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REVIEW

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Cancer Incidence in Volcanic Areas: A Systematic Review

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Abstract

Background: There are more than 1,000 active volcanoes worldwide with inhabitants within 100 km of them. Volcanoes spill several toxic metals and spew pollution through gasses, causing soil and water contamination. The dangerously active volcanoes place the nearby population at risk for volcanic hazards. This review aimed to determine whether people living in these volcanic areas have higher risk of cancer and more attention should be given to this danger. **Methods:** A systematic literature search was conducted of PUBMED, Science Direct, SCOPUS, Proquest, and Google Scholar, and from citation searching. We assessed the quality of the studies and extracted the incidence rate of cancer in the volcanic areas compared to non-volcanic areas. **Results:** The search identified 360 articles, with 11 studies meeting our selection criteria. The results reported the incidence of cancer in children was predominantly in volcanic areas with girls suffering as much as 1.4 per 100,000 per year. The highest cancer age standardized incidence rates for females, males, and overall calculation in volcanic areas were reported as 31.7/100,000/year in Catania, 10.34/100,000/year in Furnas, and 38.3/100,000/year in Catania-Messina-Enna for thyroid cancer. We observed the increasing incidence of carcinoma for some types of cancer in volcanic areas. **Conclusion:** Cancer incidence in volcanic areas was higher than non-volcanic areas and it is caused by multifactorial conditions. The concentrations of hazardous elements of volcanic products vary among volcanoes and are related to the harmful risk for the inhabitants. The negative effects of volcanic products to human health should be given more consideration.

Keywords: Natural disaster- volcano- cancer incidence- hazard risk- volcanic area

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Introduction

There are approximately 1,550 active volcanoes in the world and most of them are on the seafloor. These volcanoes particularly exist in tectonic plate boundaries. In the Pacific Ocean, the so-called 'Ring of Fire' forms a horseshoe from South America to North America, reaching to Indonesia. Alongside, there are 452 volcanoes, of which 75% are in active status. Archipelago nations host the highest population within 100 km of active volcanoes and also many inhabitants live within areas of high volcanic hazards and risk (Cottrell, 2015; Hariyono and Liliasari, 2018). Areas close to volcanic activity are characterized by non-anthropogenic pollution involving the atmosphere, soil and water. Previous research informed that some metal spills from the earth's crust cannot be easily degraded. Therefore, they have a negative impact on the ecosystems of plants, animals and humans around these volcanic areas (Yamamoto et al., 1995). A study conducted by Pellegriti in 2009 reported findings of boron (B), iron (Fe), manganese (Mg), vanadium (V), and radon (222Ra) higher than maximum permissible concentrations in drinking and irrigation water sources on the plain of Mt. Etna, which is the source of water for most of the population in the province of Catania (Pellegriti et al., 2009). In another similar study, some cancer incidence rates were reported higher in volcanic areas, such as the increasing incidence of gastric cancer in Iran and Japan (Amani et al., 2015). In some studies, incidence rates of various cancer types were increased in volcanic areas. This was possibly caused by chronic exposure to various toxic ground gas emissions. The component elements of these emissions are iron (Fe), zinc (Zn), copper (Cu), selenium (Se), nickel (Ni), cobalt (Co), cadmium (Cd) radon (Rn), mercury (Hg), arsenic (As), lead (Pb), hydrogen sulphide (H2S), and carbon dioxide (CO_2) (Kristbjornsdottir and Rafnsson, 2013). Although some of these metals, such as trace metals including iron (Fe), zinc (Zn), copper (Cu), and selenium (Se), are essential micronutrients for the body, however, the presence of these metals and gases in the volcanic load are considered to be closely related to the incidence of cancer. In addition, some of these metals and gases are carcinogenic (Malandrino et al., 2020). Increased exposure to these elements in either inorganic or organic form through inhalation, skin contact and digestion can initiate the growth of cancer (Russo et al.,

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2015; Malandrino et al., 2020).

One well-known example of carcinogenic action is the presence of high concentrations of the toxic metal, arsenic (As) in drinking water and food, which is associated with several types of cancer such as thyroid cancer through the metalation processes of arsenic (As) into dimethyl arsenic acid (DMA), also known as cacodylic acid, which is a carcinogenic substance (Hariyono and Liliasari, 2018). Another dangerous volcanic compound cadmium (Cd), which is a carcinogenic substance that can induce oxidative stress by inhibiting antioxidant enzymes, activating PI3K (phosphoinositide 3-kinase) and extracellular signal-regulated kinase (ERK) signaling pathways, deregulating cell proliferation, damaging DNA repair mechanisms and promoting tumor progression and invasiveness (Prozialeck et al., 2003; Malandrino et al., 2020). This study aimed to determine whether populations in volcanic areas have higher incidence of cancer so the people and the responsible governments should give more attention to this danger.

Materials and Methods

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Moher et al., 2009).

Information sources and search strategy

Database searching was conducted of PUBMED, Science Direct, SCOPUS, Proquest, and Google Scholar. Citation searching of reference lists was also performed. Databases were searched on May 15, 2021 without limitation on date, country, patients race, age, and gender. Keywords related to the incidence of cancer in volcanic areas are provided in Table 1. Duplicate references were removed manually.

Inclusion and exclusion criteria

Articles in English were selected without time restriction and the inclusion criteria of this review were studies in human populations and studies reporting comparison of incidence of cancer in volcanic and non-volcanic areas. The exclusion criteria were brief communications, letters, reviews, editorials, and articles that could not be accessed.

Study selection

The process of selection consisted of two steps. In the first step, we checked the titles and abstracts of all studies using predefined criteria for screening. All reviewers were involved in making the final decisions. The inclusion and exclusion criteria provided the guidance. In the second step, the selection was repeated by reading the whole paper and the final decision was made by all reviewers after discussion in case of any disagreement.

Data collection process

The collection process involved the collection of important relevant material from the articles. The data inputted into tabular form in this study included author's name, title of study, duration of study, study region, age-standardised incidence rate (ASR)/100,000, event of cancer, total population, incidence rate (IR), and p value. Data related to the metal components of the air, soil and water in the volcanic area were also collected.

Quality assessment of studies

The quality of each study was assessed by the two authors using the Joanna Briggs Institute (JBI) critical appraisal checklist for cohort studies with the scale as percentages (Goplen et al., 2019; Moola et al., 2020). Any disagreements were resolved by discussion between the authors who assessed the article. The primary outcome was the incidence of cancer in volcanic areas compared to non-volcanic areas.

Results

Study selection

The total number of the articles that we recorded from the keywords was 360 articles. After removing the duplication, a total of 246 articles were selected for the screening process. We reviewed the titles and types of articles using the inclusion and exclusion criteria. From the 246 studies, 218 were excluded and 28 studies were selected. In the next data selection, from the 28 studies, 19 were removed after the full text was read thoroughly. There were two additional included articles identified from the citation searching. At the end of selection process, the total number of studies was 11. A flowchart of the selection process is shown in Figure 1.

Characteristics of the studies

The details of the articles are provided in Table 2. The 11 articles that were included in the analysis were from Sicily (Italy) (N=7) (Pellegriti et al., 2009; Malandrino et al., 2013; Russo et al., 2015; Malandrino et al., 2016; Russo et al., 2017; Tavarelli et al., 2017; Boffetta et al., 2020), Vanuatu (N=1) (Paksoy et al.,

Table 1. Keywords for Searching Method

No.	Sources	Keyword
1.	PUBMED	(cancer[MeSH Terms]) AND (volcan*[Title/Abstract])
2.	SCOPUS	TITLE (volcanic AND cancer)
3.	SCOPUS	TITLE-ABS-KEY(volcanic AND cancer)
4.	Science Direct	(cancer OR "cancer prevalence") AND volcanic Filter : in title, abstract, or author specific keyword
5.	Proquest	noft(cancer) AND noft(volcanic) limitation in English
6.	Google Scholar	allintitle: cancer AND volcan filter : only in title

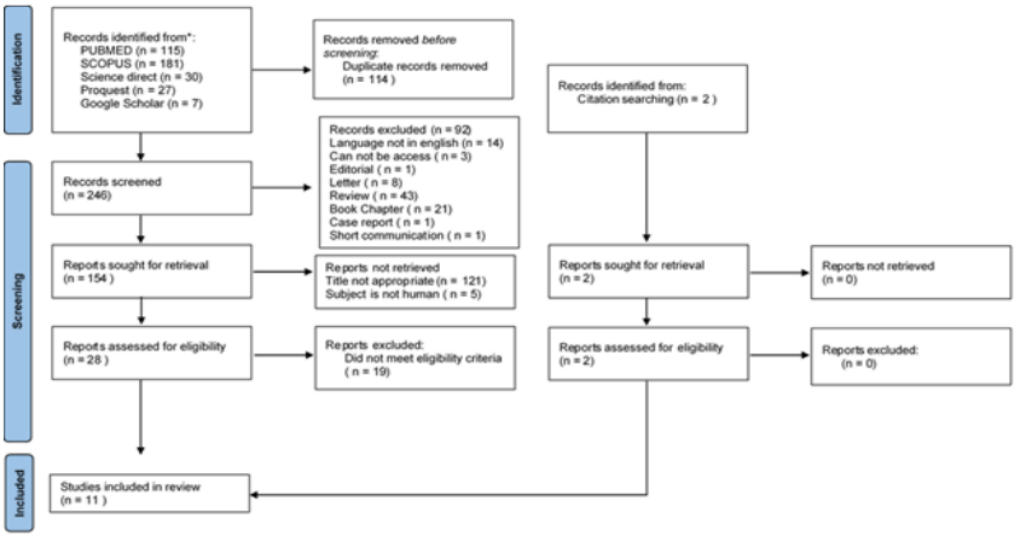

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow chart (Page et al., 2021).

1990), Iceland (N=3) (Arnbjörnsson et al., 1986), Hawaii (N=1) (Goodman et al., 1988), and the Azores (Portugal) (N=1) (Amaral et al., 2006). Studies conducted in Sicily compared Catania as the volcanic area to the rest of Sicily. The study in Iceland compared Iceland to Denmark, Finland, Norway, and Sweden as nonvolcanic areas. The study in the Azores, compared Furnas to Santa Maria. The study in Vanuatu compared that region to Papua New Guinea and Fiji. The study in Hawaii compared that region to San Francisco and New Mexico. Most of the studies investigated about thyroid cancer, indicating that the type of thyroid cancer that had higher incidence was papillary thyroid cancer. Besides thyroid cancer, two studies declared that there were other types of cancer found in residents in volcanic areas, which were cervical cancer, liver cancer, skin cancer, lymphatic leukemia, Hodgkin's lymphoma, stomach cancer, breast cancer, prostate cancer, lip cancer, and cancer in the oral cavity and thorax. From the collected articles, one study informed about thyroid cancer in children.

Risk of Bias

According to the JBI Critical Appraisal Checklist for Cohort studies, all of the studies were considered to have low risk of bias. Some studies did not identify the confounding factors and how to deal with them (Table 3).

Cancer Incidence

One study reported overall cancer crude incidence rate as 453.2 per 100,000 per year in volcanic areas and 435.97 per 100,000 per year in non-volcanic areas, indicating higher cancer incidence reported with ASR in volcanic areas. In addition, the study reported lymphatic leukemia, thyroid cancer, and prostate cancer as cancers

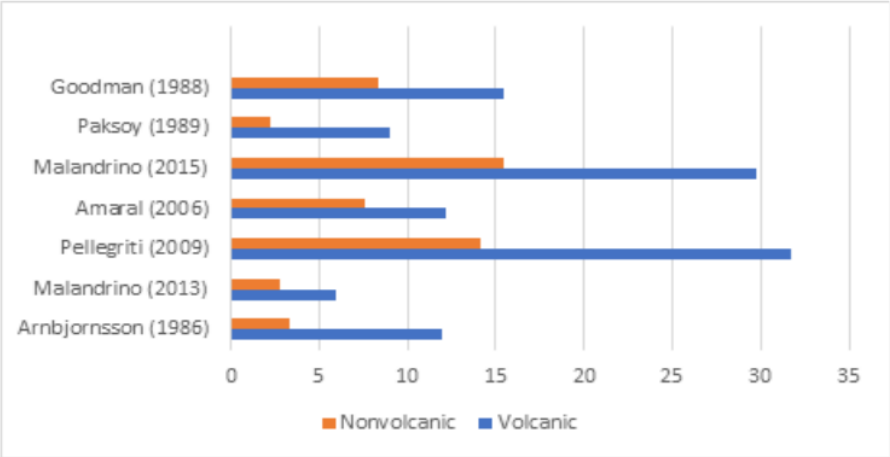

Figure 2. Cancer Age-Standardized Incidence Rate (ASR) per 100,000 per Year for Females

Table 2. Study Characteristics

No.	Study ID	Title	Study duration	Region		Volcanic					
				Volcanic	nonvolcanic	event	total population	ASR incidence per 100000/year			IR
								F	M	both	
1	Ambjornsson (1986) [2]	Thyroid cancer incidence in relation to volcanic activity	1955-1982 (volcanic) 1959 - 1975 (non-volcanic)	Iceland	Denmark, Finland, Norway, Sweden	139	< 250,000	12	4,1	NR (8.05)	NR
2	Russo (2017)	Thyroid cancer in the pediatric age in Sicily: influence of the volcanic Environment	2002-2009	Catania	other province in Sicily	23	NR	1.4	0.5	NR (0.95)	NR
3	Malandrino (2013)	Papillary thyroid microcarcinoma: a comparative study of the characteristics and risk factors at presentation in two cancer registry	2002-2006	Catania	the rest of Sicily	675	1,000,000	5.9	1.3	3.68	NR
4	Tavarelli (2017)	Anaplastic thyroid cancer in Sicily: the role of environmental characteristics	2002-2009	Catania	the rest of Sicily	12	1,072,000	NR	NR	0.07	NR
5	Pellegriti (2009) [3]	Papillary thyroid cancer incidence in the volcanic area of Sicily	2002-2004	Catania	the rest of Sicily	729	1,059,811	31.7	6.4	NR (19.05)	NR
6	Amaral (2006) [3]	Chronic exposure to volcanic environment and cancer incidence in the Azores, Portugal	1991-2001	Furnas	Santa Maria	18	1,541	12.17	10.34	NR (11.25)	NR
7	Russo (2015)	Several site-specific cancer are increased in the volcanic area in Sicily	2003-2007	Catania	the rest of Sicily	14,44	1,087,682	NR	NR	NR	453.2
8	Bofetta (2020) [12]	Exposure to emission from Mount Etna (Sicily, Italy) and incidence of thyroid cancer: a geographic analysis	2008-2012	catania-messina-enna	Palermo	NR	NR	NR	NR	38.3	NR
9	Malandrino (2016) [9]	Increased thyroid cancer incidence in a basaltic volcanic area is associated with non-anthropogenic pollution and biocontamination	2002-2006	Catania	Palermo & Messina	1228	NR	NR	NR	18.5	NR
10	Paksoy (1989) [14]	Cancer occurrence in Vanuatu in the South Pacific 1980-86	1980-1986	Vanuatu	Papua New Guinea, Fiji	269	127,800	9	3.6	6.3	NR
11	Goodman (1988) [3]	Descriptive epidemiology of thyroid cancer in Hawaii	1960-1984	Hawaii	San Francisco, New Mexico	1212	NR	15.43	6.8	11.11	NR

Table 2. Continued

No.	Study ID	Title	Study duration	Region				Non-volcanic ASR incidence per 100,000/year				p
				Volcanic	nonvolcanic	Event	total population	F	M	both	IR	
1	Arnbjornsson (1986) [2]	Thyroid cancer incidence in relation to volcanic activity	1955-1982 (volcanic) 1959 - 1975 (non-volcanic)	Iceland	Denmark, Finland, Norway, Sweden	NR	NR	3.35	1.55	2.45	NR	F p<0.001, M p<0.01
2	Russo (2017) [7]	Thyroid cancer in the pediatric age in Sicily: influence of the volcanic Environment	2002-2009	Catania	other province in Sicily	31	NR	0.6	0.1	0.35	NR	<0.05
3	Malandrino (2013)	Papillary thyroid microcarcinoma: a comparative study of the characteristics and risk factors at presentation in two cancer registry	2002-2006	Catania	the rest of Sicily	1102	4,000,000	2.78	0.68	1.76	NR	<0.01
4	Tavarelli (2017)	Anaplastic thyroid cancer in Sicily: the role of environmental characteristics	2002-2009	Catania	the rest of Sicily	31	3,941,000	NR	NR	0.05	NR	0.19
5	Pellegriti (2009) [3]	Papillary thyroid cancer incidence in the volcanic area of Sicily	2002-2004	Catania	the rest of Sicily	1,221	3,920,541	6.4	3	4.7	NR	<0.001
6	Amaral (2006) [3]	Chronic exposure to volcanic environment and cancer incidence in the Azores, Portugal	1991-2001	Furnas	Santa Maria	58	5,578	7.54	13.58	10.56	NR	NR
7	Russo (2015) [2]	Several site-specific cancer are increased in the volcanic area in Sicily	2003-2007	Catania	the rest of Sicily	57,757	3,327,708	NR	NR	NR	435.97	<0.05
8	Bofetta (2020) [12]	Exposure to emission from Mount Etna (Sicily, Italy) and incidence of thyroid cancer: a geographic analysis	2008-2012	catania-messina-enna	Palermo	NR	NR	NR	NR	24.4	NR	NR
9	Malandrino (2016) [9]	Increased thyroid cancer incidence in a basaltic volcanic area is associated with non-anthropogenic pollution and biocontamination	2002-2006	Catania	Palermo & Messina	1147	NR	NR	NR	9.6	NR	NR
10	Paksoy (1989) [14]	Cancer occurrence in Vanuatu in the South Pacific 1980-86	1980-1986	Vanuatu	Papua New Guinea, Fiji	NR	NR	2.2	0.35	1.27	NR	NR
11	Goodman (1988) [2]	Descriptive epidemiology of thyroid cancer in Hawaii	1960-1984	Hawaii	San Francisco, New Mexico	NR	NR	8.4	3.3	5.87	NR	NR

NR, data not reported; F, female; M, male; ASR, age-standardized incidence rate

Table 3. JBI Risk of Bias Quality Assessment for Cohort Studies

	Author	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Total	Risk of Bias
1	Amaral et al., 2006	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	90,91	Low
2	Arnbjömsson et al., 1986	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Unclear	Yes	72,73	Low
3	Boffetta et al., 2020	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	81,82	Low
4	Goodman et al., 1988	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	81,82	Low
5	Malandrino et al., 2013	yes	Yes	Yes	yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	90,91	Low
6	Malandrino et al., 2015	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	90,91	Low
7	Paksoy et al., 1989	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Unclear	No	63,64	Low
8	Pellegriti et al., 2009	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	90,91	Low
9	Russo et al.,2015	Yes	Yes	Yes	yes	Unclear	Yes	Yes	Yes	Yes	Unclear	Yes	81,82	Low
10	Russo et al.,2017	Yes	Yes	Yes	yes	Unclear	Yes	Yes	Yes	Yes	Unclear	Yes	81,82	Low
11	Tavarelli et al., 2017	Yes	Yes	Yes	yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	90,91	Low

JBI, Joanna Briggs Institute; Q1-Q11 indicate questions no.1 to 11 based on JBI. The risk of bias was ranked as high if the study reached up to 49% of yes score, moderate if the study reached from 50 to 69% of yes scores, and low if the study reached more than 70% of yes scores.

that were significantly higher in men in volcanic areas and thyroid cancer, breast cancer, lymphatic leukemia, Hodgkin's lymphoma, and stomach cancer as cancers that occur significantly higher in women (Russo et al., 2015). There was one study that reported the incidence of cancer among children (0-19 y.o) in volcanic and non-volcanic areas. Research by Russo in 2017 reported about the incidence of thyroid cancer in children between 2002-2009. The cancer incidence reported with ASR for females was significantly higher in volcanic areas than non-volcanic areas (ASR = 1.4 and 0.6, respectively, p=0.006) and the ASR for males was significantly higher in volcanic areas than non-volcanic areas (ASR = 0.5 and 0.1, respectively, p=0.03). Mostly, differentiated thyroid cancer was diagnosed in the younger age population (5-14 years old) without differentiation in gender (Russo et al., 2017).

The highest cancer incidence reported with ASR for females in volcanic areas was 31.7/100,000/year in Catania (Pellegriti et al., 2009), while the lowest was 5.9/100,000/year (Malandrino et al., 2013). The highest cancer incidence reported with ASR for females in non-volcanic area was 14.1/100,000/year in the rest of Catania in Sicily (Pellegriti et al., 2009), while the lowest was 2.2/100.000/year in Vanuatu (Paksoy et al., 1990) (Figure 2).

The highest cancer incidence reported with ASR for males in volcanic areas was 10.34/100,000/year in Furnas (Amaral et al., 2006), while the lowest was 1.3/100,000/year in Catania (Malandrino et al., 2013). The highest cancer incidence reported with ASR for males in non-volcanic areas was 13.58/100,000/year in Santa Maria (Amaral et al., 2006), while the lowest was 0.35/100.000/year in Vanuatu (Paksoy et al., 1990) (Figure 3).

The highest overall cancer incidence reported with ASR in volcanic areas was 38.3/100,000/year in Catania-Messina-Enna for thyroid cancer (Boffetta et al., 2020), and the lowest was 0.07/100,000/year in Catania (Tavarelli et al., 2017). The highest overall cancer incidence reported with ASR in non-volcanic areas was 24.4/100,000/year in Palermo (Boffetta et al., 2020) and the lowest was 0.05/100,000/year in Catania for anaplastic thyroid cancer (Tavarelli et al., 2017) (Figure 4).

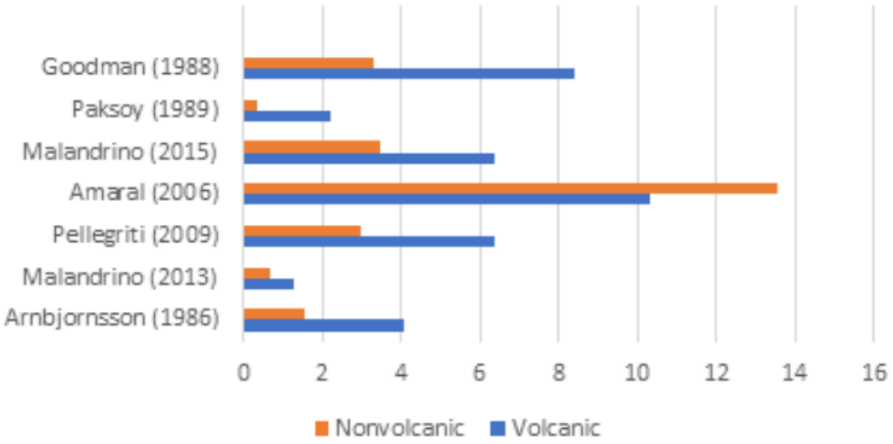

Figure 3. Cancer Age-Standardized Incidence Rate (ASR) Per 100,000 Per Year for Males

Table 4. Components Found in Volcanic Areas

No.	Region	Component contaminants in volcanic ar	Location
1	Sicily	HCO3,SO4, calcium fluoride, chloride, boron (B), iron (Fe), manganese (Mn), vanadium (V), 2 radon (222 Rn) Ca, Mg, Na, K, Si, S, B, P, Fe, Sr, Cl, Ag, Al, As, Au, Ba, Be, Bi, Br, Cd, Ce, Co, Cr, Cs, Cu, Dy, Er, Eu, Ga, Gd, Ge, Hf, Hg, Ho, I, La, Li, Lu, Mn, Mo, Nb, Nd, Ni, Pb, Pr, Pt, Rb, Sb, Se, Sm, Ta, Tb, Te, Th, Ti, Tl, Tm, U, V,W, Y, Yb, Zn, and Zr.	Water (Pellegriti et al., 2009) Volcanic Ash (Barone et al., 2021)
2	Azores, Portugal	Carbon dioxide (CO2), hydrogen sulfide (H2S), sulfur dioxide (SO2), hydrogen chloride (HCl), hydrogen fluoride (HFl), and radon (Rn)	Soil (Rodrigues et al., 2012)
3	Iceland	argon (Ar), methylene (CH2), carbon monoxide (CO), CO2, carbonyl sulfide (COS), hydrogen (H2),HF, hydrogen chloride (HCl), H2O, H2S, sulfuric acid (H2SO4), ammonium (NH4), disulfur (S2), sulfate (SO4), SiF	Gases (Arnbjörnsson et al., 1986)
4	Vanuatu	SiO_2, TiO_2, Al_2O_3, Fe_2O_3, MnO, MgO, CaO, Na_2O, K_2O, P_2O_5, F, C, SO_2l, Ca_2+,Mg_2+, Na+, K+	Lava (Bani et al., 2015)
5	Hawaii	SiO_2, TiO_2, Al_2O_3, Fe_2O_3, MnO, MgO, CaO, Na_2O, K_2O, P_2O_5, Sc, Rb, Sr, Y, Zr, Nb, Ba, La, Ce, Pr, Nd, Sm, Eu, Tb, Gd, Hf, Pb, Sr	Lava (Huang et al., 2005)

Discussion

This review presents the incidence rates of cancer in volcanic regions compared to non-volcanic regions. The highest cancer incidence reported with ASR in volcanic areas for females was papillary thyroid cancer in Catania compared to the other regions and types of cancer. The incidence was significantly higher in the volcanic areas than non-volcanic areas with p=<0.001. The mechanisms of the volcanic environment that influence the increasing of cancer incidence has not been proven yet, although some studies stated that the thyroid gland is sensitive to radiation. Mount Etna located near Catania, releases radioactive radon gas (Rodrigues et al., 2012; Hariyono and Liliasari, 2018). In these areas, radon can contaminate sources of groundwater with more than the maximum allowed concentrations (Pellegriti et al., 2009). Radon (Rn) is a radioactive compound from volcanic gases that can diffuse through soil substrates. Indoor radon (222Rn) was monitored in high concentrations in some house (>2,000 Bq/m^3) near mount Etna and high radon degassing was measured in soil samples (>10,000 Bq/m^3) (Neri et al., 2019). One study in Furnas found that indoor radon (222Rn) concentration was positively correlated with the frequency of micronucleated cells in buccal epithelial (Linhares et al., 2018). The presence of radon is strongly associated with several cancers such as thyroid and lung cancer. Radon can decay and release α particles that can penetrate to soft tissue to a lesser degree than gamma-rays and cause damage DNA and tumorigenesis. Radon can also be a gas that can decay and settle in the airways causing radiation exposure to the thyroid (Goyal et al., 2015).

In the collective data in Figure 3, the highest incidence of cancer in males was found in Portugal. The types of cancer with high incidence in Furnas compared to Santa Maria were lip, oral, and pharynx cancer. This pattern may be caused by environmental factors such as pollution from gas particles, trace elements, and radon from volcanic activity. Continuous exposure to elements in volcanic regions is possibly associated to the increasing of cancer incidence through complex mechanisms (Amaral et al., 2006). Furnas is located in soil diffuse degassing areas where fumarolic discharges and the toxic gasses are continuously released. These are carbon dioxide (CO_2), hydrogen sulfide (H2S), sulfur dioxide (SO_2), hydrogen chloride (HCl), hydrogen fluoride (HFl), and the radioactive gas radon (Rn). One study conducted by Rodrigues et al., (2012) in Furnas found that buccal epithelial cells with micronuclei (MNC) and other nuclear

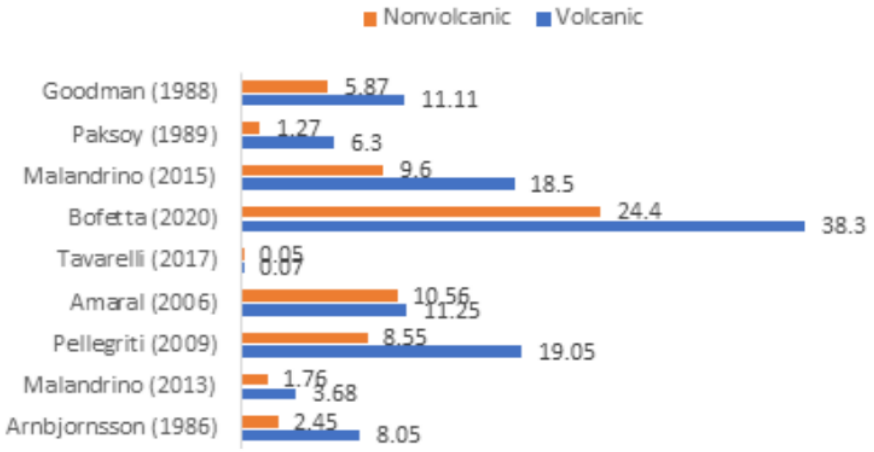

Figure 4. Cancer Age-Standardized Incidence Rate (ASR) per 100,000 per Year

anomalies (ONA) such as karyolysis, pyknosis, and karyorrhexis were higher in patients from the volcanically active environment than the non-exposed group. Higher ONA and MNC were significantly associated with exposure in the volcanically active environment. This research may be related to the increasing incidence of lip, oral, and pharynx cancers.

In our data, the overall highest incidence for cancer was thyroid carcinoma in Catania-Messina-Enna. Also, the types of cancer that appear are lip, oral cavity and thorax cancer in Furnas; and lymphatic leukemia, Hodgkin's lymphoma, stomach, breast cancer, and prostate cancer in Sicily; and liver, cervix, and skin cancer in Vanuatu. The increasing incidence of breast, thyroid, and skin cancer may be related to high radon exposure (Kristbjornsdottir and Rafnsson, 2012; Kristbjornsdottir et al., 2016). One study conducted in mice from volcanic areas showed that concentrations of aluminium (Al), lead (Pb), cadmium (Cd), and zinc (Zn) in the liver and kidneys were higher than those from non-volcanic areas. Additionally, the level of apoptotic nuclei in all organs were increased in inhabitants from volcanic areas. It may be caused by exposure to cadmium (Cd) and lead (Pb) that can degenerate DNA and stimulate the pathogenesis of cancer (Amaral et al., 2007). In addition, the presence of heavy metals such as lead (Pb), arsenic (As), cadmium (Cd), and mercury (Hg), are toxic for humans. Their presence causes genetic alteration that should be considered as an etiology for cancer initiation, for instance, the mutation of BRAF V600E. In Catania, the mutation has been found to increase the risk by 1.7-fold for papillary thyroid cancer than the other regions in Sicily. It could be possible that the radiation and genetic alteration play major roles in the carcinogenic mechanism (Goyal et al., 2015; Joneidi et al., 2019).

Some gas emissions and metal components are around volcanoes presumed dangerous to human health. One study in Catania described that six elements including arsenic (As), boron (B), molybdenum (Mo), antimony (Sb), selenium (Se), and vanadium (V) were significantly increased in drinking water samples. It was emphasized by the higher amount of those elements found in the urine specimens of local inhabitants (Malandrino et al., 2016). The rat experiment proved that rats which consumed boron (B), cadmium (Cd), and molybdenum (Mo) in drinking water presented additional neoplastic features on rat's thyroid after 10 months of goitrogenic diet (Luca et al., 2017). Nickel (Ni) is one of the components of volcanic dust that are released into the environment. In human lung cells, nickel (Ni) compounds are collected and retained in the cytoplasm and nucleus and persist for long periods of time. This retention causes DNA methylation, long-term gene silencing and also causes hypoxia in inducible genes and has been implicated in nickel-related carcinogenesis. The existence of nickel also affects the tumor associated cell migration and invasion, tumor microenvironment and survival, and its increased expression can be found in many types of cancer (Chervona et al., 2012; Chervona and Costa, 2012). Nickel has significant effects on the steroidogenic pathways. It could regulate organs upstream of the endocrine axis to affect the hypothalamus and pituitary gland and can cause abnormal secretion of pituitary hormones. The condition further affects target organs of the endocrine axis, resulting in dysfunction therein and abnormal secretion of related hormones. Studies of the negative effects of nickel in human adrenocortical carcinoma concluded that it could decrease the production of testosterone and progesterone (Lukac et al., 2020; Yang and Ma, 2021). Another dangerous component is cadmium (Cd), which can accumulate in tissues and organs especially in the kidneys. It was stated that cadmium impairs the DNA damage repair mechanism, inhibits apoptosis, induces oxidative stress, and has genotoxic effects. In the colon tumor cell line, cadmium disrupts the intestinal barrier function by decreasing the amount of E-cadherin and occludin. This leads to increased permeability for pathogens and harmful substances. High cadmium levels lead to genomic instability through multifactorial pathways which cause the promotion of cancer by activating proto-oncogenes and inactivating tumor suppressor genes through disruption of cell signaling pathway by epigenetic alteration, besides causing other diseases attributed to genomic instability (Bishak et al., 2015; Luo et al., 2019). Arsenic (As) is a pollutant that comes from many sources, including volcanic activity. It has been identified to be the causal agent of skin, bladder, lung, liver, and prostate cancers through increasing of oxidative stress, increasing inflammation, accumulation of free radical, and altering histone methylation (Filipič, 2012; Brocato and Costa, 2013). Arsenic (As), cadmium (Cd), and chromium (Cr) exposures in children and adolescents are associated with oxidative damage to DNA. They can be excreted in urine and detected as urinary biomarkers (Franken et al., 2017). Another harmful compound in volcanic emissions is sulphur dioxide (SO_2). Sulphur dioxide emission rates in Yasur (Vanuatu) vary due to volcanic activity. In PM 2.5, it can penetrate into the lung tissue, other parts of the respiratory system, and has association with mortality from 29 cancer sites. Moreover, it could disturb DNA repair, leading to DNA methylation and genotoxic effects (Bani and Lardy, 2007; Su et al., 2019).

Limitations

Our study was limited to searches of PUBMED, Scopus, Proquest, Science Direct, and Google Scholar databases for related articles in the English. Articles in the other databases and not written in English were not recorded. Most of the articles were based on case studies from Portugal and most of the cancer incidence identified was thyroid cancer. All of the articles that we found are cohort studies.

In conclusion, cancer incidence reported with age-standardised rates in volcanic areas from the data in this systematic review was higher than non-volcanic areas. This pattern is due to multifactorial causes, and one of them is exposure to the hazardous components from volcanic products. The concentration of components of volcanic products is different from one volcano to another and this is related to the harmful risk to its inhabitants. Although it is still debatable, components from volcanic products that are hazardous to human health should

be taken into consideration by local inhabitants and responsible governments.

Author Contribution Statement

The authors confirm contribution to the paper as follows: study conception and design: RGPP; data collection: YY and WA; Assessing the risk of bias : RGPP and WA; analysis and interpretation of results: RGPP and YY; draft manuscript preparation: RGPP, YY, and WA. All authors reviewed the results and approved the final version of manuscript.

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Ethics

This study did not involve the use of human (or animal) participants, therefore, did not require ethics approval.

Availability of data

Data are available by request to the corresponding author.

Data Registry

No prior registration was made for this systematic review.

Statement conflict of Interest

The authors declare that there are no conflicts of interest.

References

Amani F, Ahari SS, Barzegari S, et al (2015). Analysis of Relationships between Altitude and Distance from Volcano with Stomach Cancer Incidence Using a Geographic Information System. *Asian Pac J Cancer Prev*, **16**, 6889-94.

Amaral A, Cabral C, Guedes C, et al (2007). Apoptosis, metallothionein, and bioavailable metals in domestic mice (Mus musculus L.) from a human-inhabited volcanic area. *Ecotoxicology*, **16**, 475-82.

Amaral A, Rodrigues V, Oliveira J, et al (2006). Chronic exposure to volcanic environments and cancer incidence in the Azores, Portugal. *Sci Total Environ*, **367**, 123-8.

Arnbjörnsson E, Arnbjörnsson A, Olafsson A (1986). Thyroid cancer incidence in relation to volcanic activity. *Arch Environ Health*, **41**, 36-40.

Bani P, G B, Balcone-boissard H, et al (2015). Understanding volcanoes in the Vanuatu arc The 2009 – 2010 eruption of Gaua volcano (Vanuatu archipelago): eruptive dynamics and unsuspected strong halogens source. *J Volcanol Geotherm Res*, **2015**.

Bani P, Lardy M (2007). Sulphur dioxide emission rates from Yasur volcano, Vanuatu archipelago. *Geophys Res Lett*, **34**.

Barone G, De Giudici G, Gimeno D, et al (2021). Surface reactivity of Etna volcanic ash and evaluation of health risks. *Sci Total Environ*, **761**, 143248.

Bishak YK, Payahoo L, Osatdrahimi A, et al (2015). Mechanisms of cadmium carcinogenicity in the gastrointestinal tract. *Asian Pac J Cancer Prev*, **16**, 9-21.

Boffetta P, Memeo L, Giuffrida D, et al (2020). Exposure to emissions from Mount Etna (Sicily, Italy) and incidence of thyroid cancer: a geographic analysis. *Sci Rep*, **10**, 21298.

Brocato J, Costa M (2013). Basic mechanics of DNA methylation and the unique landscape of the DNA methylome in metal-induced carcinogenesis. *Crit Rev Toxicol*, **43**, 493-514.

Chervona Y, Arita A, Costa M (2012). Carcinogenic metals and the epigenome: understanding the effect of nickel, arsenic, and chromium. *Metallomics*, **4**, 619-27.

Chervona Y, Costa M (2012). The control of histone methylation and gene expression by oxidative stress, hypoxia, and metals. *Free Radic Biol Med*, **53**, 1041-7.

Cottrell E (2015). Global Distribution of Active Volcanoes. In: Volcanic Hazards, Risks and Disasters, Netherland, Elsevier.

Filipič M (2012). Mechanisms of cadmium induced genomic instability. *Mutat Res*, **733**, 69-77.

Franken C, Koppen G, Lambrechts N, et al (2017). Environmental exposure to human carcinogens in teenagers and the association with DNA damage. *Environ Res*, **152**, 165-74.

Goodman MT, Yoshizawa CN, Kolonel LN (1988). Descriptive epidemiology of thyroid cancer in Hawaii. *Cancer*, **61**, 1272-81.

Goplen CM, Verbeek W, Kang SH, et al (2019). Preoperative opioid use is associated with worse patient outcomes after Total joint arthroplasty: a systematic review and meta-analysis. *BMC Musculoskelet Disord*, **20**, 234.

Goyal N, Camacho F, Mangano J, et al (2015). Evaluating for a geospatial relationship between radon levels and thyroid cancer in Pennsylvania. *Laryngoscope*, **125**, E45-9.

Hariyono E, Liliasari S (2018). The Characteristics of Volcanic Eruption in Indonesia, London, IntechOpen.

Huang S, Frey FA, Blichert-Toft J, et al (2005). Enriched components in the Hawaiian plume: Evidence from Kahoolawe Volcano, Hawaii. *Geochemistry Geophys Geosystems*, **6**.

Joneidi Z, Mortazavi Y, Memari F, et al (2019). The impact of genetic variation on metabolism of heavy metals: Genetic predisposition?. *Biomed Pharmacother*, **113**, 108642.

Kristbjornsdottir A, Aspelund T, Rafnsson V (2016). Association of Cancer Incidence and Duration of Residence in Geothermal Heating Area in Iceland: An Extended Follow-Up. *PLoS One*, **11**, e0155922.

Kristbjornsdottir A, Rafnsson V (2012). Incidence of cancer among residents of high temperature geothermal areas in Iceland: a census based study 1981 to 2010. *Environ Health*, **11**, 73.

Kristbjornsdottir A, Rafnsson V (2013). Cancer incidence among population utilizing geothermal hot water: a census-based cohort study. *Int J Cancer*, **133**, 2944-52.

Linhares DPS, Garcia PV, Silva C, et al (2018). DNA damage in oral epithelial cells of individuals chronically exposed to indoor radon ((222)Rn) in a hydrothermal area. *Environ Geochem Health*, **40**, 1713-24.

Luca E, Fici L, Ronchi A, et al (2017). Intake of Boron, Cadmium, and Molybdenum enhances rat thyroid cell transformation. *J Exp Clin Cancer Res*, **36**, 73.

Lukac N, Forgacs Z, Duranova H, et al (2020). In vitro assessment of the impact of nickel on the viability and steroidogenesis in the human adrenocortical carcinoma (NCI-H295R) cell line. *Physiol Res*, **69**, 871-83.

Luo S, Terciolo C, Bracarense A, et al (2019). In vitro and in vivo effects of a mycotoxin, deoxynivalenol, and a trace metal, cadmium, alone or in a mixture on the intestinal barrier.

Environ Int, **132**, 105082.
Malandrino P, Pellegriti G, Attard M, et al (2013). Papillary thyroid microcarcinomas: a comparative study of the characteristics and risk factors at presentation in two cancer registries. *J Clin Endocrinol Metab*, **98**, 1427-34.
Malandrino P, Russo M, Giani F, et al (2020). Increased Thyroid Cancer Incidence in Volcanic Areas: A Role of Increased Heavy Metals in the Environment?. *Int J Mol Sci*, **21**.
Malandrino P, Russo M, Ronchi A, et al (2016). Increased thyroid cancer incidence in a basaltic volcanic area is associated with non-anthropogenic pollution and biocontamination. *Endocrine*, **53**, 471-9.
Moher D, Liberati A, Tetzlaff J, et al (2009). Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med*, **6**, e1000097.
Moola S, Munn Z, Tufanaru C, et al (2020). Chapter 7: Systematic reviews of etiology and In 'JBI Manual for Evidence Synthesis', Eds The Joanna Briggs Institute Adelaide, Australia,
Neri M, Giammanco S, Leonardi A (2019). Preliminary Indoor Radon Measurements Near Faults Crossing Urban Areas of Mt. Etna Volcano (Italy). *Front Public Health*, **7**, 105.
Page MJ, McKenzie JE, Bossuyt PM, et al (2021). The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*, **372**, n71.
Paksoy N, Montaville B, McCarthy SW (1990). Cancer occurrence in Vanuatu in the South Pacific, 1980-86. *Trop Geogr Med*, **42**, 157-61.
Pellegriti G, De Vathaire F, Scollo C, et al (2009). Papillary thyroid cancer incidence in the volcanic area of Sicily. *J Natl Cancer Inst*, **101**, 1575-83.
Prozialeck WC, Lamar PC, Lynch SM (2003). Cadmium alters the localization of N-cadherin, E-cadherin, and beta-catenin in the proximal tubule epithelium. *Toxicol Appl Pharmacol*, **189**, 180-95.
Rodrigues AS, Arruda MS, Garcia PV (2012). Evidence of DNA damage in humans inhabiting a volcanically active environment: a useful tool for biomonitoring. *Environ Int*, **49**, 51-6.
Russo M, Malandrino P, Addario WP, et al (2015). Several Site-specific Cancers are Increased in the Volcanic Area in Sicily. *Anticancer Res*, **35**, 3995-4001.
Russo M, Malandrino P, Moleti M, et al (2017). Thyroid Cancer in the Pediatric Age in Sicily: Influence of the Volcanic Environment. *Anticancer Res*, **37**, 1515-22.
Su SY, Liaw YP, Jhuang JR, et al (2019). Associations between ambient air pollution and cancer incidence in Taiwan: an ecological study of geographical variations. *BMC Public Health*, **19**, 1496.
Tavarelli M, Malandrino P, Vigneri P, et al (2017). Anaplastic Thyroid Cancer in Sicily: The Role of Environmental Characteristics. *Front Endocrinol (Lausanne)*, **8**, 277.
Yamamoto S, Konishi Y, Matsuda T, et al (1995). Cancer induction by an organic arsenic compound, dimethylarsinic acid (cacodylic acid), in F344/DuCrj rats after pretreatment with five carcinogens. *Cancer Res*, **55**, 1271-6.
Yang J, Ma Z (2021). Research progress on the effects of nickel on hormone secretion in the endocrine axis and on target organs. *Ecotoxicol Environ Saf*, **213**, 112034.

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