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ABSTRACT

Aim: Given that patients with cancer may commit suicide due to physical and mental problems, the present study objectives were to identify particular risk factors of different subgroup of patients including type of cancer, gender, age, type and time of suicide, and geographical region to facilitate early care and psychosocial support.

Methods: A comprehensive review of databases including Embase, Scopus, PubMed, and Web of Science was conducted for original articles published in English from January 2000 to March 2022. It is based on the PRISMA checklist.

Results: After reviewing 69 articles selected from 15 countries, the total prevalence rate of suicide among 34,157,856 patients with cancer was estimated 67,169, at 0.013 (95% CI, 0.008–0.021). The highest suicide prevalence was related to gastrointestinal cancer, estimated at 0.204 (95% CI, 0.161–0.255). A gender-based meta-analysis showed that the prevalence of suicide/suicidal ideation was higher among men, estimated at 0.013 (95% CI, 0.008–0.023) compared with women, at 0.006 (95% CI, 0.002–0.017).

Conclusion: Based on study results, suicide-prevention strategies should be aimed at patients younger than 40 years of age to effectively resolve their mental health disorders and promote their self-efficacy in successful management of the disease.

KEYWORDS

Cancer; global; meta-analysis; suicide; systematic review

INTRODUCTION

Cancer represents the second leading cause of death worldwide, with an estimated 17 million deaths in 2030, accounting for approximately one in six deaths (Ribas et al., 2018). It is predicted that the total number of new cases will quickly increase to 29.4 million in the proceeding 20 years, reaching nearly 2 million deaths (Park et al., 2016). In addition, a cancer diagnosis can cause negative emotional feelings to patients, including pain, anxiety, stress, and depression during the treatment process. Thus, having both cancer and a psychological disorder is associated with decreased quality of life, increased risk of mortality particularly by suicide, poor adherence to medication, and diminished health outcomes (Klonsky, May, & Saffer, 2016; Sinyor, Tse, & Pirkis, 2017). Patients with cancer have a

high prevalence of depression, which limits patients' ability to suppress the disease. Furthermore, it reduces patients' acceptance of their medication and leads to prolonged length of hospital stay (Amiri & Behnezhad, 2020). This negative emotion substantially increases the odds of future suicide attempts (Chochinov, 2001). Accordingly, literature has shown that individuals with cancer are at twice the risk of committing suicide compared to the general population (Ahn et al., 2015; Kye & Park, 2017; Yamauchi et al., 2014). During the years 2000 to 2016, Liu et al. found an increasing trend in suicide risk among patients with cancer which drew the attention of health professionals to this issue as preventable deaths (Liu et al., 2022). Higher suicide rates among patients with cancer were mainly mentioned to be associated with individuals with poor prognoses, such as those with stomach and pancreatic cancers, feelings of depression, lack of social support, vulnerability, interpersonal dysfunction, and prolonged unmanageable pain along with particular demographic characteristics such as age, gender, and specific cancer types (McFarland, Walsh, Napolitano, Morita, & Jaiswal, 2019).

Failure to mitigate risk of death by suicide among patients with cancer may lead to more morbidity and mortality. To obtain data in regard to suicide risk factors, it might be helpful to identify patients with cancer who are at the highest risk of suicide (Senf, Bender, & Fettel, 2022). Findings of related studies conducted between 1973 and 2002 revealed that the greatest suicide risks were found in patients with cancers of the head and neck (Kam et al., 2015). Development of study results until 2011 also confirmed that head and neck cancers were associated with the highest suicide rates, with three times more frequent suicides than in the general United States population (Zaorsky et al., 2019). Other studies reported the highest prevalence of suicide among patients with cancers of the respiratory system, followed by those with affected pharynx or cancer of plasma cells, bones and joints, the digestive system, and the nervous system (Zhang, Sun, Peng, Ma, & Tang, 2021). Male gender and age were also mentioned as risk factors for suicide among patients with cancer (Misono, Weiss, Fann, Redman, & Yueh, 2008; Spicer & Miller, 2000). The high prevalence of suicide in patients with cancer compared with the general population might be due to either patients' willingness and attitude toward self-autonomy and self-control or severe depressive symptoms (Filiberti et al., 2001). Thus, all-inclusive cancer care should incorporate appropriate psychiatric intervention along with pain management with the purpose of minimizing suicidal ideation (Akechi, Okamura, Nishiwaki, & Uchitomi, 2002).

Despite the importance of the issue, only few meta-analyses have examined the prevalence of suicide and its associated risk factors among patients with cancer through a comprehensive literature search. The present study objectives were to identify particular risk factors of different subgroup of patients including type of cancer, gender, age, type and time of suicide, and geographical region to facilitate early care and psychosocial support.

METHODS

Registration and Reporting

The systematic review was registered with PROSPERO 2022, CRD42022333866 (available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022333866). The

related methods are in line with the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Page et al., 2021).

Databases and Search Terms

A comprehensive review of databases including Embase, Scopus, PubMed, and Web of Science was conducted for original articles published in English from January 2000 to March 2022 with the following search terms: (Suicide[MeSH Terms]) AND (((((((((((((Tumor[Title]) OR (Neoplasm[Title])) OR (Tumors[Title])) OR (Neoplasia[Title])) OR (Neoplasias[Title])) OR (Cancer[Title])) OR (Cancers[Title])) OR (Malignant Neoplasm[Title])) OR (Malignancy[Title])) OR (Malignancies[Title])) OR (Malignant Neoplasms[Title])) OR (Benign Neoplasms[Title])) OR (Benign Neoplasm[Title])).

From the initial search of different electronic databases, a total of 505 articles were retrieved. After removing the duplicates, 376 articles remained for further review. To check the data relevancy, two independent researchers reviewed the titles and abstracts independently, leading to 187 articles. In the next step, the full texts of articles were deeply reviewed to collect all associated evidence that meets the eligibility criteria for the review. As a result, studies that incorporated data on the prevalence of suicide in patients with cancer or its determinants were considered for further review. Conference abstracts were also searched and the references of included articles were examined to be included as additional references. Finally, applying inclusion/exclusion criteria resulted in 69 studies which were included in the final review (Figure 1).

Inclusion and Exclusion Criteria

Studies with quantitative data on prevalence among patients with cancer and its determinants were included to find a set of articles based on the research keywords. Different types of observational studies containing cross-sectional, case-study, case-series, prospective, and cohort were involved. Additionally articles published in English between January 2000 and March 2021 were considered in the review.

Exclusion criteria were other types of studies including interventional studies, case-control, reviews, letter to the editor, books, reports, and commentaries published in languages other than English. Furthermore, studies with inadequate data on research questions and those focusing on diagnosis approaches, therapeutic methods, and medication therapies were not included in the review.

Quality Assessment

To assess the risk of bias of included studies, the Newcastle-Ottawa Scale (NOS) was used. This checklist is a standard evaluating tool to assess the quality of studies based on dimensions including case definition, selection of controls, comparability of cases and controls, and exposure/outcome in three main sections of exposure/outcome ascertainment, selection of study groups, and their comparability. To assess risk of bias, each study was evaluated by two independent researchers; in case of any discrepancy, consensus was reached by consulting with a third party. The lowest and highest NOS scores

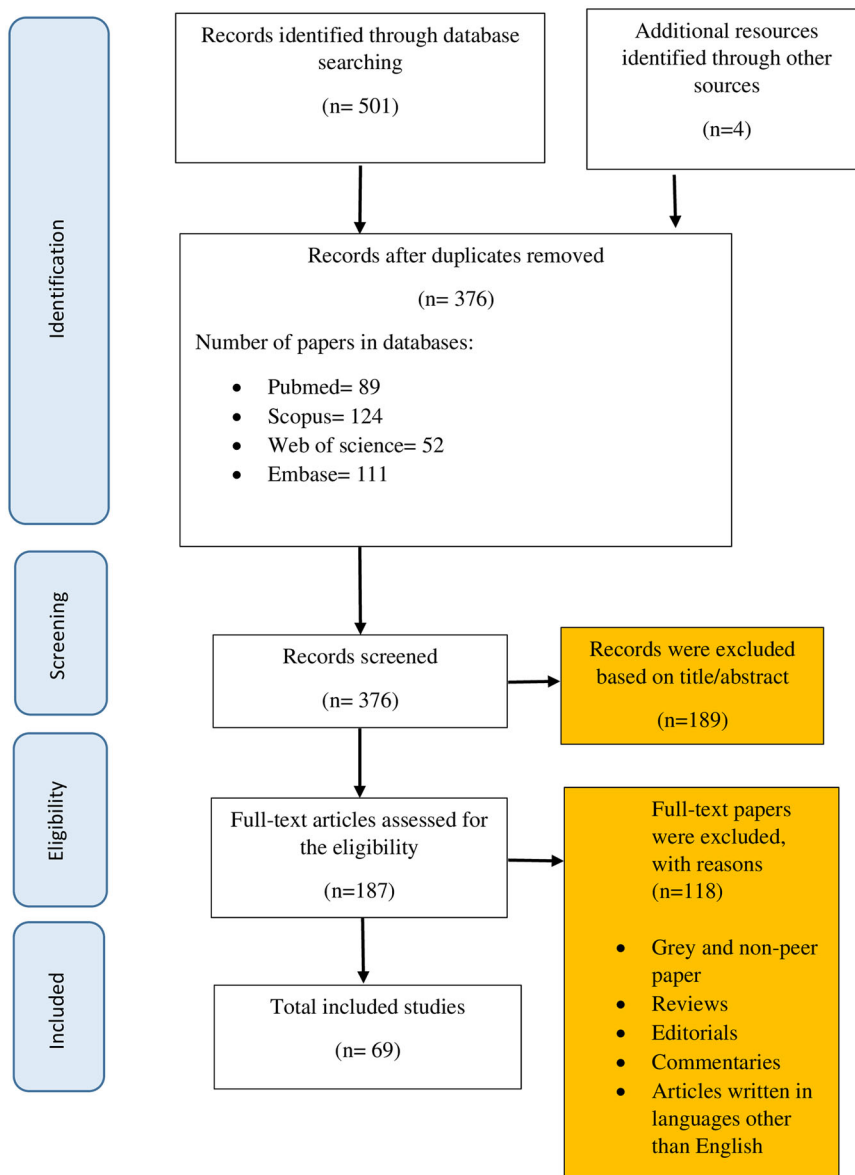


FIGURE 1. Flow diagram of our review process (PRISMA).

for each of the evaluated articles could be in a range between 0 and 10, so that an article with score below 4 was mentioned to have a low level of quality (Wells et al., 2000).

Data Extraction

A data extraction form was used to enter the data of included studies by two independent investigators. The form included requisite information including first author's name, publication date and country, data gathering tool, study design, study population,

sampling method, region based on World Health Organization (WHO) classification, type of cancer, gender, age, time of suicide, risk of bias, and outcome measures such as the prevalence of suicide and its associated factors.

Statistical Analysis

The prevalence of depression was evaluated by random-effects model. In addition, subgroup analysis was used to determine heterogeneity based on different study settings and patients' sociodemographic characteristics. Meta-analysis was performed using Comprehensive Meta-Analysis and R software. Finally, to examine the heterogeneity of preliminary studies, I^2 test was used.

Patient and Public Involvement

No patients were involved.

RESULTS

To report the findings of this review, PRISMA guidelines were employed. After reviewing 69 articles published from January 2000 to March 2021 in 15 countries, the total prevalence rate of suicide among 34,157,856 patients with cancer was estimated to be 67,169, at 0.013 (95% CI, 0.008–0.021) (Figure 2).

Meta-Analysis Based on Countries, Continents, and WHO Regions

Based on meta-analysis, 15 countries were identified among 69 studies. Among these countries, Greece and Israel had the highest prevalence of suicide in patients with cancer, at 0.549 (95% CI, 0.46–0.635) and 0.158 (95% CI, 0.139–0.179), respectively. Furthermore, Australia and the United Kingdom were reported to have the lowest prevalence of suicide among these patients. Results based on continents revealed that Asia had the highest prevalence of suicide estimated at 0.067 (95% CI, 0.025–0.165) (Table 1).

Meta-analysis based on different WHO regions also revealed that the Region of the Americas (AMR) had the lowest suicide rate at 0.006 (95% CI, 0.004–0.008). On the other hand, no studies were found to be conducted in Eastern Mediterranean region (EMR), Regional Office for Africa (AFRO), and South-East Asia regions (SEAR) (Table 1).

Meta-Analysis Based on Type of Cancer

According to the results based on cancer type, findings indicated that the highest suicide prevalence was related to gastrointestinal cancer, estimated at 0.204 (95% CI, 0.161–0.255), followed by breast cancer at 0.131 (95% CI, 0.080–0.176) and thoracic cancer at 0.116 (95% CI, 0.096–0.140), respectively (Table 2).

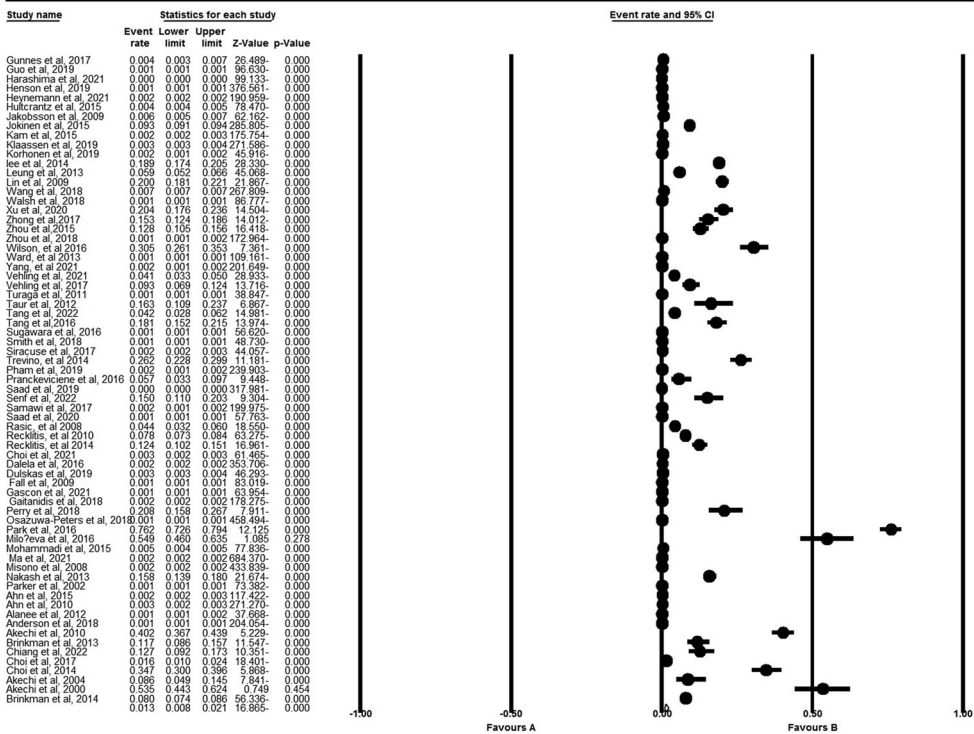


FIGURE 2. The forest plot of the prevalence of suicide among patients with cancer.

TABLE 1. Subgroup analysis based on country, continent, and World Health Organization (WHO) region.

Subgroups	Effect size and 95% interval			Test of null (2-tailed)		
	Point estimate	Lower limit	Upper limit	Z value	p value	
Countries	Australia	0.001	0.001	0.001	-48.730	.000
	Canada	0.027	0.005	0.134	-4.063	.000
	China	0.112	0.021	0.427	-2.283	.022
	Denmark	0.002	0.001	0.002	-45.916	.000
	Finland	0.006	0.005	0.007	-62.162	.000
	Germany	0.084	0.037	0.177	-5.457	.000
	Greece	0.549	0.460	0.635	1.085	.278
	Israel	0.158	0.139	0.180	-21.674	.000
	Japan	0.062	0.000	0.899	-1.086	.278
	Lithuania	0.014	0.001	0.190	-2.975	.003
	Norway	0.004	0.003	0.007	-26.489	.000
	South Korea	0.036	0.005	0.227	-3.122	.002
	Sweden	0.006	0.001	0.072	-3.971	.000
	United Kingdom	0.001	0.001	0.001	-73.382	.000
	United States	0.004	0.003	0.006	-33.081	.000
	Continents	Asia	0.067	0.025	0.165	-5.099
Australia		0.001	0.001	0.001	-48.730	.000
Europe		0.011	0.002	0.056	-5.268	.000
North America		0.006	0.004	0.009	-26.370	.000
WHO regions	AMR	0.006	0.004	0.008	-27.419	.000
	EUR	0.013	0.003	0.061	-5.329	.000
	WPR	0.051	0.019	0.129	-5.688	.000

TABLE 2. Subgroup analysis based on type of cancer.

Type of cancer	Number of studies	Effect size and 95% interval			Test of null (2-tailed)	
		Point estimate	Lower limit	Upper limit	Z value	p value
Bone	6	0.076	0.016	0.293	-3.027	.002
Breast	23	0.131	0.080	0.176	-17.289	.000
Endocrine	11	0.028	0.014	0.055	-10.037	.000
Gastrointestinal	47	0.204	0.161	0.255	-9.234	.000
Head and neck	28	0.038	0.022	0.063	-11.737	.000
Hematologic	34	0.086	0.056	0.131	-9.901	.000
Nervous system	16	0.073	0.038	0.136	-7.242	.000
Skin and Connective/soft tissue	20	0.052	0.035	0.077	-13.468	.000
Thoracic	27	0.116	0.096	0.140	-18.795	.000
Urogenital	67	0.095	0.074	0.122	-15.994	.000
Other	26	0.149	0.117	0.188	-12.159	.000

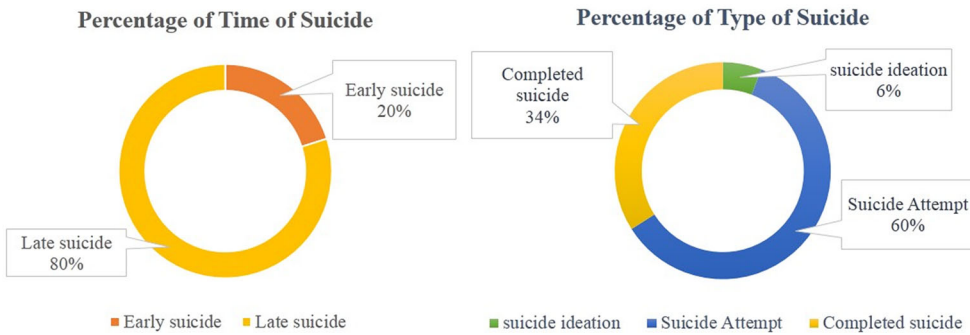


FIGURE 3. Subgroup analysis based on type/time of suicide.

Meta-Analysis Based on Type and Time of Suicide

Study findings showed that out of 67,169 patients, 6% ($n = 4,030$) had suicidal ideation, 60% ($n = 40,300$) had unsuccessful suicide, and 34% ($n = 22,839$) had completed suicide (Figure 3). Furthermore, 20% of patients had suicidal ideation during the first year after cancer diagnosis, and the rest experienced suicidal tendencies a year after being diagnosed with the disease (Figure 3).

Meta-Analysis Based on Gender

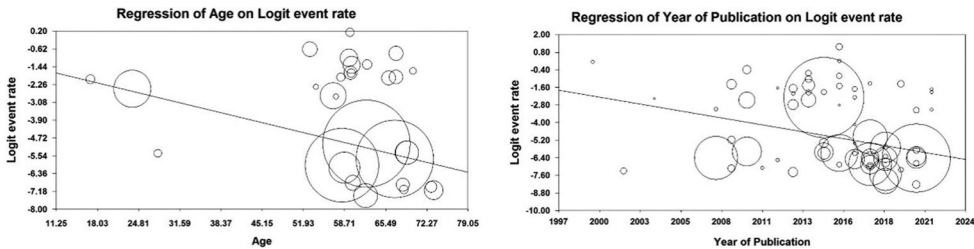
A gender-based meta-analysis showed that the prevalence of suicide/suicidal ideation was higher among men estimated at 0.013 (95% CI, 0.008–0.023) compared with women at 0.006 (95% CI, 0.002–0.017) (Table 3).

Meta-Regression Based on Age and Year of Publication

A meta-analysis affirmed a significant indirect relationship between suicide prevalence in cancer patients and year of study publication ($p < .05$), so that a unit of increase in the study year led to a decreased rate in suicide prevalence. Furthermore, an inverse relationship between patient’s age and suicide prevalence was observed based on the meta-analysis (Figure 4).

TABLE 3. Meta-analysis based on gender.

Gender	Number of studies	Effect size and 95% interval			Test of null (2-tailed)	
		Point estimate	Lower limit	Upper limit	Z value	p value
Male	45	0.013	0.008	0.023	-15.770	.000
Female	41	0.006	0.002	0.017	-10.057	.000

**FIGURE 4.** Meta regression based on age and year of publication.**TABLE 4.** Meta-regression based on quality assessment tool.

Quality	Number of studies	Effect size and 95% interval			Test of null (2-tailed)	
		Point estimate	Lower limit	Upper limit	Z value	p value
High	47	0.010	0.005	0.018	-13.935	.000
Low	6	0.046	0.005	0.335	-2.529	.011
Medium	16	0.018	0.007	0.041	-9.064	.000

Meta-Regression for Quality Assessment

In case of study quality assessment, more than half of the included studies ($n = 47$) had high quality, while 16 studies were of medium quality and the other 6 studies were of low quality (Table 4).

Publication Bias

According to Figure 5, the results of Egger's statistical test showed a p value (2-tailed) of 0.88, affirming the existence of no publication bias in the study.

DISCUSSION

Overview

Our meta-analysis of 69 studies revealed that the total prevalence rate of suicide among 34,157,856 patients with cancer was estimated at 0.013. Several factors associated with suicide among study patients were found, including age, gender, place of residence, type of cancer, and year of study publication. Knowing more about suicide in the patients with diagnosed cancer is necessary both for healthcare providers and caregivers due to being familiar with associated risk factors as well as for health authorities to organize and implement preventive measures. The average total score of suicide among patients with cancer in our review was reported to be 0.013, which was lower than the rate estimated in

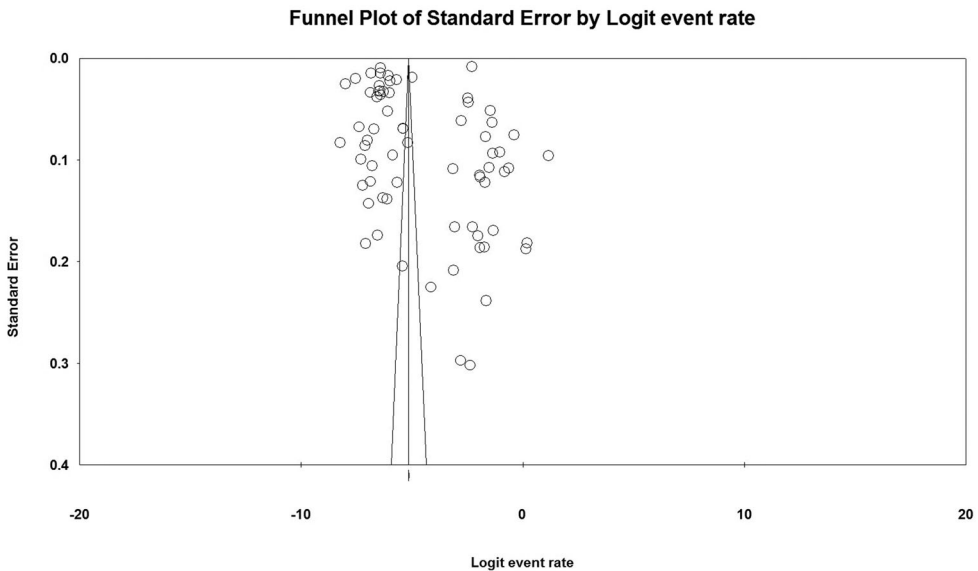


FIGURE 5. The funnel plot of publication bias.

Denmark for both male and female patients, at 1.7 and 1.4, respectively (Yousaf, Christensen, Engholm, & Storm, 2005). Furthermore, the higher prevalence of suicide among patients with cancer was observed in studies conducted by Hem et al. and Björkenstam et al., with corresponding mortality ratio of 1.55 and 2.5 (Björkenstam, Edberg, Ayoubi, & Rosén, 2005; Zaorsky et al., 2017). In another study by Zaorsky et al., an extremely high mortality rate of 4.44 was estimated, which highlighted a more than fourfold increase in suicide risk among patients with cancer (Zaorsky et al., 2017). These inconsistencies with our study findings might be due to the differences in the baseline risks of comparison groups or as a result of different characteristics of included patients with multiple primary tumors, which could threaten the validity of study results.

Gender

Our review also revealed that a greater suicide risk was correlated with male gender. Research data obtained by Kendal et al. in the United States affirmed this finding and added that the suicide prevalence was higher in men, equating to 19 deaths per 10,000 male patients compared to 4 deaths per 10,000 women (Kendal, 2007). In addition, our review affirmed a significant association between risk of suicide and cancer sites/organ system.

Cancer Type

The greatest suicide rate was found in patients with gastrointestinal cancer, followed by those with breast cancer and thoracic/lung cancers. However, the anatomic sites associated with increased suicide rates differed in various literatures. For example, a study by Misono et al. found that the highest suicide rates were associated with lung, gastrointestinal system, and head and neck cancers (Misono et al., 2008). Similar to our meta-analysis findings, the elevated suicide rates in patients with lung and gastric cancer were

related to emotional distress and lower quality of life in patients (Carlsen, Jensen, Jacobsen, Krasnik, & Johansen, 2005; Nordin & Glimelius, 1997; Sarna et al., 2002). Therefore, our analysis suggests that healthcare providers should pay more attention to patients' psychological experiences as patients with cancer encounter high levels of mental distress and psychosocial challenges.

Age

Our review revealed a high rate of suicide among adolescent and young adults with cancer. In fact, as these groups of patients are at an early stage of education, occupation, and family life, they are subjected to more psychological pressures which rapidly deteriorate their physical and mental condition. Young adult patients with cancer encounter several challenges after diagnosis, such as diminished chance to continue their job and educational growth or even maintain their family life balance (Pang et al., 2008). In addition, cancer incidence among adolescents and young adults has been proven to be considerably more common than older population (Langeveld et al., 2003; Trama, Botta, & Steliarova-Foucher, 2018). A study by Yang et al. highlighted that patients aged 20 to 24 years old had the highest rates of suicide (Yang et al., 2019). Another study also found that younger patients were more likely to have poorer survival outcomes and advanced disease at diagnosis than were older patients (Wu et al., 2017; Xiao, Cao, Qiu, Wang, & Wang, 2013).

Territory

Analyzing suicide rates among people with cancer in different countries showed higher rates in the United States, Greece, and Israel than in Europe, Asia, or Australia (Yang et al., 2019). The type of financing system in the health systems of mentioned countries together with economic costs of chronic diseases such as cancer might result in greater probability of therapy withdrawal, particularly among individuals from lower socioeconomic levels, which may bring them disappointment and a desire to end their lives or attempt suicide. On the other hand, most European countries have universal health coverage and easy access to healthcare services, which facilitate cancer therapy without imposing financial burden to citizens (Jones & Kantarjian, 2019). Studies conducted in England and the United States have asserted that urgent health promotion strategies among patients with cancer should be implemented with logical costs to eliminate depression and associated risk of suicide (Guo et al., 2019).

LIMITATION

Our study has some limitations. First, our review has been restricted to studies published in English, which might exclude relevant researches. Second, lack of data for some of the countries including EMRO, AFRO, and SEAR restricted the generalizability of our findings. Third, we were incapable of evaluating the potential confounding role of comorbidities such as medical or psychological disorders on the prevalence of suicide among patients with cancer. Furthermore, we did not mention the role of unhealthy

lifestyle or harmful behaviors such as tobacco and alcohol use as associated factors for increased risk of suicide.

CONCLUSION

This systematic review identified several risk factors that affect the prevalence of suicide among patients with cancer worldwide. Based on study results, suicide-prevention strategies should be aimed at patients younger than 40 years of age to effectively address their mental health disorders and promote their self-efficacy in successful management of the disease.

AUTHORS' CONTRIBUTIONS

Conception and design of study: Samira Raoofi, Ahmad Ghashghae, Fatemeh Pashazadeh Kan. **Acquisition of data:** Farzaneh Bagheribayati, Fatemeh Pashazadeh Kan, Samira Raoofi, Akbar Javan Biparva, Zahra Noorani Mejareh, Mohaddeseh Sanaei, Yasamin Dolati, Bahare Abdollahi. **Analysis and/or interpretation of data:** Samira Raoofi, Ahmad Ghashghae, Fatemeh Pashazadeh Kan. **Drafting the manuscript:** Sima Rafiei, Ahmad Ghashghae. **Revising the manuscript critically for important intellectual content:** Sima Rafiei, Ahmad Ghashghae. **Approval of the version of the manuscript to be published:** Samira Raoofi, Ahmad Ghashghae, Sima Rafiei, Elaheh Parnian

DISCLOSURE STATEMENT

The authors declare that they have no competing interests

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