



Chronic diseases and mortality among immigrants to Israel from areas contaminated by the Chernobyl disaster: a follow-up study

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Abstract

Objectives To examine six chronic diseases and all-cause mortality among immigrants to Israel from areas contaminated by the Chernobyl accident.

Methods The medical data were obtained from the two largest HMOs in Israel. In the assessment of chronic diseases, individuals were divided into three groups: less exposed ($n = 480$), more exposed ($n = 359$), and liquidators ($n = 45$) and in the mortality analysis, into two groups: less exposed ($n = 792$) and more exposed ($n = 590$).

Results Compared to the less exposed, adults from the more exposed group had increased odds of respiratory disorders (OR = 2.34, 95% CI 1.21, 4.54) and elevated odds, with borderline significance, of ischemic heart disease (OR = 2.01, 95% CI 0.97, 4.20). In addition, the liquidators had increased odds of hypertension compared to the less exposed (OR = 2.64, 95% CI 1.24, 5.64). The Cox proportional-hazards model indicated no difference in the ratio of all-cause mortality between the exposed groups during the follow up period.

Conclusions Our study, conducted approximately two decades after the accident, suggests that exposure to radionuclides may be associated with increased odds of respiratory disorders and hypertension.

Keywords Chernobyl · Cesium-137 · Iodine-131 · Radiation

Introduction

The accident at the Chernobyl nuclear power plant on April 26th 1986 was the most severe in the history of the nuclear power industry, causing a massive release of radionuclides over large areas of the former Soviet Union (FSU). The total release of radioactive substances was about 14 EBq, including: 1.8 EBq of short-lived iodine-131 (^{131}I , half-life of 8 days), and 0.085 EBq of long-lived cesium-137 (^{137}Cs , half-life of 30 years) (IAEA 2006). Millions of residents of contaminated areas received radiation exposure from ingestion of radioactively contaminated products, inhalation of contaminated airborne dust, and from radionuclides deposited on the ground. Radioactive iodine exposure is primarily to the thyroid gland, while radioactive cesium exposure can involve all body organs (Ostroumova et al. 2016).

Four years after the accident, ecological (Abelin et al. 1994) and epidemiological studies (Astakhova et al. 1998; Cardis et al. 2005) reported increased rates of childhood thyroid cancer among those living in the Chernobyl-contaminated areas. At that time, it was not clear whether the observed increase was due to radiation or due to the increase in detection efficiency for thyroid cancer. In the 2000 report of the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) 1800 thyroid cancer cases were confirmed among those aged under 18 years at the time of the accident (UNSCEAR 2000). By 2006, this number had climbed to more than 6000 cases of thyroid cancer (UNSCEAR 2011).

While an increased risk of thyroid cancer from post-Chernobyl exposure to ^{131}I in children and adolescents has been well-documented (Cardis and Hatch 2011; Ivanov

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et al. 2012; UNSCEAR 2015; Zablotska et al. 2015), the risks of other cancers or chronic conditions remain uncertain (Davis et al. 2006; Noshchenko et al. 2010; Ostroumova et al. 2016). Due to the paucity of well-designed studies, it is premature to conclude that radiation from the Chernobyl accident did not have a significant effect on the incidence of other tumors or chronic diseases.

Between the years of 1989–1996 Israel absorbed an estimated 700,000 immigrants from FSU, of whom approximately 140,000 migrated from the contaminated areas of Belarus, Russia, and Ukraine (Quastel et al. 1997b; Wishkerman et al. 1997). In 1990, medical staff at the Soroka Medical Center and the Faculty of Health Sciences at Ben-Gurion University of the Negev (BGU) established a clinic to address the needs of immigrants from the contaminated areas and to initiate a study to assess their health status and radiocesium body burdens (Kordysh et al. 1995; Quastel et al. 1995, 1997a). Kordysh and colleagues, who used a subset of the study population, found an increased risk of self-reported bronchial asthma among boys (5.4%) and girls (3.4%) from the more exposed areas compared to boys and girls (1.9 and 1.6%, respectively) from the less exposed areas. A similar increase was observed among children who were potentially exposed in utero (Kordysh et al. 1995). Quastel et al., found that girls from more exposed areas had significantly higher levels of thyroid-stimulating hormone (TSH), though within the normal range, than girls from the less exposed areas (Quastel et al. 1997a, b).

In the mid-nineties, Cwikel and colleagues recruited a subset of the BGU study population with additional immigrants selected by snowball sampling to examine the prevalence of post-traumatic stress disorder, depression, hypertension and other self-reported acute and chronic disorders (Cwikel et al. 1997b). The authors found that psychological symptoms and hypertension were significantly higher among immigrants from the more exposed areas compared to immigrants from the less exposed areas (Cwikel et al. 1997b). In addition, immigrants from the more exposed areas had higher odds of self-reported heart disease (RR = 1.88, 95% CI 1.09, 3.22) compared with immigrants from the less exposed areas. The authors concluded that based on their results, the Chernobyl accident was a powerful stressor, having a strong impact on both mental and physical health (Cwikel et al. 1997a).

Because the evidence to date regarding a post-Chernobyl increase in risk of non-thyroid cancers and other chronic diseases is uncertain, it is important to monitor the exposed population for all cancer types and chronic diseases, in order to understand the outcome of Chernobyl-related exposures over time. Therefore, in this study, we used a subset of the BGU study population to examine six chronic diseases and all-cause mortality among immigrants

to Israel from the contaminated areas about two decades after the accident.

Methods

Study population

The study population is a subset of a previous study conducted in the early nineties at Ben-Gurion University, Israel, to examine the health status of immigrants from areas contaminated by the Chernobyl accident (Cwikel et al. 1997a, b; Kordysh et al. 1995; Quastel et al. 1995, 1997a, b). Immigrants were divided into three exposure groups: immigrants from less exposed areas, immigrants from more exposed areas, and liquidators—workers who were involved in the clean-up and recovery operation. The terms ‘more exposed’ and ‘less exposed’ were based on past residence in regions of higher or lower ^{137}Cs exposure as documented by the IAEA ^{137}Cs contamination map published in 1991 (UNSCEAR 2000). ‘More exposed’ regions were contaminated with $\geq 37 \text{ GBq/km}^2$ and ‘Less exposed’ regions were defined as having less than this level of ^{137}Cs contamination. In this follow-up study, about 46% of the individuals from the less exposed group were from Kiev, Ukraine and 68% of the more exposed were from Gomel, Belarus.

In 2004, using the Israeli Ministry of Interior’s database we were able to locate and identify the unique identity numbers of 1447 immigrants who were interviewed in the original BGU study. In 2005, this verified database was used to collect dates of death of all-cause mortality from the time participants entered the study up until January 1st 2005. The analysis of all-cause mortality included the less exposed ($n = 792$) and the more exposed ($n = 590$).

In order to collect medical information, Clalit and Maccabi Health Maintenance Organizations (HMOs) were contacted. These two organizations, which insure and provide health care services for the majority of the population in Israel (Plotnik and Kedar 2015), provided information on chronic diseases for 884 individuals in three exposure groups: less exposed ($n = 480$), more exposed ($n = 359$), and liquidators ($n = 45$).

Data collection

A detailed description of the data collection process in the original BGU study was previously published (Kordysh et al. 1995; Quastel et al. 1997a). Briefly, between the years 1991–1995 an in-person interview and a physical examination was conducted on more than 1600 immigrants who visited the clinic on a voluntary basis. All immigrants signed an informed consent to participate in the study.

Detailed information was collected on residential and exposure history, medical and smoking history, dietary history, and socio-demographic characteristics. This process also included body burden measurements of ^{137}Cs (Quastel et al. 1995).

In 2004, the databases of Clalit and Maccabi HMOs were used to collect information on chronic diseases, smoking, and health care services utilization for the three exposed groups. Unfortunately, data were not available for immigrants who participated in the BGU study and were not registered with Clalit or Maccabi HMOs. More specifically, information was collected from medical records for the diagnosis of several chronic diseases including: hypertension [International classification of disease (ICD) 9 codes 401–405], disorders of thyroid gland (codes 240–245), ischemic heart disease (codes 410–414), diseases of the respiratory system (codes 490–496 and 472–476), and malignancies (codes 140–208 and 230–234). In addition, hypertension measurements, information on smoking, and the number of visits to the primary health care clinic during 2004 were also recorded.

Statistical analysis

Descriptive analyses were conducted using Chi-square and Student's *t* tests to compare the distribution of socio-demographic characteristics among the three exposure groups. The smoking status variable that was used in the descriptive analyses combines smoking data from the original BGU study and the follow-up study (smoking or smoked, never smoked). Logistic regressions were used to calculate odds ratios (OR) and 95% confidence intervals (CI) of chronic disease among the three exposure groups, controlling for sex and age. Poisson regressions were used to assess the differences in the number of visits to the primary care physician during 2004, between the three exposure groups. In addition, hazard ratios (HR) and 95% confidence intervals for all-cause mortality using Cox proportional hazard models were used to evaluate whether survival differed between the more exposed and the less exposed groups.

Results

The demographic characteristics of participants were similar between the less exposed ($n = 480$) and the more exposed group ($n = 359$), with significant differences only in the year of immigration. The less exposed immigrated to Israel later than the more exposed (Table 1). Compared to the first two groups, the liquidators ($n = 45$) had higher percentage of smoking (53.3%) and had higher percentage of immigration in years 1992–1995 (57.8%).

Table 1 Main characteristics of less exposed ($n = 480$), more exposed ($n = 359$) and liquidators ($n = 45$), follow-up of the Ben-Gurion University Study, Israel, 2005

	Less exposed <i>n</i> (%)	More exposed <i>n</i> (%)	Liquidators <i>n</i> (%)
Gender			
Male	192 (40.0)	132 (36.8)	35 (77.8)
Female	288 (60.0)	227 (63.2)	10 (22.2)
Age at the time of the accident (years)			
0–9	138 (28.8)	110 (30.6)	
10–20	56 (11.6)	51 (14.2)	
≥20	286 (59.6)	198 (55.2)	45 (100)
Mean age at the time of the accident, years (SE)	25.1 (0.8)	24.3 (1.0)	
Smoking status ^a			
Smoking or smoked	100 (30.7)	52 (22.7)	24 (53.3)
Never	226 (69.3)	177 (77.3)	21 (46.7)
Year of immigration to Israel			
1989–1990	171 (35.6)	187 (52.1)	8 (17.8)
1991	279 (58.1)	150 (41.8)	11 (24.4)
1992–1995	30 (6.3)	22 (6.1)	26 (57.8)

^a Included only those age 16 and above at the time of the BGU interview

The analyses of chronic disease between the exposure groups, for those aged 20 and above at the time of the accident, indicated no significant difference in the prevalence of hypertension, diabetes, thyroid disorders and malignancies. Individuals from the more exposed group had an increased odds of respiratory disorders (OR = 2.34, 95% CI 1.21, 4.54) compared to the less exposed, when adjusted for age and sex. The more exposed group also had elevated odds, with borderline significance, of ischemic heart disease compared to the less exposed (OR = 2.01, 95% CI 0.97, 4.20). In addition, the liquidators had increased odds of hypertension (OR = 2.64, 95% CI 1.24, 5.64) compared to the less exposed, when adjusted for age and gender (Table 2). The results of the chronic disease analyses did not change when smoking was included in the model. In addition, no differences in the odds of these six chronic conditions were observed between the two exposed groups for those ages 0–9 years and 10–20 years at the time of the accident (data not shown).

The frequency of visits to the primary care physician was analyzed using Poisson regression models adjusted for age and gender. The results indicated that the more exposed (age ≥20 years at the time of the accident) and the liquidators had a significantly higher mean number of visits (7.09 and 8.34, respectively) in 2004 than the less exposed

Table 2 Odds ratio (95% confidence interval) for chronic diseases among the less exposed, more exposed, and the liquidators, ≥ 20 years old at the time of the accident, follow-up of the Ben-Gurion University Study, Israel, 2005

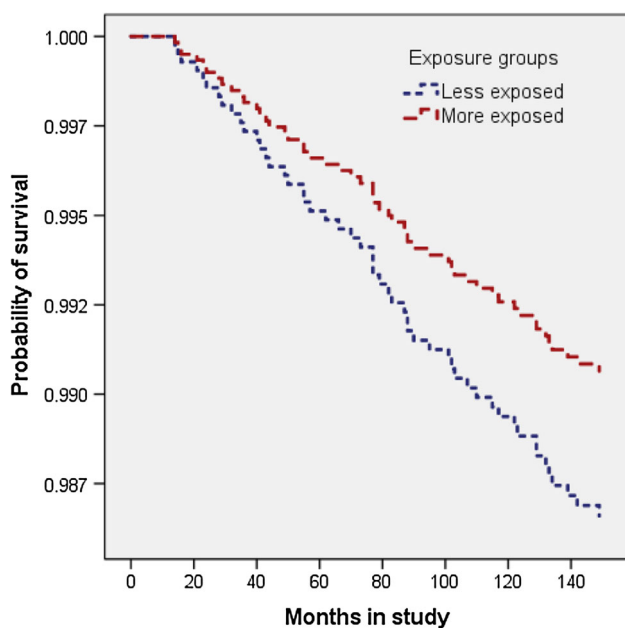
	Less exposed ($n = 286$)	More exposed ($n = 198$)		Liquidators ($n = 45$)	
	n (%)	n (%)	OR (95% CI) ^a	n (%)	OR (95% CI) ^a
Hypertension	89 (31.1)	72 (36.4)	1.14 (0.74, 1.78)	20 (44.4)	2.64 (1.24, 5.64)
Diabetes	20 (7.0)	18 (9.1)	1.18 (0.60, 2.38)	6 (13.3)	2.77 (0.94, 8.15)
Ischemic heart disease	19 (6.6)	25 (12.6)	2.01 (0.97, 4.20)	5 (11.1)	2.16 (0.65, 7.18)
Thyroid disorders	25 (8.7)	14 (7.1)	0.73 (0.36, 1.46)	4 (8.9)	2.85 (0.80, 10.09)
Respiratory disorders	16 (5.6)	25 (12.6)	2.34 (1.21, 4.54)	4 (8.9)	1.72 (0.51, 5.81)
Malignancies	12 (4.2)	11 (5.6)	1.18 (0.50, 2.80)	2 (4.4)	1.18 (0.24, 5.87)

^a Odds ratios and 95% confidence intervals comparing to less exposed group estimated using multiple logistic regressions adjusted for age and sex

Table 3 Frequency of visits to the primary care physician during 2004, by age and exposure, follow-up of the Ben-Gurion University Study, Israel, 2005

Age	Less exposed ($n = 480$)	More exposed ($n = 359$)		Liquidators ($n = 45$)	
	Mean (SD)	Mean (SD)	IRR (95% CI) ^a	Mean (SD)	IRR (95% CI) ^a
0–9	2.88 (4.1)	3.01 (3.6)	1.02 (0.88, 1.11)		
10–20	2.95 (3.1)	3.08 (3.5)	1.01 (0.85, 1.34)		
≥ 20	5.71 (6.2)	7.09 (6.5)	1.19 (1.10, 1.27)	8.34 (7.3)	1.71 (1.52, 1.93)

^a Incidence rate ratio and 95% confidence intervals estimates comparing to less exposed group using Poisson regression adjusting for age and gender

**Fig. 1** Survival probability between 1992 and 2004 among the less exposed ($n = 792$) and the more exposed ($n = 590$), follow-up of the Ben-Gurion University Study, Israel, 2005

(5.71) (incidence rate ratio (IRR) = 1.19, 95% CI 1.10, 1.27) and (IRR = 1.71, 95% CI 1.52, 1.93), respectively (Table 3).

The all-cause mortality analysis indicated that from the beginning of the BGU study until the end of 2004, 34 (4.3%) individuals from the less exposed group and 18 (3.1%) individuals from the more exposed group had died. The Cox proportional-hazards model indicated no difference in the hazard ratio of all-cause mortality between the less exposed and the more exposed, adjusted for age and sex (HR = 0.70, 95% CI; 0.39, 1.24) (Fig. 1). The results did not change when smoking was added to the model.

Discussion

In this follow-up study of immigrants to Israel from areas contaminated by the Chernobyl disaster, we found that immigrants from the more exposed areas had statistically significant increased odds of respiratory disorders compared to immigrants from the less exposed areas. Our study also found an elevated, though not statistically significant, odds of ischemic heart disease among the more exposed and the liquidators compared to the less exposed. In addition, our results indicated that the mean number of visits to the primary care physician in 2004 was higher among the more exposed (7.09) and the liquidators (8.34) compared to the less exposed (5.71). The results of the

analyses above include only those age ≥ 20 years at the time of the accident.

A number of studies of the health effects of radiation from the Chernobyl accident have been conducted over the last 30 years. These studies provided important information regarding the association between exposure to several radionuclides and health, especially between ^{131}I and thyroid cancer (Ivanov et al. 2006a; Ostroumova et al. 2014; Tronko et al. 2012; Zablotska et al. 2011). The increased risk of thyroid cancer from post-Chernobyl exposure to ^{131}I in children and adolescents has been well documented but the risks of other disorders remained uncertain. Little is known of non-carcinogenic effects on the immune system associated with exposure to long term low dose radiation (Cardis and Hatch 2011; Saenko et al. 2011). Most well designed studies to date have found no association between Chernobyl exposure and non-thyroid cancers (Hatch et al. 2015; Ostroumova et al. 2016) and other health outcomes, but some studies have indicated an increased incidence of leukemia, cardiovascular diseases, and other health outcomes among the liquidators (Ivanov et al. 2006b; Krasnikova and Buzunov 2014; Zablotska 2016).

The Chernobyl liquidators, or accident recovery workers, are of particular interest, as they tended to receive relatively high levels of exposure through their work on the industrial site of the power plant and in the surrounding area (Kesminiene et al. 2008). The average external doses of the liquidators who were working during 1986 and 1987 were 146 and 96 mGy, as recorded by the national registries of Belarus, the Russian Federation and Ukraine (UNSCEAR 2011). In our study, the liquidators had statistically significant increased odds of hypertension compared to immigrants from the less exposed areas (OR = 2.64, 95% CI 1.24, 5.64). In addition, we found elevated, but not statistically significant, increased odds of three other chronic conditions (diabetes, disorders of the thyroid gland and ischemic heart disease). The failure to achieve a statistically significant excess of those three conditions among the liquidators could reflect insufficient statistical power, given the relatively small number of liquidators ($n = 45$).

Our findings of increased odds of hypertension among the liquidators are in line with previous studies. Ivanov and colleagues conducted a study to assess the risks of cerebrovascular diseases and hypertension among liquidators using data from the Russian National Medical and Dosimetric Registry (Ivanov et al. 2005, 2006b). The authors found dose-related increased risk of essential hypertension [Excess Relative Risk (ERR) = 0.36, 95% CI; 0.005, 0.71] (Ivanov et al. 2006b). However, the authors noted that they did not adjust for important risk factors such as excessive weight, smoking, and alcohol consumption. Following the studies of Ivanov and colleagues, the UNSCEAR indicated

in its 2008 report, that further studies were required before it can be concluded whether radiation exposure due to the Chernobyl accident has increased the risk of cardiovascular and cerebrovascular disease and associated mortality (UNSCEAR 2011).

The increased odds of respiratory disorders in our study population, among those age ≥ 20 years at the time of the accident, has been previously observed and reported in the early stage of the BGU study (Kordysh et al. 1995). In line with our results are the findings of Svendsen and colleagues who conducted a longitudinal prospective cohort study to investigate the association between ^{137}Cs levels in the soil and basic and post-bronchodilator spirometry measures of children. The authors used repeated measurements from 1993 to 2010. In 2015, the authors reported that children from the regions closer to Chernobyl areas continued to have respiratory health deficits that were associated with ^{137}Cs whole-body burden (Stepanova et al. 2008; Svendsen et al. 2010, 2015). The authors concluded that impairment in respiratory function among children may be of greater public health concern than previously recognized (Svendsen et al. 2015).

The observed increased odds of hypertension in this follow-up study were consistent with earlier findings of the BGU study as reported by Kordysh and Cwikel (Cwikel et al. 1997b; Kordysh et al. 1995). Cwikel and colleagues indicated that the systolic blood pressure (>140 mmHg) was significantly higher among immigrants from the more exposed areas compared to immigrants from the less exposed areas (20 vs. 16%, respectively) (Cwikel et al. 1997b). However, we could not find other well-designed English studies reporting increase in the odds of hypertension among the residents of the contaminated areas near Chernobyl.

Mortality ratio in our study did not differ significantly between the less exposed and the more exposed groups. However, while the Cox proportional-hazards model indicated no significant difference in the mortality ratio, the mortality was surprisingly higher among the less exposed (4.3%) compared to the more exposed (3.1%). There is no clear explanation for the observed differences in the mortality, perhaps it is due to chance alone. It is important to mention that the mortality analysis in our study is not likely to suffer from a loss to follow-up bias as it was record-based and included all of the BGU study population who were identified by the Israeli Ministry of Interior.

While our study provides a unique opportunity to evaluate the health status of immigrants who were presumably exposed to radioactive contamination it also has several limitations. There might be a bias in the selection of study participants. Our study population was a subset of the BGU study population. The BGU study population was a sample that was similar to the demographic make-up of the FSU

immigrant population to Israel (Cwikel et al. 1997b). However, this population may be different from the subjects who stayed in the former USSR and continued to be exposed over the years. Therefore, our findings are less generalizable to other populations from Chernobyl-affected areas who are still residing in the area contaminated with long-lived ^{137}Cs . In addition, in this follow up study, we were able to locate and identify 1447 (90.5%) immigrants out of the 1600 who participated in the BGU Study. The database of the Ministry of Interior could not identify 153 identification numbers because either the immigrants had left the country or their identification number was incorrectly typed in the records of the BGU study. In addition, out of the 1447 immigrants who were included in the mortality analysis (excluding 65 liquidators), only those registered with Clalit or Maccabi HMOs were included in the chronic disease analyses. Individuals who were registered with the other two small HMO's in Israel were not included in this analyses. It is important to mention that the Israeli National Health Insurance Law from 1995 made membership in one of the four existing HMOs compulsory for all citizens and gave them the freedom to select and participate in any one of them regardless of factors such as age, gender, or health condition. Because citizens have the freedom to choose which HMO to be registered with, we assume that those who participated in our follow-up study have similar characteristics to those who did not participate and therefore our follow-up sample represents the earlier BGU study population.

In addition, the number of liquidators was small ($n = 45$), limiting statistical power and precluding accurate quantitative risk estimates. The overall sample size of our follow-up study did not allow us to assess the risk of thyroid cancer, a major outcome of the Chernobyl accident. Another major limitation is that the data were obtained from medical records and as a result, important updated information (physical activity, alcohol consumption, dietary, subsequent stressful life events, occupation, education or other socioeconomic factors) was not available. Therefore, the observed differences in the odds of respiratory disorders and hypertension do not necessarily imply an effect of radiation exposure.

Conclusion

Our follow-up study, conducted approximately 20 years after the accident, suggests that exposure to radionuclides may be associated with increased odds of respiratory disorders and hypertension. Our results attest to the need to continue monitoring those who were exposed to radionuclides, as we have observed long-term health differences between the exposed groups. Additional well-designed follow-up studies are still needed to evaluate the health

effects associated with long-term exposures to low concentrations of radioactivity.

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Compliance with ethical standards

All procedures performed in our study involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study was approved the Helsinki Committee of the Soroka University Medical Center.

Conflict of interest The authors declare that they have no conflict of interest.

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