

## RADIATION INDUCED THYROID CARCINOMA IN ROMANIA – EFFECTS OF THE CHERNOBYL FALLOUT, A SYSTEMATIC REVIEW OF OBSERVATIONAL STUDIES

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### Abstract

**Introduction.** The development of thyroid carcinoma is a complex process, in which both genetic and environmental factors play an important role. The rising incidence of thyroid neoplasm determines researchers to investigate factors implicated in this phenomenon. This article aims to elucidate the effects of the Chernobyl nuclear disaster on the Romanian population, studying the existing literature on radiation induced thyroid carcinoma. We analyzed the main studies published on this matter.

**Methods.** We used the PubMed and Google Scholar databases to search for articles upon the effects of the Chernobyl nuclear disaster on the incidence of thyroid carcinoma in the Romanian population. After a careful review of the existing literature, we selected the relevant and accessible studies, the first observation being that data on thyroid related effects of the Chernobyl nuclear disaster are scarce.

**Results.** From the selected studies, results show that there is a possible link between the Chernobyl fallout and the incidence of thyroid carcinoma. Multiple factors have been studied that play an important role in the increasing number of thyroid carcinoma cases, such as: better diagnostic techniques, incidentalomas, microcarcinomas and radiation exposure. In consequence it is difficult to measure the influence that the Chernobyl nuclear fallout has on thyroid carcinoma incidence.

**Conclusion.** Especially in pediatric patients, there seems to be a convincing evidence of radiation related thyroid carcinoma, while in adult patients the rising incidence due exclusively to nuclear fallout is not that clear. Further studies must be done on this matter to clearly see the influence radiation has on the incidence of thyroid cancer.

**Keywords:** thyroid neoplasm, Chernobyl, incidence, radiation

### Background and aims

The incidence of thyroid carcinoma is increasing, due to better diagnostic techniques and exposure to

environmental and genetic factors [1,2,3,4]. Genetic predisposition plays an important role in the development of cancer, the most common genetic mutation associated with thyroid carcinoma is the BRAF V600E mutation, which is related to the MAPK (mitogen activated protein kinase) signaling pathway, regulating cell growth [5]. Of

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the environmental factors an important role is played by ionizing radiation from natural (background) and artificial sources. [1,3]

The Chernobyl nuclear power plant disaster occurred in 1986 April 26 and resulted in the release of many volatile radioactive materials from the reactor's core, which continued for several days after the initial explosions. Due to changing wind directions, the radioactive cloud interested many parts of Europe. The radioactive materials were deposited mostly in Belarus, Russia, Ukraine, but also in many other European countries depending on wind speed and direction and rainfall. In the initial days and weeks after the accident the short half-life radionuclides were the most important contributors to the extrinsic and intrinsic effects of radiation (Iodine-131 ( $^{131}\text{I}$ ) especially), later the significance of Cesium radio nuclides ( $^{134}\text{Cs}$  (Caesium 134), especially  $^{137}\text{Cs}$  (Caesium 137),) started to grow, and it became the most important factor, especially over large distances [6]. Currently the radioactive material is located at a depth of 0-30 cm from the surface [7]. Due to wind, precipitation patterns at that time and geometric characteristics, radioactive deposits vary from region to region [7,8].

Of the emitted radioisotopes  $^{131}\text{I}$  and  $^{137}\text{Cs}$  were the most important for the Romanian population. The main contributor for the thyroid doses was  $^{131}\text{I}$ .  $^{137}\text{Cs}$  was and still is the main source of radiation for other organs and tissues. Exposure to  $^{131}\text{I}$  happened mainly via internal radiation causing high radiation induced thyroid carcinogenesis, while  $^{137}\text{Cs}$  via both internal and external radiation [7,9]. Exposure to  $^{131}\text{I}$  occurred in the first few weeks after the nuclear accident, while exposure to  $^{137}\text{Cs}$  is continuous at low rates due to the long half life [8].

$^{131}\text{I}$  is the most common radionuclide used in endocrinology, both for benign and malignant pathologies. It has a half-life of  $T_{1/2}=8$  days. It is a beta (606 keV -89%) and gamma (364 keV) emitter. Possible ways of exposure are: intrinsic and extrinsic contamination.  $^{137}\text{Cs}$  is the most common radioactive form of cesium. It is produced

by nuclear fission, a byproduct of uranium and plutonium fission. The half-life of cesium-137 is 30 years. It is a beta (511 (94.6%), 157 keV) and gamma (662 keV) emitter. It moves easily in the air, and dissolves in water. External or internal exposure to  $^{137}\text{Cs}$  increases the risk of cancer. Internal exposure results in distribution of the radioactive material mainly in the soft tissue. It is used in medicine, for therapeutic purposes and for medical devices and gauges. It can be found in the environment due to nuclear tests and nuclear accidents, such as Chernobyl [10,11,12,13].

### Methods

We performed an initial search of medical literature using the following databases: PubMed, Scopus and Google Scholar.

In the PubMed and Scopus databases using the keywords "thyroid cancer, Chernobyl" we found 707 studies. An additional filter was applied to include only articles on the Romanian population, which resulted in 5 studies. Of these five articles one study had only the abstract available and another one had no application in radiation related thyroid carcinoma.

On the Google Scholar database we applied the same search words and found 743 studies. After a careful review of the abstracts, seven were selected with implications in our field of research.

We selected articles published after 1995 that studied thyroid carcinoma incidence in the Romanian population after the Chernobyl nuclear disaster. The following exclusion criteria were applied: studies published before 1995, abstracts without available full text. Consequently we included 10 articles in our literature review.

### Results

During our search of the available literature and applying our established criteria we only found ten articles regarding the effects of the Chernobyl fallout on the Romanian population. (Table I.)

**Table I.** Studies on radiation induced thyroid carcinoma in Romania due to the Chernobyl nuclear fallout.

Author	Year	County
Sali et al. [14]	1996	Not specified
Sălăgean et al. [15]	1996	Cluj, Mures
Davidescu et al. [17]	2004	Eastern territory of Romania, otherwise not specified
Szántó et al. [16]	2009	Not specified
Piciu et al. [18]	2012	Not specified
Catana et al. [22]	2012	Mures and border counties, otherwise not specified.
Lisencu et al. [20]	2013	Not specified
Piciu et al. [1]	2013	Not specified
Stanciu et al. [21]	2015	Sibiu
Chiosila et al. [19]	2016	Not specified

## Discussion

All the studies invariably point out the increasing number of thyroid carcinoma cases (Table I). According to the year of publishing: two studies [14,15] appeared between 1995 and 2000, two [16,17] between 2000-2010, and six studies [1,18,19,20,21,22] after 2010.

Thyroid carcinoma is the most frequent endocrine neoplasm, which in the last two decades presented an important increase in incidence [3,4]. It is difficult to determine the factors implicated in this surge of incidence. For the immediate vicinity of the contamination zone the deterministic effect of radiation on the incidence of thyroid carcinoma is very clear, while for the rest of Europe there is no clear link. Multiple factors play a role in the process of carcinogenesis, both intrinsic (genetic inheritance) and extrinsic (environmental factors). The lack of studies and <sup>131</sup>I dose data and the long carcinogenesis period makes it very difficult to estimate the role that the Chernobyl related radiation plays on the incidence of thyroid carcinoma [8].

Authors of the studies published before 1996 [14,15] point out that thyroid carcinoma has a latency period of at least 10 years, in consequence data gathered before 1996 may not be representative of the actual situation, but both studies found an increase in the number of cases. Outside the immediate affected countries (Belarus, USSR, and Ukraine) which had high contamination rates, in other European countries researchers must take into account this latency period. Most likely this is why the initial studies hadn't shown a clear link between thyroid carcinoma and radiation despite the initial fears. Sali et al. [14] concluded that during the nine year period 1986-1995 no major health risk related to the Chernobyl event in Romania has been described, in the context of a lack of correct data upon <sup>131</sup>I contamination, which was the main radioactive substance that determined thyroid carcinogenesis. Multicenter and comparative studies should be designed to elucidate the still continuing argument upon the thyroid effects of the Chernobyl nuclear fallout.

Szántó et al. [16] report two peaks of increasing incidence, one between 1992 and 1999, the second between 2000 and 2007, with a 3 to 5 fold increase, while Catana et al. [22] found a 2 to 5 fold increase in incidence between 1990 and 2009, mostly due to papillary thyroid neoplasm.

The researchers observed that the incidence of thyroid cancer started to rise in the year 1992 and it was stationary between 1984 and 1991. The maximum incidence of radiation induced thyroid carcinoma is concentrated in 5-10 years after the disaster, with a larger margin of 1-20 years, depending on the exposure rate [16]. Piciu et al. [1] shows a vast increase of thyroid carcinoma cases in Romania since 1970, with a maximum increase of 511% between the years 2001-2010 in contrast to 1970-1980.

Many of the above mentioned studies (Table I) focused on pediatric population. The most affected subgroup was the pediatric population at the time of the incident.

According to data from the UNSCEAR 2008 report [8], the most vulnerable population to radiation exposure were between 0-14 years at the time of the accident, and data suggests a surge of incidence of thyroid carcinoma between 1991-2005. For the exposed population of Belarus, Ukraine and Russia the incidence of thyroid carcinoma was higher in the subgroups that were under the age of 14 at the time of the accident, the detectable peak of incidence was between 1991 and 1995 [8]. Also studies indicate no effect on babies born after or adults during the event [8]. Davidescu et al. [17] report that there is no radiation related rise in incidence in unborn children at the time of the accident, fact reinforced by the UNSCEAR report [8], while Lisencu et al. [20] report a major increase in incidence in children born after the Chernobyl event and those who were under 18 years, in contrast to those born after, although researchers mention that thyroid lesions discovered in children present a higher rate of malignancy. Piciu et al. [18] describe a different trend line in the incidence of thyroid carcinoma between adult and pediatric patients; 10-15 years after the Chernobyl nuclear fallout there is an increasing number of thyroid carcinomas in children, but this trend becomes stationary after 2005, while in the cases of adult patients there is a constant increase, fact that suggests a link between child thyroid carcinoma cases and the Chernobyl nuclear fallout. Sălăgean et al. [15] in a 10 year period between 1982 and 1992, studies the effects of the Chernobyl nuclear accident on the incidence of leukemia and thyroid carcinoma in children in two counties (Cluj, Mureș). Although the reported thyroid doses were different, in Cluj County the actual dose was higher than the one reported in Mures County; the study doesn't report a difference in incidence between the two regions.

Microcarcinomas play an important role in the increasing number of cases according to most studies [1,16,21,22]. The first reported case in Romania is from the year 1996 [1].

All the studies report a rise in the papillary form of thyroid cancer, while the follicular form is decreasing mostly due to salt iodination [21].

Stanciu et al. [21] on thyroid carcinoma incidence in Sibiu County conclude that during the period of 2011-2013 the incidence of thyroid carcinoma doubled; in 2011 it was 3.98/100000, while the measured incidence in 2013 was 6.91/100000. Most cancers identified by this study were papillary carcinomas which presented more aggressive features than previously reported, with latero cervical and lung metastases. Also, they found a decrease in follicular carcinoma cases probably due to salt iodination. The aim of the study was to determine thyroid carcinoma incidence in Sibiu County depending on demographic and environmental factors. The study also reported a higher incidence in females and in urban population.

Catana et al. [22] attribute the increase in thyroid neoplasm to papillary and medullar forms while the

researchers observed a decrease in anaplastic form.

We can observe an increase in the number of research papers on this matter (Table I.), while there were only 2 papers published before 1996, after 2010 this number reached six, a fact that shows the preoccupation of professionals to define the role that the Chernobyl nuclear disaster related radiation plays in thyroid carcinoma incidence.

The question remains why there is this increase in incidence? Researchers conclude that while thyroid carcinoma incidence is most probably increasing due to better diagnostic techniques and standardized evaluation protocols, these could not be the only determining factors, radiation exposure due to the Chernobyl nuclear disaster should be considered. Further studies should be conducted.

The limitation we faced in writing our literature review was the quality and the lack of articles published on this matter. Another vulnerability of our article is the limitation present in all the articles included in our literature review, namely the dosimetry of <sup>131</sup>I contamination of Romania during the accident is estimative based on cesium deposits and may not represent reality.

### Conclusions

Thyroid neoplasm is the most frequent endocrine malignant tumor with a rapid increase in incidence in the last two decades. Also thyroid carcinogenesis is a long process which makes it difficult to study the determining and predisposing factors. Intrinsic along with extrinsic factors such as radiation, the evolution of diagnostic methods and protocols must be considered.

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