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Health Hazards from Chemical Substances and Ionizing Radiations

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Abstract

Chemical substances and ionizing radiation (IR) are known to probe the DNA-damaging effects and hence the risk of cancer can emerge. This small cohort study aimed to evaluate the lifetime fatal cancer risk (FCR) and non-fatal cancer risks (NCR) from IRs and compared them with the risks of other chemical substances (Nickel, Arsenic, Benzene & Asbestos) in nuclear medicine (NM) workers. The procedure for the FCR and NCR risk calculation was followed through the guidelines of ICRP and UNSCEAR using 'probability coefficient'. A high-capacity TLD reader was used to calculate whole-body AAED (annual average effective dose) (mSv). All occupational cancer risks were compared with the risks from other chemical substances through the Mann-Whitney U test. The FCRs were decreased from 7.854×10^{-4} to 3.836×10^{-4}, similarly, NCRs were also decreased from 1.57×10^{-4} to 7.672×10^{-4} in NM workers from 2015-2019. The fatal/non-fatal cancer risks from IR in INMOL hospital's NM workers were found considerably lower than the risks from other carcinogenic substances. Significant differences existed between the IR fatal/non-fatal cancer risks with the risk values of other chemical substances. The standard risk value (2.80×10^{-2}) of IR dose-effect can be used to compare the lifetime cancer risk from the other chemical substances in the occupational workers who are continuously being exposed to toxic substances occupationally.

Keywords: Ionizing Radiation (IR), Annual Average Effective Dose (AAED), Fatal and Non-Fatal Cancer Risks, Nickel, Asbestos, Benzene, Asbestos.

1. Introduction:

The relationship between tumor occurrence and carcinogens and chemicals has been studied for years and there is a need to develop sound quantitative dose-response models and methods to quantify the cancer risks [8]. Chemical substances and ionizing radiation (IR) are known to induce DNA-damaging agent, which is a great health hazard in the form of cancer. Nuclear medicine (NM) personnel is being continually exposed to chronic low-dose IRs from radioactive sources, radiopharmaceuticals (Tc-99m and I-131), and imaging modalities like single-photon emission computed tomography (SPECT) and positron emission tomography (PET). A cohort study of medical radiation workers deriving from the National Dose Registry of Canada (NDR) confirmed the association of higher incidence of thyroid cancer among medical workers who had professional exposure to ionizing radiation [1]. The current small cohort study assessed the lifetime fatal cancer risk (FCR) and non-fatal cancer risks (NCR) from ionizing radiations in nuclear medicine (NM)

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workers during 2015-2019. We also compared the IR risks with the risks of other chemical substances (Nickel, Arsenic, Benzene & Asbestos). The occupational NM workers were working in INMOL (Institute of Nuclear Medicine & Oncology) hospital and are chronically exposed to low-doses of occupational medical radiations. Today, various procedures in radiology, expose a large number of health professionals and technicians in medicine, dentistry, and veterinary medicine to the hazards of radiation while performing different procedures [2]. External exposure is from radioactivity in the working environment and internal exposure is from inhalation, ingestible or topical accidents of radionuclides. Workers in nuclear plants also get exposed to nuclear ionizing radiation [3-6]. For example, the element plutonium was of greatest concern at the Sellafield plant for occupational exposures [7].

We were keen to find out whether the cancer risks from the exposure of IR are greater than, less than, or have equal weightage from the risks of other chemical substances. There is a rising incidence of mesothelioma in the European male population from asbestos exposure. A high dose of chemical exposure is required to cause cancer, however, the cancer risks from persistent low dose exposure still need to ascertain [8-9]. A causal relationship with the exposure of asbestos has been linked to the risk of mesothelioma and other cancers [10]. The most hazardous agents known through various studies were sparingly soluble nickel compounds for causing lung cancers [11]. The chances of cancer increased if exposure to nickels was on the highest level [12-14]. Respiratory cancers occur in most nickel species, however, evidence of disease has only been documented for nickel sub-sulfide and nickel oxide [15]. More than 130 deaths have been reported from nickel workers during 1948-1956 [16]. Evidence of Benzene for causation of acute non-lymphocytic leukemia (ANLL) has been found with higher exposures of the personnel to benzene. Researchers have observed inconsistent results for the association of peak exposures of benzene and causation of ANLL. A little evidence of increasing standardized mortality ratio (SMR) has been observed for acute nonlymphocytic leukemia (ANLL), chronic lymphatic leukemia, and non-Hodgkin's lymphoma, and possibly non-lymphocytic leukemia with increasing low-level cumulative exposure to benzene [17]. The International Agency for Research on Cancer (IARC) has classified arsenic as a group 1 carcinogen as it is known to cause cancers in nearly any human organ [18]. Blackfoot disease, endemic in Taiwan, and liver cancers were observed and associated with higher consumption of high-arsenic artesian well water in females [19]. A peak exposure greater than 100 ppm to benzene is a predictor of the risk of lymphohematopoietic cancers [20].

2. Materials & Methods

2.1 Measurement of Annual Average Effective Dose (AAED):

A high-capacity TLD (Thermoluminescent dosimeter) reader (Harshaw model 8800) from Thermo-Scientific was used to calculate whole-body AAED (annual average effective dose) (mSv) in nuclear medicine staff from 2015-2019. The average employment history of working in this department for the workers was 15 years. The monitoring and management of the dosimetry were done in software RaDLab. The AAED doses with a maximum yearly allowable limit of 20 mSv were averaged over 5 consecutive years to calculate the risks.

2.2. Probability Coefficient and Lifetime Cancer Risks Calculations:

The procedure for the cancer risk calculation was followed through the guidelines of ICRP (Publication 60) and UNSCEAR [21-23]. The assessment of lifetime fatal and non-fatal cancer risks was done by using the 'probability coefficient' for stochastic effects by considering 35 years as a working lifetime limit. "The probability coefficient for fatal cancer risk (FCR) is 4.0×10^{-2} (detriment per Sv) and for non-fatal cancer risk (NCR) is 0.8×10^{-2} (detriment per Sv). The lifetime risk was calculated by multiplying the level of mean annual exposure by 35 years and by the coefficient 4.0×10^{-2}/Sv lifetime for fatal cancer risk and 0.8×10^{-2}/Sv for lifetime non-

fatal cancer risk" [21-23]. The average annual risk (AAR) was also calculated by taking 60 years of average life expectancy.

2.3. Comparison of Cancer Risks with other Risks from Carcinogens:

All risk values of FCR, NCR along with respective (average annual risk) AARs were compared with the combined lifetime occupational exposure (35 years) risks from other carcinogen substances (Nickel, Arsenic, Benzene & Asbestos) through a non-parametric Mann-Whitney U test. A p-value less than 0.050 was considered significant. In Mann-Whitney U, the following formula of z scoring is used if we use a normal approximation [24]:

$$z = \frac{U - \frac{n_x n_y}{2}}{\sqrt{\frac{n_x n_y (N+1)}{12}}}$$

Where, $U = \sum_{i=1}^{n} \sum_{j=1}^{m}$, $S(Xi, Yi)$; n_x = samples of observations in one group $\{x_1, x_2, \ldots x_n\}$; n_y = samples of observations in one group $\{y_1, y_2, \ldots y_n\}$ and $N = n_x + n_y$

The standard lifetime risks for these substances were calculated from their limit of average exposure values (AEV) along with their respective risk coefficients over the basis of 8 working hours, 240 days per year, over 35 years, as mentioned by [21-23].

2.4. Average Exposure Values (AEV) for Carcinogens:

Following AEVs were considered for Nickel, Arsenic, ionizing radiation (IR), Benzene and Asbestos: 1000 ($\mu g.m^{-3}$)/8 hours, 200 ($\mu g.m^{-3}$)/8 hours, 20 mSv/year, 16000 ($\mu g.m^{-3}$)/8 hours and 0.1 ($fibre.cm^{-3}$)$^{-1}$/8hours, respectively [21-23, 25-26].

2.5. Risk Coefficients:

Following risk coefficients were considered for Nickel, Arsenic, ionizing radiation (IR), Benzene and Asbestos: 4×10^{-4} ($\mu g.m^{-3}$)$^{-1}$, 1.5×10^{-3} ($\mu g.m^{-3}$)$^{-1}$, 4×10^{-2} $(Sv)^{-1}$, 6×10^{-6} ($\mu g.m^{-3}$)$^{-1}$ and 2×10^{-1} ($fibre.cm^{-3}$)$^{-1}$, respectively [21-23, 25-26].

3. Results and Discussion

3.1. AAEDs and Lifetime Cancer Risks:

A declining trend was observed in mean AAED values, i.e., from 0.561 - 0.274 (mSv), between the years 2015-2019. Fatal cancer risks (FCR) were decreased from 7.854×10^{-4} to 3.836×10^{-4}, similarly, non-fatal cancer risks (NCR) decreased from 1.57×10^{-4} to 7.672×10^{-4}, during 2015-2019 (**Table 1**). The mean values of all risks from IR during 2015-2019 were found fairly lower than the allowable maximum (20 ms) IR exposure's risk value, i.e., 2.80×10^{-2}.

Medical and nuclear industries make up the largest contribution to the exposed occupational groups. Medical professionals who conduct fluoroscopically-guided procedures and deal with the radionuclides for nuclear medicine-based treatments have a much higher radiation exposure than general workers in medicine [26]. A study confirmed the association of higher incidence of thyroid cancer among medical workers who had professional exposure to ionizing radiation [1]. Leuraud et al (2015) [26-27] had concluded a strong link between protracted low-dose exposure and resulting mortality from tumors like leukemia, lymphoma, and multiple myeloma in France, the UK, and the USA [27-28]. The workers of the Sellafield plant of British Nuclear Fuels reported a significant positive association between combined radiation doses and mortality from leukemia, multiple myeloma, all lymphatic and hematopoietic cancers. Breast cancers were also associated with plutonium exposure [29]. Valuckas et al (2007) [30] also determined the status of occupational exposure among medical radiation workers in Lithuania from 1991-2003. They concluded that the levels of radiation doses and cancer risk needs further examination and evaluation. A relative risk model has been applied to a study of 1669 workers of Mayak, who were exposed to plutonium between 1948 and 1958 [31]. A study from a Canadian cohort of 45468 persons with low-dose whole-body radiation exposure between 1957-1994 was carried out. The excess relative risks of leukemia and all solid cancers were 52.5 per Sievert [32]. We assessed the lifetime fatal cancer risk (FCR) and non-fatal cancer risks (NCR) from ionizing radiations in nuclear medicine (NM) workers who were exposed to low-dose IRs [0.088(min.) to 1.99(max.)] mSv during 2015-2019. We compared these calculated IR risks in NM

workers to the risks of other chemical substances (Nickel, Arsenic, Benzene & Asbestos). Our results are favorable in concluding that the lifetime fatal and non-fatal cancer risks were declining in nuclear medicine workers. INMOL hospital ensures the entire and required standard operating procedures (SOPs) for radiation protection. We have noticed that the lifetime fatal/non-fatal cancer risks from IRs of INMOL hospital's NM workers, were found considerably lower than the standard lifetime cancer risks from other chemical substances (Nickel, Arsenic, Benzene & Asbestos). We can always compare the risk values from the available standard IR risk value (i.e., 2.80×10^{-2} from the exposure of 20 mSv/year) based on the probability coefficient and the measurement of average dose exposed values in radiation workers. The standard IR risk coefficient i.e., (2.80×10^{-2}) was found in the middle of cancer risk values of mentioned other chemical substances. The IR standard risk coefficient may be for the indication and comparison of lifetime cancer risks from the other carcinogens. 50 years of applying preventive measures, resulted in a significant reduction in radiation exposure of medical workers in the low-level exposure to ionizing radiation. However, low-dose exposures of any type of carcinogen should not be ignored. Although, medical radiation exposure forms the largest contributor to the occupational and environmental sources of radiation [1, 27-28]. However, the risks from other carcinogenic substances should not also be underestimated for occupational workers.

3.2. Cancer Risks from Other Carcinogens (Comparisons):

The range of lifetime risks (for both FCR & NCR) is 4.33×10^{-2} to 0.2×10^{-2} for carcinogens: Nickel, Arsenic, Benzene & Asbestos. Table 2 shows the average exposure value (AEV), risk coefficients, and the calculations of fatal/non-fatal cancer risks in the case of other carcinogens. The mean of lifetime risk (all substances) was 0.02692±0.0124. For Nickel and Arsenic, the standard lifetime risks were greater than the risk from IR (2.80×10^{-2}, i.e., from the permissible limit: 20 mSv). Further, the substances Benzene and Asbestos showed lesser values of their standard lifetime risks as compared to the risk from IR (i.e., 2.80×10^{-2}). However, in all of our nuclear medicine workers', the fatal/non-fatal cancer risks (FCR & NCR) from the IRs, were found considerably lower than the standard lifetime cancer risks from other carcinogenic substances (Nickel, Arsenic, Benzene & Asbestos). The significant differences (p-value 0.015<0.050; Z score: -2.506) were found between IR risk values of following FCR, NCR, FCR-AAR & NCR-AAR, and the risk values of other carcinogen substances when compared through the Mann-Whitney U test. See Table 3.

Finland reported an increase in cancer incidence related to nickel exposure from copper/nickel smelters and nickel refineries [33]. Exposure of workers to insoluble nickel compounds caused a small increase in cancers over 20 years of exposure. Nasal, lung, and stomach cancers increased in refinery workers that had exposure to low levels of nickel sulfate or other nickel compounds. The study of Anttila et al 1998 however, could not rule out the relationship between gastric cancer and the working environment, it could be a chance finding. Based on various studies and quantitative estimates of lung cancer risk by the U.S. Environmental Protection Agency (EPA), Lippmann (1994) [34] concluded that it is the 10 ìm fibers that were responsible for the causation of Mesotheliomas. Stayner et al. (1996) performed a study on the relative risk of lung cancer to the length of fibers of chrysotile and its duration of exposure [35-36]. study with small numbers of persons exposed to benzene and polycyclic aromatic hydrocarbons (PAH) and occurrence of breast cancer was convincingly pointing towards their association [37]. Nickel, apart from its many uses in modern industry, has detrimental effects on humans. Its carcinogenic effects have been of major concern and interest to researchers, especially for lung cancers. Natural killer (NK) cell activity and other immune processes are suppressed by nickel, facilitating mutation and cancer. Nickel causes DNA damage again increasing mutational

tendencies. In Wales, the risk of lung cancer was observed in various prospective studies, especially in nickel refineries [38]. Lung and nasal cancer risks were calculated in workers of Clydach nickel refinery, South Wales. The risk of cancer was strongly related to the exposure of workers at the refinery to nickel near the 1920s and 1930s [39]. Asbestos is carcinogenic as proven in numerous studies and any level of asbestos exposure is hazardous for working personnel and this must be minimized [40]. A study by Taiwan also found that exposure to arsenic is linked to cancer risks [41].

4. Conclusions:

In nuclear medicine workers, the low-dose ionizing radiation lifetime cancer risks were found less than the risks from other carcinogens chemical substances. The standard IR risk coefficient value is also useful in comparing the lifetime cancer risks from other cancer-causing chemical substances (Nickel, Arsenic, Benzene & Asbestos). Such standard dose-effect indicators must be in use for a first-quick comparison in the occupational workers who are continuously being exposed to toxic substances during their duty.

5. Recommendation:

There is a diverse range of toxic exposures, there is a need to develop the ranking of risks from different toxic exposure in more, different occupational workers with more profound average exposure values. There should be more studies on the more exact quantifications of finding cancer risks from low-dose chronic ionizing radiations as well as from other chemical cancer-causing substances. We must present more detailed studies in which guidelines for the occupational health & safety of workers should be described.

Limitations:

This was a single-centered study. Not all chemical carcinogens were included for the comparison. The study only covered a 5-year trend for cancer risk.

The authors report no conflict of interest.

Table 1. Measurements of AAEDs (mSv) and Lifetime Fatal & Non-Fatal Cancer Risks in Nuclear Medicine Staff

Years	*No. of Workers*	*AAED (mSv) (Mean)*	*AAED (mSv) Min.*	*AAED (mSv) Max.*	*FCR*	*AAR- FCR*	*NCR*	*AAR- NCR*
2015	26	0.561±0.428	0.08	1.40	7.854×10^{-4}	1.309×10^{-5}	1.570×10^{-4}	2.618×10^{-6}
2016	27	0.457±0.472	0.09	1.99	6.398×10^{-4}	1.066×10^{-5}	1.279×10^{-4}	2.132×10^{-6}
2017	32	0.383±0.404	0.01	1.83	5.362×10^{-4}	8.936×10^{-6}	1.072×10^{-4}	1.787×10^{-6}
2018	34	0.336±0.381	0.01	1.58	4.704×10^{-4}	7.840×10^{-6}	9.408×10^{-5}	1.568×10^{-6}
2019	34	0.274±0.320	0.01	1.36	3.836×10^{-4}	6.393×10^{-6}	7.672×10^{-5}	1.278×10^{-6}

Key: AAED= Annual Average Effective Dose, FCR=Fatal Cancer Risk, AAR= Average Annual Risk, NCR= Non-Fatal Cancer Risk, mSv=Mili-Sievert

Table 2. Comparison of FCR and NCR with the Other Lifetime Risks from other Cancer Causing Substances

Substance/Source	AEV-Average Exposure Value (Exposure Limit) [21-23]	Risk Coefficient [21-23]	Lifetime Risk for Occupational Exposure Over 35y
Nickel (standard)	1000 $(\mu g.m^{-3})/8h$	4×10^{-4} $(\mu g.m^{-3})^{-1}$	4.33×10^{-2}
Arsenic (standard)	200 $(\mu g.m^{-3})/8h$	1.5×10^{-3} $(\mu g.m^{-3})^{-1}$	3.28×10^{-2}
Ionizing Radiation (IR)	20 (mSv/a)	4×10^{-2} $(Sv)^{-1}$	2.80×10^{-2} (Standard) Mean FCR (2015-2019): 0.00056308±0.000155 Mean NCR (2015-2019): 0.00011258±0.00003108
Benzene (standard)	16000 $(\mu g.m^{-3})/8h$	6×10^{-6} $(\mu g.m^{-3})^{-1}$	1.05×10^{-2}
Asbestos (standard)	0.1 $(fibre.cm^{-3})^{-1}/8h$	2×10^{-1} $(fibre.cm^{-3})^{-1}$	0.2×10^{-2}

Table 3. Mann-Whitney U Test (between IR risk values of following FCR, NCR, FCR-AAR & NCR-AAR, and the risk values of other carcinogen substances)

Variable	Mean IR Values (2015-2019)	Z-Score	p-value
IR FCR	0.00056308±0.000155	-2.411	0.0015 (significant)
IR AAR-FCR	0.00000938±0.00000259		
IR-NCR	0.00011258±0.00003108		
IR AAR-NCR	0.000001877±0.000000518		
Life Time Risk (All Substances)	0.02692±0.0124		

Key: IR= Ionizing Radiation, FCR=Fatal Cancer Risk, AAR= Average Annual Risk, NCR= Non-Fatal Cancer Risk

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