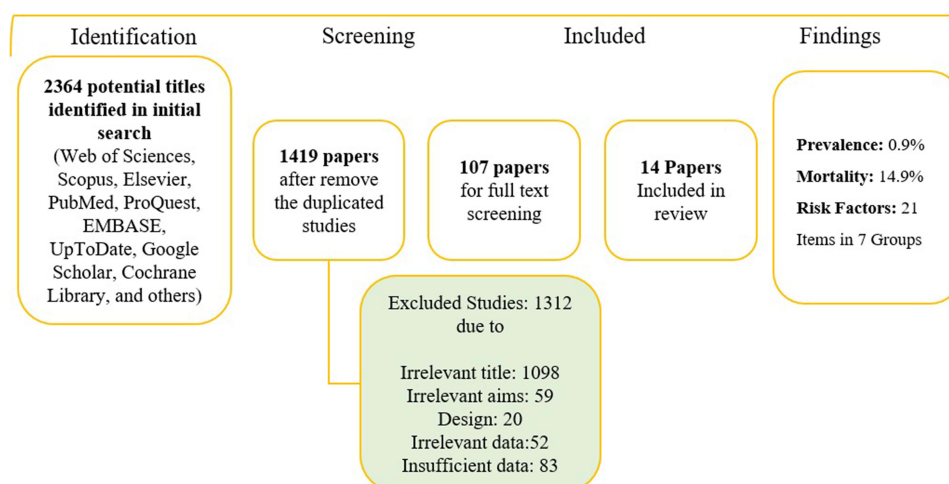


Figure 1 Flow Chart for Study Selection and Results.

Table 1 Characteristics of Studies (n = 14)

Studies	Design	Pub Date - Country	Participants
Wu et al ²⁴	CS	2013 - Taiwan	Case: 591 SCZ Patients Control: 2527 Health Peoples
Hauck et al ²¹	CS	2020 - Canada	Overall: 108610 SCZ: 1145non-SCZ: 107465
Kugathasan et al ²⁵	CS	2018 - Denmark	SCZ: 36962 Non-SCZ: 184810
Kurdyak et al ²⁶	CS	2012 - Canada	SCZ: 842non-SCZ: 71668
Jakobsen et al ²⁷	CS	2008 - Denmark	SCZ: 15710
Lin et al ²⁸	CS	2010 - Taiwan	SCZ: 7353
Wu et al ²⁹	CS	2015 - Taiwan	Total AMI: 834 SCZ: 591
Lin et al ³⁰	CS	2014 - Taiwan	Total: 59806 SCZ: 5748
Fleetwood et al ³¹	CS	2021 - Scotland	SCZ: 923 Healthy Peoples: 227506
Kugathasan et al ³²	CS	2018 - Denmark	SCZ: 684 Healthy peoples: 104334
Attar et al ³³	CS	2019 - Denmark	SCZ: 726 Healthy peoples: 1425
Attar et al ³⁴	CS	2020 - Sweden	SCZ: 1008 Non-SCZ: 285325
Westman et al ³⁵	CS	2018 - Sweden	SCZ: 13895
Al-Seddik et al ³⁶	CS	2019 - Lebanon	SCZ: 329

Abbreviation: CS, Cross Sectional.

Prevalence of AMI in Patients with Schizophrenia

The prevalence of AMI in patients with schizophrenia was not high. In 4 articles, the prevalence of AMI in schizophrenic patients was reported. The results of meta-analysis showed that the prevalence of AMI in schizophrenic patients is 0.9% (0.6–1.4%) (Figure 2). There was no publication bias ($t = 1.28$, $P = 0.163$) (Figure 3). The reported prevalence rates were 0.41% (30/7353), 1.1% (173/15,710), 1.2% (4/329) and 1.45% (537/36,962) (Table 2).

Mortality Rate of AMI in Patients with Schizophrenia

In 5 studies, the mortality rate of AMI has been reported that the results of meta-analysis showed the mortality rate due to AMI in schizophrenic patients is 14.9% (7.4–27.6%) (Figure 4). There was no publication bias ($t = 0.78$, $P = 0.244$) (Figure 5). The mortality rate of AMI in patients with schizophrenia reported in various ranges from 3.9% to 44.9% for early deaths, with one-year mortality reported at 21% and 33.5% (Table 3).

Risk Factors for AMI in Patients with Schizophrenia

Thirteen studies were screened qualitatively and the risk factors for AMI were assessed in 7 dimensions including cardiovascular, metabolic disorders, socio-economic-demographic status, lifestyle and others. The effect of the nature of schizophrenia and the role of the health care system have also been reported. A total of 22 risk factors were extracted. The highest reported risk factors were metabolic disorders included diabetes and hyperlipidemia/dyslipidemia. Hypertension and

Prevalence of AMI in Schizophrenia Patients

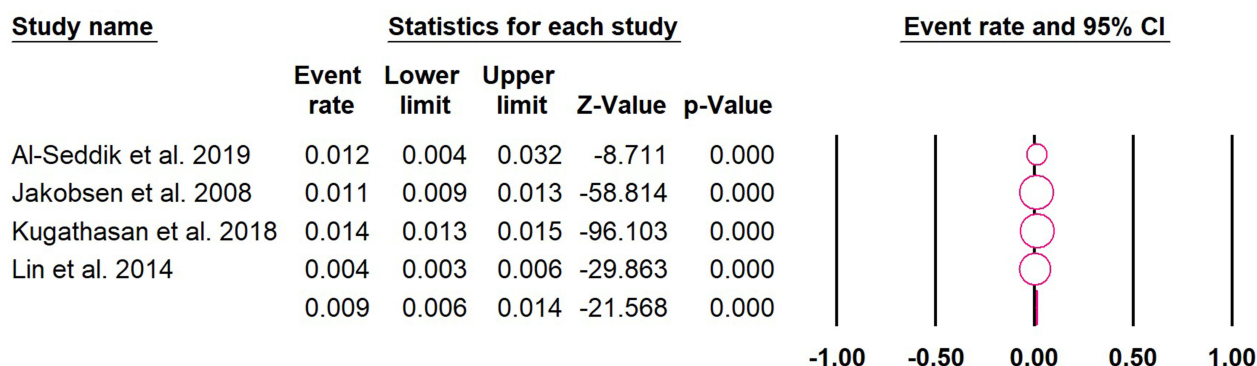


Figure 2 Prevalence of AMI in Schizophrenia Patients.

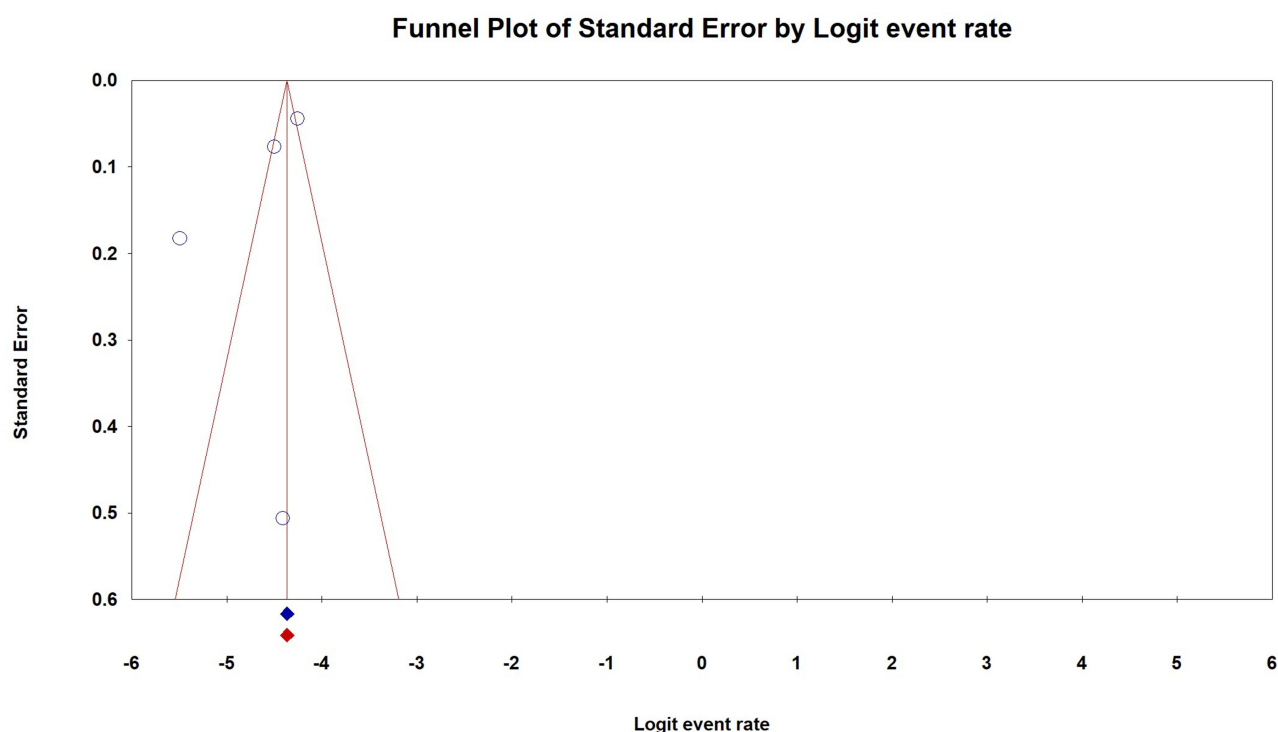


Figure 3 Funnel Plot for Included Studies in Prevalence Meta-analysis.

heart failure have been reported as cardiovascular risk factors. Low socio-economic status, age under 65, male gender and living in rural areas are more reported than other socio-economic-demographic factors. Drug abuse, smoking and alcohol use have also been reported as risk factors for AMI. The nature of schizophrenia has also been suggested as a risk factor for AMI through the use of antipsychotic medications. The health care system is also known to be risk factor by lack of proper cardiac care after MI in SCZ patients. Other reported risk factors included COPD, asthma and anemia (Table 4).

Discussion

The aim of this study was to review the prevalence, mortality and risk factors of AMI in schizophrenic patients. Patients with schizophrenia are at risk for myocardial infarction, which can lead to higher mortality than others. The prevalence of AMI in SCZ patients was 0.9%, and AMI mortality in schizophrenic patients is estimated at 14.9%, which is reported at 13.4% to 13.8% in United States AMI patients.³⁷

Table 2 The Prevalence of Acute Myocardial Infarction in Schizophrenia Patients

Studies	Participants	AMI Prevalence in SCZ Patients (%)
Kugathasan et al ²⁵	SCZ: 36962 Non-SCZ: 184810	537 (1.45)
Jakobsen et al ²⁷	SCZ: 15710	173 (1.1)
Lin et al ²⁸	SCZ: 7353	30 (0.41)
Al-Seddik et al ³⁶	SCZ: 329	4 (1.2)

SCZ patients are at risk for acute myocardial infarction and other CVDs and its related mortality. One of these causes is the nature of the schizophrenia disorder. These patients experience high levels of stress, anxiety, depression, and social isolation,^{38,39} and these symptoms seem to be risk factors for cardiovascular disease and myocardial infarction. Stress and anxiety have been identified as risk factors for coronary artery disease.^{40–42} In addition, the degrees of depressive symptoms are directly related to cardiovascular disease,^{40,43} and can also be effective in the incidence and progression of CVDs by the development of metabolic syndromes.^{44,45} Therefore, controlling the symptoms of schizophrenic patients may be effective in preventing AMI. However, it should be noted that controlling the symptoms with high doses of antipsychotic drugs (APDs) or long-term administration can worsen the condition of patients. Some studies have shown that one of the causes of progression of cardiovascular disease and AMI in schizophrenic patients is the use of antipsychotic drugs.^{46,47} APDs such as clozapine can reduce left ventricular ejection fraction (LVEF),⁴⁶ and also cause insulin resistance, hyperglycemia and weight gain.^{48–50} APDs increase the risk of diabetes, hypertension and hyperlipidemia.⁵¹ The incidence of diabetes, especially type 2 diabetes, following weight gain and insulin resistance and changes in leptin levels are side effects of taking APDs, especially second-generation drugs in schizophrenic patients.^{48–50,52} These factors may explain the effect of antipsychotic drugs on the incidence and severity of cardiovascular disease and AMI in SCZ patients. Weight gain has been reported as a factor for cardiovascular disorders in patients taking lipogenic APDs. This side effect has been reported in clozapine and olanzapine and other similar medications.^{47,53,54} Monitoring the use of medications and replace drugs with known cardiovascular complications and less side effects, can be useful in preventing cardiovascular complications. In addition, it is recommended that non-pharmacological methods be used to control schizophrenia as much as possible.

Another factor that may cause schizophrenia patients to have a cardiac infarction is the lifestyle. Schizophrenia affects patient’s lifestyles and lifestyle affects the severity of schizophrenia symptoms.^{55,56} SCZ patients are more likely than other

Mortality Rate of the AMI in Schizophrenia Patients

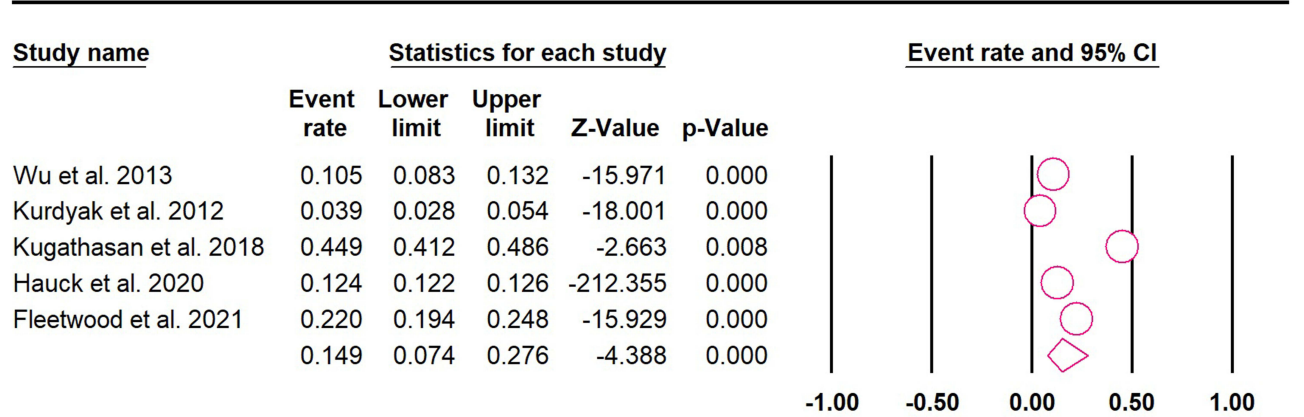


Figure 4 Mortality Rate of AMI in Schizophrenia Patients.

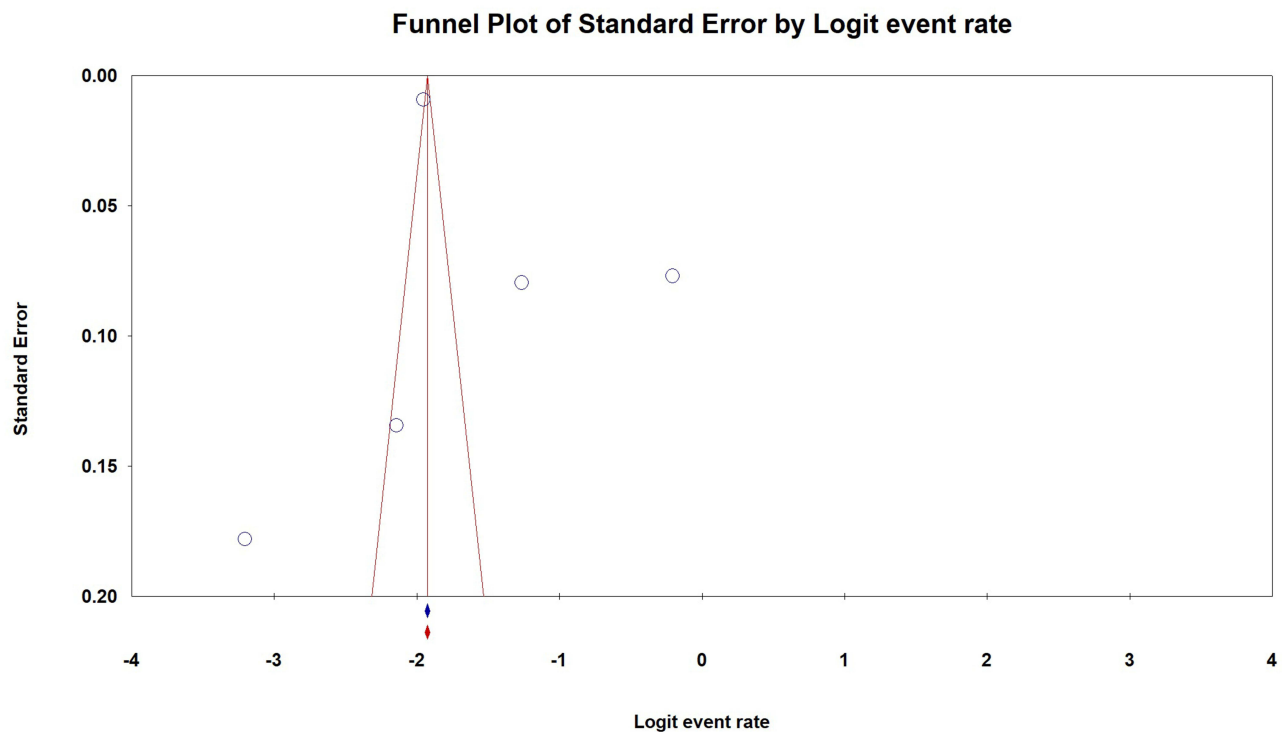


Figure 5 Funnel Plot for Included Studies in Mortality Meta-analysis.

healthy populations to develop cardiovascular disease due to an unhealthy lifestyle.^{57,58} And as we know, cardiovascular diseases are also very much related to lifestyle.^{59–61} Smoking, drug abuse, inactivity, unhealthy diet, and poor sleep patterns are all reported CVDs factors in schizophrenic patients.^{10,59–63} One of the factors of the incidence and severity of myocardial infarction is smoking,⁶⁰ which the high levels of smoking has been reported in patients with SCZ.^{58,64} Tobacco use increases the risk of cardiovascular mortality by 86% over 20 years.⁶⁵ Smoking also increases C-reactive protein (CRP) levels in schizophrenic patients.⁶⁶ Recent studies have reported that smoking affects the severity and location of coronary artery occlusion, which can also affect the severity of MI.⁵⁹ Therefore, it is possible to prevent or exacerbate cardiovascular disease in SCZ patients by offering smoking cessation programs. The effect of diet on the incidence and severity of cardiovascular disease has also been confirmed.^{57,67} In patients with schizophrenia, multiple periods of food poverty and food insecurity have been reported.^{68,69} In patients with mental disorders, food poverty is more common in those who smoke.⁷⁰ And in patients

Table 3 The Mortality Rate of Acute Myocardial Infarction in Schizophrenia Patients

Studies	Participants	Mortality (%)
Wu et al ²⁴	Case: 591 SCZ Patients Control: 2527 Health Peoples	62 (10.49)
Hauck et al ²¹	Overall: 108610 SCZ: 1145Non-SCZ: 107465	142 (12.4)
Kurdyak et al ²⁶	SCZ: 842Non-SCZ: 71668	33 (3.9)
Fleetwood et al ³¹	SCZ: 923 Healthy Peoples: 227506	203 (22)
Kugathasan et al ³²	SCZ: 684 Healthy peoples: 104334	307 (44.9)

Table 4 Risk Factors for Acute Myocardial Infarction in Schizophrenia Patients

Cardiovascular Risk Factors	
Hypertension	Wu et al, ²⁴ Hauck et al, ²¹ Kugathan et al, ²⁵ Kurdyak et al, ²⁶ Lin et al, ²⁸ Al-Seddik et al ³⁶
Heart Failure comorbidity	Fleetwood et al, ³¹ Attar et al, ³⁴ Attar et al ³³
Metabolic Disorders	
Diabetes	Wu et al, ²⁴ Hauck et al, ²¹ Kugathan et al, ²⁵ Kurdyak et al, ²⁶ Lin et al, ²⁸ Fleetwood et al, ³¹ Kugathan et al, ³² Attar et al, ³⁴ Attar et al, ³³ Al-Seddik et al ³⁶
Hyperlipidemia/Dyslipidemia	Wu et al, ²⁴ Kugathan et al, ²⁵ Al-Seddik et al ³⁶
Socio-economic/Demographic	
Low Income/Low Socio-economic status	Wu et al, ²⁴ Hauck et al, ²¹ Kurdyak et al, ²⁶ Fleetwood et al ³¹
Female Gender (2)	Hauck et al ²¹
Male Gender	Kurdyak et al, ²⁶ Lin et al, ³⁰ Fleetwood et al ³¹
Rural Area Residence	Hauck et al, ²¹ Kurdyak et al, ²⁶ Lin et al ²⁸
Age (10 younger compared to non-SCZ participants/Mean age < 65)	Hauck et al, ²¹ Lin et al, ³⁰ Fleetwood et al, ³¹ Attar et al, ³⁴ Westman et al ³⁵
Unemployment	Attar et al ³⁴
Life Style	
Alcohol Use	Wu et al, ²⁴ Fleetwood et al ³¹
Drug abuse	Lin et al, ²⁸ Kugathan et al ³²
Smoking	Attar et al ³⁴
Schizophrenia Nature	
Antipsychotic Medications	Wu et al, ²⁹ Lin et al ³⁰
Receptor-bindings: D1, D3, 5-HT2A, 5-HT2C, 5-HT6, α 2, and H1 receptors	Lin et al ³⁰
Health Care System	
Low cardiac care after MI	Kugathan et al ³²
Other Factors	
COPD	Kugathan et al, ²⁵ Kurdyak et al, ²⁶ Fleetwood et al, ³¹ Attar et al ³⁴
Asthma	Kurdyak et al ²⁶
Anemia	Attar et al ³³

with schizophrenia with nutritional deficiencies, they are more likely to develop lifestyle-related diseases.⁵⁶ Physical inactivity has been reported in 65% of schizophrenic patients.⁵¹ Poor diet and lack of physical activity can make the symptoms of schizophrenia and the cognitive impairment be worse.⁷¹

Another potential risk factor is sleep disorders. Many of schizophrenic patients report sleep disturbances before the severity of their symptoms.⁷² Some patients with schizophrenia have comorbidities such as sleep apnea.⁷³ Sleep apnea and sleep disorders are known to be factors for CVD and CAD.^{74,75} Therefore, monitoring the lifestyle of schizophrenic patients seems to be very important.

Recommendations

1. Monitor the dose of APDs and the duration of treatment with them.
2. Use non-pharmacological therapies and counseling as much as possible.
3. Effective lifestyle change programs are designed and implemented.
4. The diet of schizophrenic patients should be planned and controlled.
5. Schizophrenia patients should be checked in periods for cardiovascular disease.

Limitations and Implications

In this review study, we conducted a comprehensive search in databases to find all of the eligible papers. In addition, the list of references in potent studies was screened to find more papers. In this study, we reported the potent risk factors for progression of CVDs and AMI. The results of this study are comprehensive and can be used by clinicians and researchers.

A limitation of this review is that the included studies were conducted in different countries, and geographic variability may have contributed to heterogeneity in mortality rates. So this difference should be considered by readers.

Conclusions

In this systematic review, we synthesized evidence on acute myocardial infarction (AMI) in patients with schizophrenia. The prevalence of AMI in this population was estimated at 0.9%, while the mortality rate associated with AMI was approximately 14.9%. Multiple risk factors were identified, including metabolic disorders (diabetes, hyperlipidemia/dyslipidemia), cardiovascular conditions (hypertension, heart failure), and socio-demographic factors such as male gender, age under 65, low socio-economic status, and living in rural areas. Lifestyle factors (smoking, alcohol use, drug abuse), the nature of schizophrenia (including antipsychotic medication use), and limitations in the health care system also contribute to the risk of AMI.

Overall, this review highlights the prevalence, mortality, and multifactorial risk profile of AMI in patients with schizophrenia, emphasizing the need for early detection, targeted preventive strategies, and improved cardiac care in this vulnerable population.

Data Sharing Statement

This study has a review design and the raw data are available in references studies. All of the related data reported in study.

Ethics Approval and Consent to Participate

This study approved in Kurdistan University of Medical Sciences with ID: IR.MUK.REC.1403.235. In this systematic review study, all aspects of ethics in medical research were observed based on the Declaration of Helsinki and the journal guidelines.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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