ASSESSMENT OF IMPACTS OF HEMATOLOGICAL PARAMETERS OF CHRONIC IONIZING RADIATION EXPOSED WORKERS IN HOSPITALS

SAMAN SHAHID1, NASIR MAHMOOD2, MUHAMMAD NAWAZ CHAUDHRY1, SHAHARYAR SHEIKH1 AND NAUMAN AHMAD1

1Department of Allied Health Science and Chemical Pathology, University of Health Sciences, Lahore, Pakistan.
2Department of Neurosurgery, Sheikh Zayed Hospital, Federal Postgraduate Medical Institute Lahore, Pakistan.

Abstract

This study examined the impact on hematological parameters for medical workers that work on ionizing radiation equipment. Comparison of mean values of CBC (complete blood count) parameters with the normal range and comparisons based on the T-tests between radiation exposed (RE) workers and radiation unexposed workers was done. Most of the parameters were below the normal range and were disturbed in majority of the RE workers. Most affected parameter was MCH (mean corpuscular hemoglobin) which was found to be lower in majority of radiotherapy workers. From T-test, statistically significant differences (p<0.05) were observed in the mean values MCHC (MCH concentration) and lymphocytes (LYM). A decline was observed in platelet-count, hematocrit and lymphocytes, whereas, an increase was observed in neutrophils in association with Annual average effective dose (AAED) (0.29-1.91) mSv. These associations were although weak but significant. Long term work on radiations at even low doses (<20 mSv) can impact health and results into an altered immune response or anemia.

Introduction

There is a worldwide concern about the use of ionization radiations (IR) in the medical field such as X rays, gamma (γ) rays and particles: α-particle, β-particle, protons and neutrons. Radiations are being extensively used in diagnosis as well as in therapeutic use for cancer patients. Therefore, the frequent use of machines by technicians such as X-ray diagnostic units as well as therapy units, CT-scans, PET (positron emission tomography), SPECT (single photon emission computed tomography), gamma cameras, brachytherapy units, 60Co teletherapy units, linear accelerators, dose calibrators, radioimmunoassay counters and different radiopharmaceuticals pose health risks to occupational workers (Jabeen et al., 2010; Masood et al., 2013). Ionization radiations influence human health as they break chemical bonds of the molecules and damage DNA by the production of free radicals and hence proliferative cells can undergo apoptosis (Vakifahmetoglu et al., 2008). Stem cells are found radiosensitive and their damage by radiations can result into non-performance of the functional cells. Long term exposure to even low doses of radiation can affect proliferating cells (Fliedner et al., 2012). Ionizing radiation exposure is sensitive for those tissues (i.e., bone marrow, the gastrointestinal tract and skin) which turnover rapidly as well as to those tissues (i.e., central nervous system, lung, heart, liver, kidney and gonads) which turnover slowly (Dainiak and Sorba, 1997). Hematopoietic system is one of the most radiosensitive systems because its functional cells transport oxygen in the blood, which prevent immune system against viruses, bacteria, etc. This system also provides blood coagulation to safe intact blood vessels (Smirnova, 2010). This study examines the impact of ionizing radiations (IR) on the complete blood count (CBC) parameters of hospital workers who work in radiotherapy (RT), radiology (RT) and nuclear medicine (NM) departments. This research provides a study on radiation induced hematopoietic system alterations for the hospital radiation exposed workers or technicians etc. for their health and safety measures concerns. It is known that bone marrow system is highly radiosensitive and analysis of hematopoietic system for such workers is highly emphasizing. Blood forming cells are located in bone-marrow and such cells are highly susceptible to radiation damage (Edwards, 1977). This study not only provides various comparisons of CBC parameters between radiation exposed workers with the control group (radiation unexposed workers) but also includes correlation analysis with the control variable that is, Annual Average Effective Dose (AAED) in mSv (millisievert: measure of radiation dose). Pakistan Nuclear Regulatory Authority (PNRA) follows International Atomic Energy Agency (IAEA) and International Committee on Radiological Protection (ICRP) guidelines on dose range limits for occupational radiation exposures (Jabeen et al., 2010). According to IAEA guidelines, the annual effective dose should be controlled below 20mSv for radiation workers. In Pakistan, a Radiation Dosimetry Laboratory (RDL) regularly monitors occupational exposure of all workers that the exposure may not exceed the recommended limits by PNRA by Film Badge dosimeters (FBD) service mostly and remaining by thermoluminescent dosimeters (TLD) (Jabeen et al., 2010).
Ionizing radiations (IR) can damage stem cells of hematopoietic system which is radiosensitive and as a result alteration in the production of bone marrow stromal cells is observed which are important to regulate this system. An exposure to IR can reduce bone marrow production where blood forming cells both immature and rapidly dividing cells locate. Dividing cells of the hematopoietic system are highly radiosensitive which divide rapidly and may show effects at even at low doses of long term ionizing radiations such as X-rays or γ-rays (Smirnova, 2010). For the last 30 years, the fluoroscopically guided interventional procedures have increased X-ray exposure. These occupational health concerns are quite important to the cardiologists, radiologists, surgeons and other technicians working with the fluoroscopy techniques (Klein, 2009). Several studies suggest that chronic exposure of low-dose radiation has a genotoxic effect on somatic DNA of professionally exposed workers as well. A few studies focus on interventional cardiologists who work in cardiac catheterization laboratories and are exposed to low doses of ionizing radiation (Andreassi et. al., 2005; Roguin et. al., 2012; Venneri et. al., 2009).

There were 92 radiation workers in this research who were working in different radiation departments (diagnostic or therapeutical) and were exposed to x-rays or γ rays in the range of Annual Average Effective Dose (AAED) 0.29-1.91 mSv. This study focus on those workers’ hematology through complete blood count (CBC) test, who are being long-term exposed (although low dose) from radiation machines such as X-ray machines or linac (linear accelerator). Health hazards from acute radiation dose impacts of radiations are although, well documented but there is a little concern and unawareness in such workers related to the impacts of chronic low-dose regular or periodic radiation exposure. Therefore, this research will be beneficial to initiate awareness among occupational ionizing radiation workers and further to mitigate the effects.

Materials and Methods

Blood Sample Collection and Background Information: Blood samples (1-ml from each individual) of 147 non-smoker individuals were collected by taking volunteers and informed consents from radiation exposed (RE) workers (n=92) and control group (n=55) who were radiation unexposed (RU) workers. The control group individuals were not found to be exposed from any type of artificial or ionizing natural radiations. Blood was collected in CBC vials and sent for a CBC test soon after its collection. Information regarding age, sex, duration of radiation exposure, dietary habits and occupation was taken on a designated Performa. All individuals were in having balanced food intake with non-alcoholic habits.

CBC (Complete Blood Count) Test: The collected blood was mixed well and inserted into the following machines: Abacus+ and Medonic and CBC parameters were analyzed. Nine CBC parameters were considered for this study and these were: hemoglobin (HB in g/L), white blood cells (WBC in $10^9$/L), platelet count (PLT in $10^9$/L), hematocrit (HCT in %), red blood cells (RBC in $10^12$/L), mean corpuscular hemoglobin (MCH in g/L), mean corpuscular hemoglobin concentration (MCHC in %), lymphocytes (LYM in %) and neutrophils (NEUT in %) were analyzed in all groups.

Statistical Analysis & Calculations: All statistical calculations were performed in software SPSS-21. All of nine CBC parameters’ mean values and mean values of those CBC parameters which were either below the normal range or above the normal range, were calculated for all groups, i.e., for RT (radiotherapy) workers (n=20), RD (radiology) workers (n = 41), NM (nuclear medicine) workers (n = 31) and RU (radiation unexposed) workers (n = 55). A T test (independent samples test) was conducted on the mean values of all nine CBC parameters to analyze those parameters which show significant difference between all radiation exposed (RE) workers (n = 92) and radiation unexposed (RU) workers (n = 55). Another T- test (independent samples test) was conducted on those CBC parameters which were either in below or above with the normal range between all radiation exposed workers (RE) i.e., from three different departments, i.e., radiotherapy, radiology and nuclear medicine workers (total n = 92) and radiation unexposed (RU) workers (n = 55).

In Pakistan, annual average effective dose (AAED) range was recorded between 1.39-1.80 (mSv) for the nuclear medicine department, 1.22-1.71 (mSv) for radiology department and 1.05 -1.45 (mSv) for radiotherapy department during 2003-2007 (Jabeen et al., 2010) and AAED ranges were between 0.51-1.91 (mSv) for the nuclear medicine department, 0.29-0.80 (mSv) for radiology department and 0.50-1.72 (mSv) for radiotherapy department during 2002-2011 (Masood et al., 2013). The range of the duration of radiation exposure among radiation workers was between 05-25 years during of the employment history. The AAED range 0.29-1.91 (mSv) was considered for the statistical analysis in this study. A Bivariate correlation analysis was conducted to see the correlation between CBC parameters with an independent variable, i.e., AAED (mSv) for all radiation exposed (RE) workers (n = 92). The r-values (Pearson coefficients) were obtained and analyzed to observe the strength and direction (±) of the correlation between a respective significant CBC parameter and AAED (mSv) as a control variable. The p-values obtained were checked for significance or non-significance of a CBC parameter with the variable i.e., AAED (mSv).
Further, Linear Regression analyses were performed and R-square (coefficient of determination) values were observed for the analysis of the proportion of variance in the dependent variables (CBC parameters) which can be subjected to be predictable from the independent variable AAED (mSv). The Linear Regression analyses were performed for variable AAED (mSv) to predict CBC parameters’ change. The measure of strength of CBC parameter’s association was analyzed with an independent variable AAED (mSv) to analyze R (square) values, model’s coefficients, t-test values and p-values in order to handle the estimation of an affected CBC parameter which was significant in correlation with independent variable AAED (mSv). Finally, regression equations were developed between independent variable AAED (mSv) and the respective dependent variable i.e., a specific CBC parameter. Regression equations mentioned in scatter plots figures accordingly. Odds ratios were calculated to find out the association of measure between radiation exposure and having an altered (low or high) CBC parameter. Pearson chi-square test used to evaluate significance of a respective parameter through p-value (p < α = 0.05).

Results

**Analysis of Background Information**: Background information for all individuals included in this study has been presented in Table 1. Among all RT workers (n = 20), most of the workers were male (80%) and mostly (50%) were from the age group (26-50 years). Among all RD workers (n = 41), most of the workers were male (80.4%) and mostly (68%) were from the age group (26-50 years). Among all NM workers (n = 31), most of the workers were male (77.4%) and mostly (67.7%) were from the age group (26-50 years). In the category of radiation unexposed workers (n = 55) most of the individuals were male (62%) and mostly (62%) were from the age group (26-50 years). Radiation unexposed workers were from miscellaneous profession, for example, office workers, teachers, physicians, etc. All radiation exposed workers and radiation unexposed workers included were from Lahore city.

<p>| Table 1. Background Information for Radiation Exposed (RE) Workers and Radiation Unexposed (RU) Workers |</p>
<table>
<thead>
<tr>
<th>Parameters</th>
<th>Occupationally Radiation Exposed (RE) Workers (n=92)</th>
<th>Radiation Unexposed (RU) Workers (n=55)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Radiotherapy (n=20)</td>
<td>PP* %</td>
</tr>
<tr>
<td>18-25</td>
<td>3</td>
<td>15</td>
</tr>
<tr>
<td>26-50</td>
<td>10</td>
<td>50</td>
</tr>
<tr>
<td>51 &amp; above</td>
<td>7</td>
<td>35</td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
<td>16</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>4</td>
</tr>
</tbody>
</table>

*PP: Percentage Prevalence

**Hematological Profiles:**

Comparison of Mean Values of CBC Parameters with the Normal Range:

Table 2, shows nine CBC parameters’ mean values (indicated “total”), mean values of those CBC parameters which were below the normal range (indicated “low”) and mean values of those CBC parameters which were above the normal range (indicated “high”) of all four groups of individuals that is, RD workers, RT workers, NM workers and RU workers. This Table (2) is explained on the basis of Table 3 in which percentages of the all individuals have been mentioned who were having their one or more CBC parameter(s) in either low or high range when compared with the normal range mentioned in Table 2.

Most affected CBC parameter was MCH, which was found in the lower range (mean=25.87) in 60% of the radiotherapy workers when compared with RD and NM departments as well as with the RU workers. The second most affected CBC parameter was MCHC which was found in the lower range (mean=30.22) in 50% of the radiotherapy workers when compared with RD and NM departments as well as with the RU workers. The third most affected CBC parameter was LYM which was found in higher range (mean=49.43) in 39% of the radiology workers when compared with RT and NM departments as well as with the RU workers. Overall in all, 40.2% of all (n = 92) RE workers two CBC parameters were more affected in lower range, i.e., MCH.
(mean=24.99) and MCHC (mean=30.57) as compared to the controls the RU workers. It can also be observed from the column labeled “total” in Table 2 that collective mean values of all CBC parameters are within the normal range but there is a little shift towards lower range in the CBC parameter MCH (mean=27.21 for RT, mean=27.87 for RD and mean=27.84 for NM) in all three department’s workers whereas, and MCHC is also on a slight lower range (mean=31.87) for RT workers only.

Table 2. Mean values of complete blood count (CBC) for radiation exposed (RE) workers and radiation unexposed (RU) workers. Column labeled as “low” shows mean of CBC parameter below normal range, column labeled as “high” shows mean of CBC parameter above normal range and column labeled as “total” shows mean of CBC parameter of each individual. The number in the parenthesis describes the number of individuals whose CBC parameters were found disturbed (low or high).

Table 3. Number of workers expressed in percentages whose CBC parameters were either in low range/high range.

Key (Tables 2 and 3): HB: Hemoglobin, WBC: White Blood Cells, PLT: Platelet Count, HCT: Hematocrit,

RBC: Red Blood Cells, MCH: Mean Corpuscular Hemoglobin, MCHC: MCH Concentration, LYM: Lymphocytes, NEUT: Neutrophils
Table 4. T test analysis of significantly different mean CBC values between radiations exposed (RE) workers and radiation unexposed (RU) workers.

<table>
<thead>
<tr>
<th>Blood Parameters</th>
<th>t-test for Equality of Means</th>
<th>95% Confidence Interval of the Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>t</td>
<td>p-value (&lt; 0.050)</td>
</tr>
<tr>
<td>MCHC</td>
<td>-4.688</td>
<td>0.000</td>
</tr>
<tr>
<td>LYM</td>
<td>2.238</td>
<td>0.027</td>
</tr>
<tr>
<td>LYM (high)</td>
<td>2.943</td>
<td>0.005</td>
</tr>
</tbody>
</table>

Table 5. Correlation analysis between Annual Average Exposed Dose AAED (mSv) with CBC parameters in radiation exposed (RE) workers.

<table>
<thead>
<tr>
<th>mSv</th>
<th>PLT Pearson Correlation</th>
<th>HCT Pearson Correlation</th>
<th>LYM Pearson Correlation</th>
<th>NEUT Pearson Correlation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>p-value (&lt;0.050)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.021</td>
<td>0.024</td>
<td>0.026</td>
<td>0.014</td>
</tr>
</tbody>
</table>

* Correlation is significant at the 0.05 level (2-tailed).

Table 6. Risk Estimate and Chi-Square Tests

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Odds Ratio for Exposed Workers</th>
<th>95% Confidence Interval (CI)</th>
<th>Pearson Chi-Square</th>
<th>df</th>
<th>p-value (&lt;0.05)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MCHC (low)</td>
<td>6.842</td>
<td>2.488</td>
<td>18.811</td>
<td>16.574</td>
<td>1</td>
</tr>
<tr>
<td>NEUT (low)</td>
<td>9.692</td>
<td>1.238</td>
<td>75.910</td>
<td>6.745</td>
<td>1</td>
</tr>
<tr>
<td>ANC (low)</td>
<td>6.897</td>
<td>1.540</td>
<td>30.891</td>
<td>8.139</td>
<td>1</td>
</tr>
</tbody>
</table>

*df: degree of freedom

Most of the radiation exposed (n = 92) workers (9.8%) had low HB (mean=10.35) as compared to RU workers (0%). Most of RE workers (5.4%) had low WBC (mean=2.7) as compared to RU workers (0%). Most of RE workers (11%) had low PLT (mean=108.9) as compared to RU workers (7.3%). Most of RE workers (8.7%) had low HCT (mean=30.13) as compared to RU workers (5.5%). Most of RE workers (16.3%) had high RBC (mean=5.96) as compared to RU workers (9.1%). Most of RE workers (40.2%) had low MCH (mean=24.99) as compared to RU workers (29.1%). Most of RE workers (40.2%) had low MCHC (mean=30.57) as compared to RU workers (9.1%). Most of RE workers (32.6%) had high LYM (mean=49.66) as compared to RU workers (20%).

Overall, seven CBC parameters: HB, WBC, PLT, HCT, MCH, MCHC and NEUT were in the lower range of radiation exposed (RE) workers and two CBC parameters RBC and LYM are in high range as compared with the mean values CBC of non-radiation exposed (RU) workers. It is observed of course, that majority of RE workers had their CBC parameters affected because of the long term use of radiation works in the hospitals.

CBC Parameters Related to Intradepartmental Comparisons between Radiotherapy, Radiology and Nuclear Medicine Workers

Results from both Tables 2 and 3 indicated that the majority of RD, RT and NM workers had their CBC parameters were in the low range. Most of the RT workers (20%) had low HB (mean= 10) as compared to RD workers (7.3%) and NM workers (6.5%). Most of RD workers (9.8%) had low WBC (mean=2.46) as compared to RT workers (5%) and NM workers (0%). Most of the RD workers (17.1%) had low PLT (mean=106.4) as compared to RT workers (15%) and NM workers (0%). Most of RT workers (15%) had low HCT (mean=31.6) as compared to RD workers (7.3%) and NM workers (6.5%). Most of the RD workers (19.5%) had high RBC (mean=6.13) as compared to RT workers (5%) and NM workers (19.4%). Most of the RT workers (60%) had low MCH (mean=25.87) as compared to RD workers (31.7%) and NM workers (38.7%). Most of the RT workers (50%) had low MCHC (mean=30.22) as compared to RD workers (41.5%) and NM workers (32.3%).
Most of the RD workers (39%) had high LYM (mean=49.43) as compared to RT workers (5%) and NM workers (16.1%). Most of the RT workers (25%) had low NEUT (mean=28.16) as compared to RD workers (17.1%) and NM workers (6.5%).

Overall, in both radiology and radiotherapy personnel most of the CBC parameters had been affected as compared to nuclear medicine department personnel. In the majority of radiotherapy (RT) workers, following five CBC parameters were found in lower range: HB, HCT, MCH, MCHC and NEUT. While in majority of radiology (RD) workers following two CBC parameters were found in lower range: WBC and PLT and two CBC parameters were in higher range: RBC and LYM. It can be concluded that blood parameters had been more altered in radiotherapy and radiology workers as compared to nuclear medicine workers. Moreover, majority of CBC parameters were either low or high for the RT, RD and NM workers as compared to RU workers.

**Comparisons based on the T tests Between Radiation Exposed (RE) Workers and Radiation Unexposed (RU) Workers**

Comparisons based on the T test (Table 4) were conducted to find out those CBC parameters which show the significance of difference between radiation exposed (RE) personnel (n = 92) and radiation unexposed (RU) personnel (n = 55). The descriptive of T test shows that significant differences were existed in the mean values of CBC parameters: MCHC, and LYM between those who were exposed to radiation (n=92) and those who were not exposed to radiation (n = 55). The results of this T test indicated that the difference between the mean scores of those exposed to radiation and those not exposed to radiation for MCHC is $t = -4.688$ standard deviation units (95% CI: -1.79 to -0.73; p trend: 0.000 < α; α=0.05) and for LYM is $t = 2.238$ standard deviation units (95% CI: 0.38 to 6.15; p trend: 0.027 < α; α=0.05). Whereas, another T test shows that significant differences existed in the mean high values of the LYM between those who were exposed to radiation (n = 92) and those who were not exposed to radiation (n=55). The results of this second T-test indicated that the difference between the mean scores of those exposed to radiation and those not exposed to radiation for mean high values of LYM is at $t=2.943$ standard units (95% CI: 1.99 to 10.77; p trend: 0.005 < α; α = 0.05).

**Correlation Analysis between Annual Average Exposed Dose (AAED) and CBC Parameters**

Correlation analyses were performed for the CBC parameters to see the strength of the association with AAED (mSv) as a control variable. Table 5 showed that the correlation is significant at $p < \alpha$ (α = 0.05) for following four CBC parameters: PLT ($p = 0.021 < \alpha$), HCT ($p = 0.024 < \alpha$), LYM ($p = 0.026 < \alpha$) and NEUT ($p = 0.014 < \alpha$) with the Annual Average Effect Dose (AAED) overall range 0.29-1.91 (mSv) for all three departments: radiotherapy (RT), radiology (RD) and nuclear medicine (NM) during the years 2003-2011. It is observed that following three significant CBC parameters, i.e., PLT ($r = -0.240$), HCT ($r = -0.235$) and LYM ($r = -0.232$) were having weak negative relationships with Annual Average Effective Dose (AAED) in mSv. Whereas, parameters NEUT ($r = +0.254$) was having a weak positive relationship with Annual Average Effect Dose (AAED) in mSv.

**Regression Analysis:** Four regression models were developed and scatter plots were generated (Figs. 1-4) in order to estimate the effect of an independent variable AAED (mSv) on respective four CBC parameters (PLT, HCT, LYM and NEUT) which were significant for both in male and female workers’ samples in correlation analysis (as dependent variables). Regression analysis indicated that 5.8% of variance (R-square=0.058) in PLT, 5.5% (R-square=0.055) in HCT, 5.4% (R-square=0.054) in LYM and 6.5% (R-square=0.065) in NEUT can be predicted from the variable AAED (mSv). It is now concluded that for every unit increase in AAED (mSv), there is -37.774 unit decrease in PLT, -2.401 unit decrease in HCT, and -5.129 unit decrease in LYM is predicted. Whereas, NEUT is found to be higher by 7.181 points for every increase of one point on the variable AAED (mSv). In all these analyses, variable AAED (mSv) is found to be different than zero ($p < \alpha = 0.05$).

**Odds Ratio and Pearson Chi-Square Test:** Odds ratios were calculated to find out the association of measure between radiation exposure and having an altered (low or high) CBC parameter. The odds of developing low MCHC were 6.84 times higher, the odds of developing low NEUT were 9.69 times higher and the odds of developing a low ANC were 6.89 times higher for those who were radiation exposed compared to those who were not exposed to occupational radiations. Only parameters, i.e., MCHC (low), NEUT (low) and ANC (low) were found significant at $p < \alpha = 0.050$ (Table 6).
Fig. 1. Scatter plot: PLT vs. AAED (mSv) = x
Model equation: PLT= y = 281.266 + (-37.774) x
R=0.240, R Square= 0.058 (p-value<0.05), N=92
(PLT: platelet count; AAED: annual average effective dose; mSv millisievert)

Fig. 2. Scatter plot: HCT vs. AAED (mSv) = x
Model equation: HCT = y = 44.929 + (-2.401) x
R=0.235, R Square=0.055 (p-value<0.05), N=92
(HCT: hematocrit; AAED: annual average effective dose; mSv millisievert)
Discussion

It is well known that dividing cells of the hematopoietic system are highly radiosensitive (Smirnova, 2010). Role of the functional cells of the lymphopoiesis and granulocytopoiesis system is very important for immune protection against infections. Thrombocytopoiesis is one of the most radiosensitive hematopoietic cell lines in humans. Radiation injury or damage of hematopoiesis system can lead to hemorrhage and anemia (Smirnova,
2010). However, these alterations are dependent on an effective radiation dose range and exposure time (Ismail and Faafar, 2011). It is found in this study that radiation exposed (RE) workers’ CBC parameters had been more altered as compared to the control group i.e., radiation unexposed (RU) workers. Erythropoietic system produces mature erythrocytes for the circulation. There is a swift proliferation of the two immature forms of erythropoietic system, i.e., erythroblast and basophilic proerythroblasts and they found to be more sensitive as compared to other immature forms, i.e., polychromatic erythroblast, normoblast and reticulocytes and therefore, as a result cell apoptosis can be occurred by Radiations (NATO handbook, 1996). Myelopoietic marrow cell renewal system produces mature granulocytes i.e., neutrophils, eosinophils, and basophiles, for the circulating blood. Neutrophils have an important role in preventing infections. Stems cells and those cells which are found in developing phases, i.e., dividing and differentiating are more radiosensitive. That’s why, myeloblast, progranulocytes and myelocyte stages are more radiosensitive as compared to the other immature forms i.e., metamyelocyte and band forms. Thrombopoietic cell renewal produces platelets, which are produced by megakaryocytes in the bone marrow in the peripheral circulating blood. Platelets and mature megakaryocytes are relatively radioreistant but the stem cells and immature megakaryocytic stage is very radiosensitive and they can be declined by higher doses of ionizing radiations (NATO handbook, 1996).

Table 3 indicate percentage of those individuals which were having either lower or higher values of their respective CBC parameter compared to the normal range. Overall, there were four most affected CBC parameters, i.e., most affected CBC parameter was only MCH, which was found low in majority of RT workers (60%), the second most affected parameter was MCHC which was found low in majority of RT workers (50%), third most affected parameter was LYM which was found high in majority of RD workers (39%). It indicates that overall, radiotherapy workers were more affected for CBC parameters MCH and MCHC probably because of the extensive use of gamma rays and energetic particles for therapeutic purposes for patients. These personnel can be accidentally exposed to the radiations from linac-based radiotherapy machines. This may happen if the worker receives primary beam radiations or this could be the secondary beam from patient scatter-radiations (Fondevila, 2009). Radiation induced anemia is due to the hemolysis of red blood cells, called hemolytic-anemia (NATO handbook, 1996). This suggested that the Impact of IR is significant as evidenced by a reduction in the MCH, MCHC and an increase of LYM. The radiation causes anemia in the radiation workers due to apoptosis at the stem cell level within the bone marrow. The stem cells are precursors to all blood cell lines and hence a reduction can be noted in the number of cells getting to mature. As a result of hypoxia, the bone marrow gets stimulation for the production of the red blood cells. It is evident that hematopoietic system is the most sensitive of radiation and cells which divide rapidly or are relatively non-specialized may incline to show effects at lower doses of radiation (Jefferson Lab, 2012). Lower doses of occupational ionizing radiations are found to influence the hematopoietic system in exposed workers and among the other radioreistant mature forms, lymphocytes are found most radiosensitive (Edwards, 1977).

Table 2 has two columns labeled “low” and “high” for each group which define CBC parameters’ mean values which were in low range or in high range as compared to the normal range. Whereas, Table 3 has two columns “low%” and “high%” to mention percentage of the individuals who were having low values or high values of their respective CBC parameter compared to the normal range. Findings from such “low” and “high” indicated for the comparison between total RE workers (n=92) and RU workers (n=55) that most of the CBC parameters i.e., HB, WBC, PLT, HCT, MCH, MCHC & NEUT were found low in majority of RE workers whereas, RBC and LYM were found high in majority of RE workers as compared to RU workers. That is, most of the CBC parameters have been affected by the radiations and mostly were found in the lower range. Ionizing radiations (IR) can damage, stem cells of the hematopoietic system and as a result can alter the production of bone marrow stromal elements which are important to maintain this system. An exposure to IR can reduce bone marrow production where blood forming cells, both immature and rapidly dividing cells located. Therefore IR induces a decline in circulating hematopoietic cells and further redistribution and apoptosis (programmed cell death) of mature cells of the blood can be occurred. Mature blood cells from the bone marrow are transported out of the bone marrow in order to enter into the blood stream and hence they perform their respective functions. Such cells are resistant to ionizing radiation, but their precursor cells (the pluripotent stem cells) are quite susceptible to radiations. Stimuli like hypoxia because of IR, causes a release of erythropoietin from kidney leading to RBC production. Furthermore, the stimulus to the bone marrow causes higher production of the red blood cells. The retic count increased after IR as a result of compensatory mechanism started in the bone marrow. MCHC is not increased because of hemolysis of RBCs as a result of radiations. The cell counts increase, but MCHC does not increase correspondingly. Ionizing radiations cause apoptosis in the homeopathic stem cells, which consider precursors to all blood cells and hence there could be a hampering in the provision of mature cells into the blood stream and then there would be a development of plenty of immature cells in the bone marrow (Dainiak, 2002). A study by Caciari et al., (2012) indicating that the mean of total white blood cell were significantly decreased in exposed workers as compared to the controls.

The lymphocytes have been found to be the most radiosensitive cells (IAEA, 1997). At low doses, ionizing radiation can affect the immune system by suppressing it or stimulating it whereas; relatively higher doses of
radiation can suppress immune responses because of the destruction of cells (UNSCEAR, 2012; IAEA, 2011). It was reported that T-lymphocytes were affected to the individuals who were exposed to ionizing radiation and hence altered immune response was reported (Godekmerdan et al., 2004). The immune system has an important role in fighting with the cancerous disease and radiations can increase or decrease this system which can lead to the cancer development. Leukocytes are among the most sensitive lymphocytes to ionizing radiation and hence radiations can lower white blood cells and platelets and, as a result, there would be a lowered immunity to viruses or bacteria. Because lymphocytes are highly radiosensitive and therefore immune system is susceptible to ionizing radiations (UNSCEAR, 2012; Godekmerdan et al., 2004). In a study it was found that the subgroups of peripheral blood lymphocytes were affected for those who were operating X-ray machines for a long time (Godekmerdan et al., 2004; Hrycek et al., 2002). Level of CD4+ T lymphocytes in this exposed group was significantly lower than in the control group (Hrycek et al., 2002). Therefore, it can be concluded that ionizing radiation can modulate the immune system response.

Intradepartmental comparisons, i.e., between RT, RD and NM revealed that workers of both RD and RT departments had more CBC parameters affected as compared to NM department workers. In RT workers, five CBC parameters, i.e., HB, HCT, MCH, MCHC and NEUT were in the lower range as compared to RD and NM workers. Whereas, in RD workers, four CBC parameters were affected, i.e., WBC and PLT were in the low range and LYM and RBC were in the higher range as compared to NM and RT workers. It means both RT and RD workers had more CBC parameters affected as compared to NM workers. Therefore, it can be stated that both RT and RD workers are more affected in their CBCs as compared to NM workers. It is known that radiation workers are prone to significantly alter their blood parameters and they can be further suffered from leukopenia, anemia or leukemia (Edwards, 1977). Moreover, a long term exposure to the radiations for medical workers indicated that they may have effects on their immune system (Oskouii et al., 2013). Finding of the T test indicated that two mean values of following CBC parameters: MCHC and LYM were found significantly in their difference between total RE workers (n=92) and RU workers (n=55) among mean values of the all remaining CBC parameters. A second T test was conducted between all CBC parameters’ mean low values and mean high values between RE workers (n=92) and RU workers (n=55). Finding of the second T test indicated that mean of high values of LYM was found significant in their difference among total RE workers (n=92) and RU workers (n=55). LYM (high) explained that as a result of IR, the compensatory mechanism has started in the bone marrow to cover the reduced number of lymphocytes.

Correlation analysis showed that the following four significant at \( p < \alpha \) (\( \alpha = 0.05 \)) CBC parameters, i.e., PLT, HCT and LYM had weak negative associations with AAED (mSv) whereas two significant at \( p < \alpha \) (\( \alpha = 0.05 \)) CBC parameter NEUT had a weak positive association with AAED (mSv). All other CBC parameters were not found significant in correlation with AAED (mSv) and therefore not included in correlation associations. This suggested that, PLT, HCT and LYM may decline with the annual average dose of exposure ranging 0.29-1.91 (mSv). These parameters, though weak, but were found significant in association with AAED (mSv). Rotations can decrease granulocytes, lymphocytes, and platelets, due to decline in hematopoietic stem and progenitor cells and hence there would be a delayed re-population and individuals can be vulnerable to infections (NATO handbook, 1996; Dainiak, 2002). Moreover, radiation-induced apoptosis and redistribution of lymphocytes would be occurred from the circulation of the lymph-nodes as they're highly radiosensitive cells found in the capillary bed (Dainiak, 2002).

It has been observed that long term use of ionizing radiations of radiation workers can affect their immune system even at low doses of radiations as leukocytes and lymphocytes are highly radiosensitive (UNSCEAR, 2012; Gridley et al., 2002; Kluciński et al., 2005). Granulocytes may show an initial increase (i.e., granulocytosis: demargination of granulocytes) before they deplete and there would a gradual decline in the HCT and red cell count occurs after the exposure of moderate doses (Dainiak, 2002; Storer, 1966). A decline in HCT (hematocrit) and increase in neutrophils are indicated by correlation analysis with the radiation dose range 0.29-0.91 (mSv) in our study. It is known that ionizing radiation affects bone marrow and lymphocytes can decline along with a temporary sharp increase in granulocytes (Division of Environmental Health, A Fact Sheet). This suggests that radiations can disturb immunity of those workers who are long term exposed to low doses of ionizing radiation (Zykovová et al., 1984; Soldatov and Ushakov, 1995). Because white blood cells, lymphocytes are the most sensitive to X-ray radiations therefore, lymphopenia can be happen depends on the absorbed dose (Anderson and Warner, 1976). It was reported in some studies, that lymphocytes of radiation workers were slightly lower than the control group although the difference was not statistically significant. Radiological workers were found under the influence of the gradual decline of neutrophils, leukopenia and lymphopenia; due to the modulations or alterations in leukocytes (Hrycek and Stieber, 1994; Klajnowicz, et al., 1998). Another investigation also indicated that the absolute number of peripheral blood lymphocytes was slightly lower than for radiology department workers as compared to the control group but there was no statistical significance found (Hrycek et al., 2002). Regression models were developed and scatter plots were generated for four significant CBC parameters found in correlation with AAED (mSv) in order to estimate the effects of an independent variable AAED (mSv) on respective significant CBC parameter as the dependent
variable. It was discovered in this study, that the odds of developing low MCHC were 6.84 times higher and the odds of developing low NEUT were 9.69 times higher for those who were radiation exposed compared to those who were not exposed to occupational radiations. It has been discussed that the decreased number of circulating lymphocytes and granulocytes by radiations can lead to infections and long term work on radiations can induce anemia. Therefore, long-term damage caused by IR can induce various hematological diseases etc. (Andreassi et. al., 2005; Roguin et. al., 2012; Venneri et. al., 2009).

Conclusion

Hematopoietic system is found to be sensitive for radiation workers because mostly CBC parameters were observed suppressed, however a weak (though significant) association has been linked with the AAED (0.29-1.91 mSv). Changes in blood parameters have been noted. Although these workers were working under <20mSv of radiation doses, this may lead that long term use of radiations can show harmful effects on blood parameters. Significant differences were found with the parameters: MCHC and I.YM by the T-test. Radiotherapy and radiology workers were more affected than nuclear medicine workers. The corresponding safety measures should be kept in mind for such workers saving the workers from any accidental exposure. Furthermore, regular checkups of radiation workers and effective monitoring of all blood parameters should be under taken in order to diagnose an early change in their entire health. The long-term impacts of low ionizing radiation doses on the immune functions in relation to human health should be evaluated. It has been discussed that the decreased number of circulating lymphocytes and granulocytes by radiations can lead to infections and long term work on radiations can induce anemia.

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