PATH ANALYSIS : PUBLIC HEALTH IMPACTS OVERVIEW IN HIGH NATURAL BACKGROUND RADIATION AREA IN BOTTENG, WEST SULAWESI OF INDONESIA

by Elanda Fikri

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Abstract

Introduction: The effect of ionizing radiation exposure in a human being is chromosome aberrations. Botteng has the highest annual radiation exposure rate in Indonesia, which is 6.15 ± 0.81 mSv/year. The people in Botteng were exposed to the low dose radiation, continuously. The purpose of this research is to describe the pathway radiation exposure to inhabitants and the cytogenetic response in the high natural background radiation area

Methods : This is statistical research by cross-sectional. The population is 61 residents, who were chosen randomly from 9 different exposure rate areas. The path analysis model is used to determine the linear relationship between internal and external radiation dose to the frequency of chromosomal aberrations in lymphocyte cells.

Results: The results concluded that the external radiation dose rate is 5.49 mSv / year, the internal radiation dose rate is 10.34 mSv / year, the effective dose rate of lymphocyte cells is 1.92 mSv / year, and the mean of chromosome aberrations frequency is 0.00082 of approximately 14.695 metaphase cells observed. The result of the analysis showed that there was no significant correlation between the external dose and the chromosome aberrations frequency. There is a linear relationship between the internal dose and the chromosome aberrations frequency (f count = 6.634 and p-value 0.013 <0.05). The internal and external radiation dose simultaneously affects the effective dose (R2 = 0.901, p-value = 0.000> 0.05), The Internal and external radiation doses affect the chromosome aberrations frequency of peripheral blood lymphocytes only through effective doses (R2 = 0.093, p-value = 0.017> 0.05).

Conclusion: This study provide an effective recommendation for further research as an effort to improve public health in areas with high natural background radiation.

Keywords: chromosome aberrations frequency, high natural background radiation, radioecology, public health, radioadaptive response

Introduction

Exposure of ionizing radiation sources from nature [6] humans occurs continuously and is inevitable for every living being on Earth. The estimated average annual exposure from natural background radiation sources is 2.4 mSv with a range of 1-10 mSv/year. The natural background radiation sources in question consist of external exposure from cosmic radiation (0.4 mSv/year) and terrestrial gamma radiation (0.5 mSv/year), as well as internal exposure, namely inhalation (1.3 mSv/year, especially Radon) and ingestion (0.3 mSv/year[14].

Exposure to ionizing radiation comes from cosmic rays and radionuclides in soil, indoor and outdoor air, water, food chain, and so on leads to chronic exposure originating from external and internal radiation. Those chronic exposures resulted in an annual effective dose for the inhabitants. An area with several chronic exposures that causes inhabitants' effective dose to be above the specified level is known as High Natural Background Radiation (HNBR) areas[2].

The average data of environmental gamma radiation dose rate in Indonesia is 68 nSv/hour. Areas with a dose rate above the average rate were North Sumatra 186.08 ± 3.72 nSv/hour, West Kalimantan 349.48 ± 57.21 nSv/hour, and West Sulawesi 487±103 nSv/hour (Iskandar, et al. al., 2008). In the results of the 2013 study in West Sulawesi, a dose rate of 272 ± 3 nSv/hour was obtained[3].

Mamuju Regency has the highest dose rate in West Sulawesi. Measurements of the external radiation level are taken whose radiation source comes from outside the human body. The average level of exposure to gamma radiation in Mamuju Regency is 631.4 ± 569.5 nSv/hour. The results of a follow-up survey conducted in several villages in Mamuju Regency showed that Botteng Village, Simboro District, is the village with the highest gamma radiation level, namely 700 – 1000 nSv/hour with an annual average of 6.15 ± 0.81 mSv[4].

Ionizing radiation exposure that occurred in Botteng Village, Mamuju Regency is exposed by low dose chronic radiation exposure. Our Understanding evolved from "small dose may cause harm" to "small dose definitely will cause harm". Every ionizing exposure causes DNA damage, which is detrimental to health and leads to higher risks of genetic abnormalities. High natural background radiation area inhabitant needs multidisciplinary observation of science continuously, for supporting inhabitant's health. The researcher is interested in conducting an epidemiological study of environmental health, using the principle of node theory. This paper is a cross-sectional study, environment epidemiological review on the relationship between natural ionizing radiation exposure for detriment of inhabitant's health. The Pathway model is presented here to demonstrate the direct and indirect mechanism relations between natural ionizing radiation exposure to the detriment of inhabitant health. The pathway is expected to provide recommendations for further public health research.

Methods

The research method is using the dynamics principle of environmental epidemiological, namely the node theory.
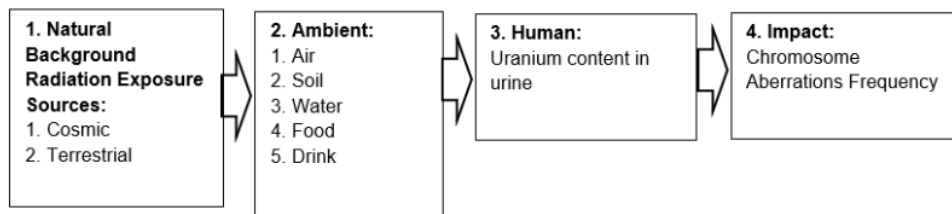

Figure 1. The dynamics principle of environmental epidemiological

The research used a cross-sectional research design, meaning that the research variables (external radiation dose, internal radiation dose, effective dose, and Chromosome Aberrations Frequency) were collected simultaneously. The study was conducted by processing and analyzing secondary data from a survey conducted by PTKMR – BATAN. Data processing and analysis were carried out in August. The total population of the study was 61 people, selected randomly, from 9 hamlets in Botteng Village, Mamuju Regency.

Cosmic and terrestrial natural radiation sources contained in the air, soil, water, food, and drink expose the inhabitants by means of internal exposure and external exposure. The calculation of the external dose is carried out by installing a survey meter, namely the Exploranium GR 135 device. The calculation of the internal dose is carried out by taking samples of food, soil, water, and air for further measurement of the internal radiation dose using a Gamma Spectrometer, while the calculation of the chromosome aberrations frequency is carried out by taking peripheral blood samples and observing the chromosome aberrations frequency using the staining method of Fluorescence In Situ Hybridization (FISH) by Whole Chromosome Probe (WCP) labeled with Fluorescent Isothiocyanate (FITC).

The obtained secondary data of external and internal radiation doses are then processed to determine the effective dose using the following equation [5]:

$$E_T = H_p(10) + \sum_j e(g)_{j,ing} I_{j,ing} + \sum_j e(g)_{i,inh} I_{j,inh}$$

ET   = Effective Dose (Sv).
$H_p(10)$ = Equivalent dose of radiation penetration at a depth of 10 mm obtained from individual dosimetry readings (Sv).
$e(g)_{j,ing}$ = Effective dose bound per unit input through digestion for radionuclide J by age group g as stated in the attachment of BAPETEN Regulation No. 4 of 2013 (Sv.Bq-1).
$e(g)_{j,inh}$ = Effective dose bound per unit of intake through inhalation for radionuclide J by age group g as stated in the attachment of BAPETEN Regulation No. 4 of 2013 (Sv.Bq-1).
$I_{j,ing}$ = Digestive input of radionuclide J (Bq).
$I_{j,inh}$ = Inhalation of radionuclide J (Bq).

The path analysis model is used to determine the linear relationship between internal and external radiation dose to the frequency of chromosomal aberrations in lymphocyte cells. The pattern of the large relationship between internal and external exposure doses directly and indirectly to the frequency of chromosomal aberrations in lymphocyte cells, through effective doses as moderator variables, inhabitant in areas with high natural radiation background. To find out the direct and indirect relationship, it was tested in two structures of path analysis.

Results
Levels of Internal Radiation Dose, External Radiation Dose, and Effective Dose and Chromosome Aberrations Frequency in Lymphocyte Cells

The area of West Sulawesi, Mamuju Regency, Botteng Village, covers 9 Hamlets. Data based on univariate analysis with a central tendency (mean value) results are presented in the following table:

Table 1. Overview of External, Internal, Effective Radiation Doses, and Chromosome Aberrations Frequency in Peripheral Blood Lymphocyte Cells in Communities with High Natural Background Radiation Area, Botteng Village, Mamuju Regency, West Sulawesi.

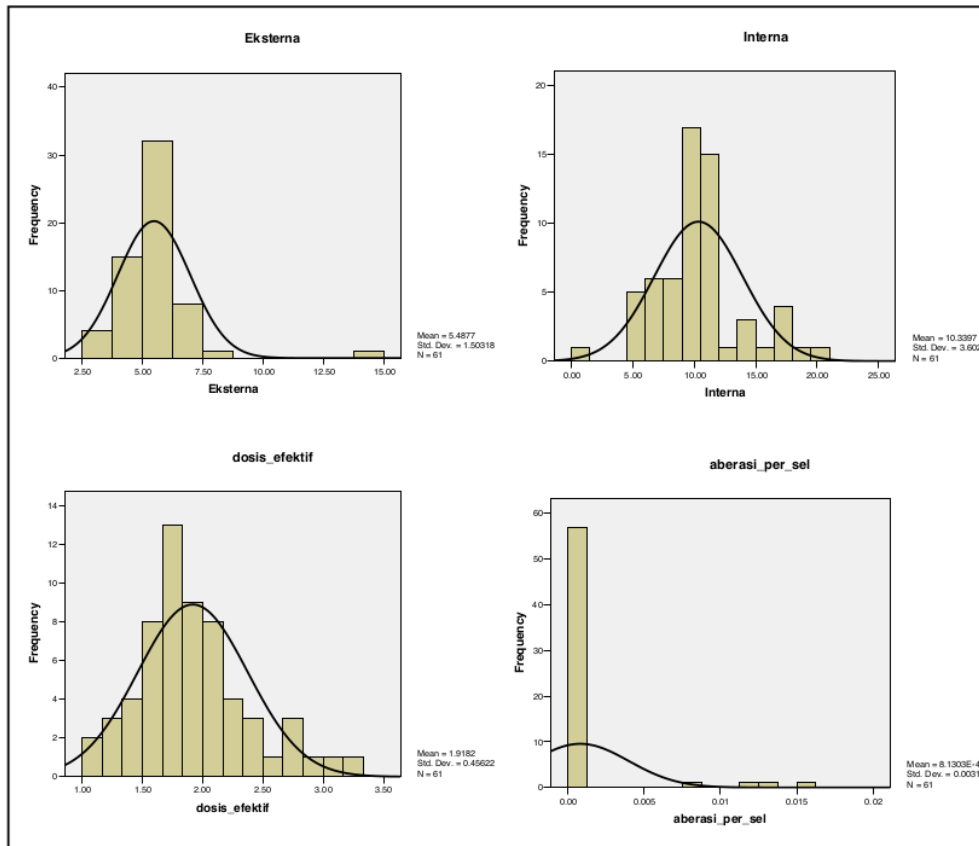| Variables	N	Mean	Median	Minimum - Maximum	95 % CI
External Dose	61	5.488	5.370	2.630 – 14.590	5.102 – 5.873
Internal Dose	61	10.340	10.120	1.230 – 20.61	9.417 – 11.262
Effective Dose	61	1.918	1.860	1.130 – 3.230	1.801 – 2.035
Chromosome Aberrations Frequency per cell	14.695	0.00082	0.000	0 – 0.2	0.000 – 0.002

Figure 2. Overview of External, Internal, Effective Radiation Doses, and Chromosome Aberrations Frequency in Peripheral Blood Lymphocyte Cells in Communities

The univariate analysis results showed that the average dose of external and internal radiation received by the inhabitants of Botteng Village, West Sulawesi was higher than the world annual dose reported by UNSCEAR[1].

The chromosome aberrations frequency of peripheral blood lymphocytes for 61 residents of Botteng Village, has an average value of 0.00082 from approximately 14,695 metaphase cells observed manually with a microscope. The lowest chromosome aberrations frequency of peripheral blood lymphocytes was 0 and the highest was 2 with a median value of 0. The residents of Botteng Village experienced the highest chromosome aberrations frequency of peripheral blood lymphocyte of 1.80 mSv/year. The examination results of chromosome aberrations in peripheral blood lymphocyte cells of inhabitants in Botteng Village, West Sulawesi, showed that there were no chromosomal abnormalities in the form of dicentric or acentric fragments, as well as rings. Only a few cells contain 1-4 dicentrics.
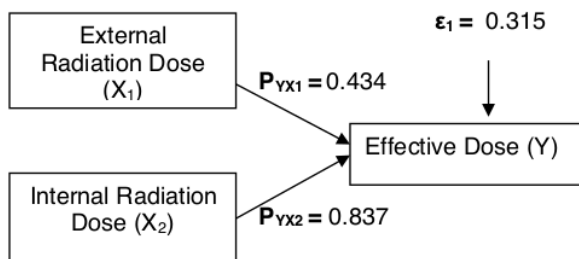
Path Analysis of Structure 1

External Radiation Dose (X_1) → $P_{YX1} = 0.434$ → Effective Dose (Y)

Internal Radiation Dose (X_2) → $P_{YX2} = 0.837$ → Effective Dose (Y)

$\varepsilon_1 = 0.315$

Figure 3. Structure 1 Empirical Causal Relationship of X_1 and X_2 variable towards Y

Overall Simultaneous Hypothesis Test Results of Structure 1

Table 2. Overall Simultaneous Hypothesis Test Results of Structure 1

	R	R^2	$\varepsilon_1 = \sqrt{1 - R^2}$	F	Standard Error	p-value
Model 1	0.949	0.901	0.315	262.483	0.14636	0.000

Based on table 2, the F value is = 262.483 with p-value = 0.000 <0.05, meaning that H_0 is rejected. Thus, the external (X_1) and internal (X_2) radiation dose has a simultaneous and significant effect on the effective dose (Y). The coefficient of determination for structural 1 is R^2 = 0.901, then the magnitude effect of other variables outside the model (error) on the effective variable dose (Y) is 1 = 0.315. This means that 90.1% of the Effective dose (Y) can be predicted by the external radiation dose (X_1) and the internal radiation dose (X_2). And 9.9% is affected by other variables outside the model. So it can be concluded that the effective dose received by lymphocyte cells is strongly affected by the amount of external and internal radiation dose.

Path Analysis of Structure 2

External Radiation Dose (X_1)

Internal Radiation Dose (X_2)

Effective Dose (Y) → $P_{ZY} = 0.304$ → Chromosomal Aberration Frequency (Z)
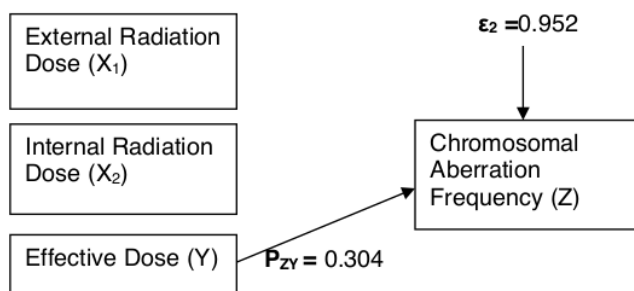
$\varepsilon_2 = 0.952$

Figure 4. Path Diagram of Structure 2 Path Analysis

Overall Simultaneous Hypothesis Test Results of Structure 2

Table 3. Overall Simultaneous Hypothesis Test Results of Structure 2

Model	R	R^2	$\varepsilon_2 = \sqrt{1 - R^2}$	F	Standard Error	p-value
Model 1	0.328	0.108	0.944	2.295	0.00308	0.87
Model 2	0.326	0.106	0.945	3.446	0.00305	0.039
Model 3	0.304	0.093	0.952	6.025	0.00305	0.017

Based on the table 3, obtained with p-value of = 0.87 > 0.05, therefore H0 is accepted. Model 2 and model 3 have p-value 0.039 < 0.05 and p-value 0.017 < 0.05, respectively.

The coefficient of determination for structural 2 is $R2 = 0.093$, therefore the magnitude of other variables effects outside the model (error) towards the effective variable dose (Y) is 1 = 0.952. This means that 9.3% of the chromosome aberration frequency dose (Z) can be predicted by the effective dose (Y) and 90.7% is affected by other variables outside the model.

Table 4. Summary of Hypothesis Test Results After Trimming

Direct Effects Between Variables	Path Coefficient	Standard Error	F-count	p-value	Conslusion
X_1 towards Y	0.434	0.013	10.485	0.000/2 =0.000	Sig.
X_2 towards Y	0.837	0.005	20.209	0.000/2 = 0.000	Sig.
Y towards Z	0.304	0.001	2.455	0.017/2 = 0.0085	Sig.

Based on the hypothesis test results, the empirical causal model between the external dose (X1), internal dose (X2), and the effective dose (Y) with the frequency of chromosomal aberrations (Z) can be visualized in the following diagram:
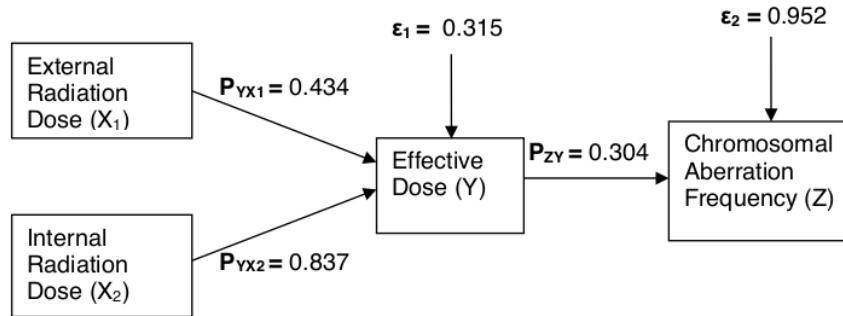

Figure 5. Empirical Causal Model between X_1, X_2, Y, and Z

The structural equations based on the results of hypothesis test are:

$$Y = 0.434X_1 + 0.837X_2 + 0.315$$
$$Z = 0.304Y + 0.952$$

Model Fit Test

The model fit test is needed to determine whether the proposed hypothetical model is fit or consistent with the empirical data. The model fit test is done by comparing the theoretical correlation matrix with the empirical correlation matrix. If the two matrices are identical or appropriate, then the proposed hypothetical model is concluded to be perfectly acceptable. The coefficient of determination for each structure obtained is presented in the following table:

Table 5. Coefficient of Determination

	Before Trimming	After Trimming
$R_{Y.X_1X_2}^2$ (Structure 1)	0.901	0. 901
$R_{Z.X_1X_2Y}^2$ (Structure 2)	0.108	0.093

Determining Chi-Square Statistics

Based on the Chi-Square table with d = 2 at the significance level α = 0.05 resulted in $X^2_{tab} = X^2_{(0.05:2)} = 5.11$, hence, $X_2 = 0.983903 < X^2_{tab} = 5.99$, therefore H_0 is accepted. Meaning that the empirical model obtained is appropriate or suitable (model fit) with the data.
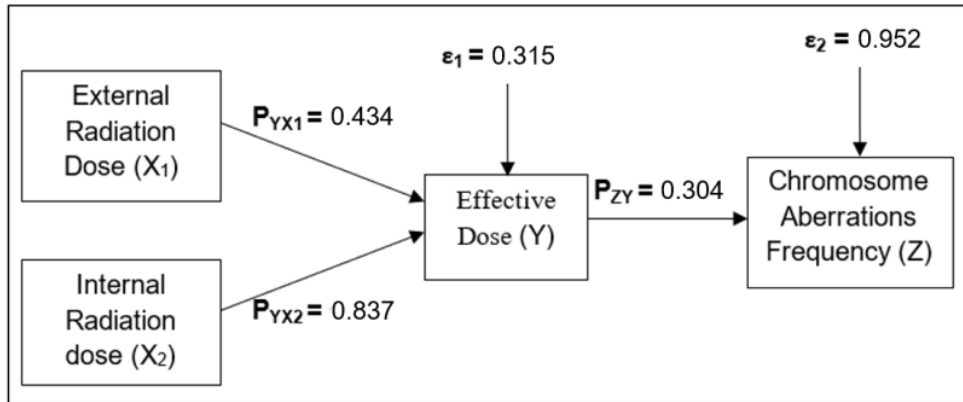
Causal Model

Figure 6. Causal Model Natural Ionizing Radiation Exposure and its Implications on The Chromosome Aberrations Frequency

Table 6 Direct, Indirect, and Total Effect Endogent Variables

Exogenous Variables	Path Coefficient	Correlation with endogent variable (Z)			R-Simultaneous
		direct	indirect (Y)	Total	
Externall radiation dose (X₁)	0.434	-	0.132	0.132	
Internal radiation dose (X₂)	0.837	-	0.254	0.254	
Effective Dose (Y)	0.304	0.304	-	0.304	
ε₁	0.315				
ε₂	0.952				
X₁. X₂ → Y					0.901
X₁. X₂. Y					0.093

The external and internal radiation dose simultaneously and significantly affects the effective dose, amounting to R2 = 0.901 and determination error ε1 = 0.315. This means that 90.1% of the effective dose can be predicted by external and internal radiation dose, 9.9% is affected by other variables besides the model. The external and internal dose of radiation has a significant effect on the chromosome aberrations frequency only through an effective dose of R2 = 0.093 and determination error ε1 = 0.952. Meaning that 9.3% of the chromosome aberrations frequency can be predicted by external, internal, and effective radiation doses, meanwhile, 90.7% is affected by other variables outside the model.

The Result from this research is: (1) The external dose variable (X1) does not have a direct effect on the frequency of chromosome aberrations (Z) but has an indirect determination through the effective dose (Y) of 0.304. Thus, the frequency of chromosomal aberrations in lymphocyte cells, cannot be explained by the level of external radiation dose, without going through the effective dose, (2) The internal dose variable (X2) does not have a direct effect on the frequency of chromosome aberrations (Z) but has an indirect determination through the effective dose (Y) of 0.254. Thus, the frequency of chromosomal aberrations in lymphocyte

cells, cannot be explained by the internal radiation dose level, without going through the effective dose, (3) The effective dose variable (Y) determines the frequency of chromosomal aberrations in lymphocyte cells (Z). Thus, the frequency of chromosomal aberrations can be explained by the dose, directly equal to 0.304, and (4) The external dose (X1), internal (X2), and effective dose (Y) variables have a simultaneous effect on the frequency of chromosome aberrations (Z), of 0.093 or 9.3%.

Discussion
High Natural Background Radiation

Table 7. Average Dose of Natural background radiation (External and Internal) in Botteng Village Inhabitants and World Annual Dose according to UNSCEAR, 2010

Types of natural background radiation exposure	Average dose of natural background radiation	
	Botteng Village Inhabitants, Mamuju Regency, West Sulawesi	World Annual Dose (UNSCEAR, 2010)
External	5.49 mSv/year	0.9 mSv/year
Internal	10.34 mSv/year	1.6 mSv/year

Natural background radiation sources in question consist of external exposure from cosmic rays (0.4 mSv/year) and terrestrial gamma radiation (0.5 mSv/year), as well as internal exposure, namely inhalation (1.3 mSv/year, especially Radon) and ingestion (0.3 mSv/year)[1].

Exposure to natural background radiation generally originates from soil or rocks and mineral materials containing the thorium series (Th-232), uranium-series (U-238), and potassium-40[3]. Areas with high natural background radiation generally contain these substances geographically and are scattered in the environment, thus the radiation levels in the environment are difficult to control. Efforts to reduce external radiation exposure to the body are called, "remedial action".

Efforts to improve the public health degree are necessary by carrying out promotive and preventive activities, by increasing the knowledge of health workers and the inhabitants regarding high natural background radiation. Efforts are made by training local health workers regarding high natural background radiation and controlling health impacts. After the workers were trained, counseling regarding high natural background radiation, and controlling health impacts can be carried out to the inhabitants in areas with high natural background radiations.

Both external and internal dose levels of natural background radiation will produce an effective dose of radiation that is accepted by the inhabitants. In knowing the exposure to natural background radiation correlation pattern, it is necessary to know the effective dose of radiation received by lymphocyte cells, because the lymphocyte cells can typically change when exposed to high natural ionizing radiation.

Average Effective Dose of Lymphocyte Cells in Botteng Village Inhabitants and Dose Limit Value for Community Members according to BAPETEN Regulation No. 4 of 2013

An area with several chronic exposures that causes the effective dose to be above the specified level to the inhabitants, the area is commonly referred to as High Natural Background Radiation (HNBR) (1 mSv/year or 0.12 mSv/year in lymphocyte cell) [2]. Based on the results of univariate analysis of internal, external, and effective doses received by the inhabitants in Botteng Village, it shows that Botteng Village is an area with high natural background radiation.

One of the biological effects caused by ionizing radiation exposure to the body is chromosome aberrations. The chromosome aberrations that can only occur by ionizing radiation exposure are chromosome aberrations in lymphocyte cells. This biological effect can affect the health condition of the inhabitants in the future.

Correlation of Internal and External Radiation Dose towards Effective Dose

Based on the Path analysis in structure 1, the external and internal radiation dose simultaneously and significantly affects the effective dose, amounting to R2 = 0.901 and

determination error ε_1 = 0.315. This means that 90.1% of the effective dose can be predicted by external and internal radiation dose, 9.9% is affected by other variables besides the model.

Radioactive materials in the environment expose the human body in two ways, namely exposure to external radiation, and internal radiation exposure. External radiation exposure is ionizing radiation exposure from outside the body. The Path Coefficients P_{YX1} = 0.434, every 1 dose of external radiation received contributes 0.434 effective dose of the inhabitant HNBR (p-value=0.000)

Meanwhile, internal radiation exposure is ionizing radiation exposure in which radionuclides contaminated the body, radionuclides contaminated the body through the respiratory tract (inhalation), ingestion (ingestion). The two exposures have different radiation patterns to the body. Path Coefficients P_{YX2} = 0,837, every 1 dose of internal radiation received contributes 0.434 effective dose of the inhabitant HNBR (p-value=0.000). The internal dose comes from radiation exposure sources that enter the body. This resulted in the contribution of the internal dose towards the lymphocyte cells' effective dose, greater than the external dose. The radioactive materials pathways of exposure to the body can be through inhalation and ingestion. Factors that can affect it, namely the transfer of radioactive materials to food materials, food sanitation, large concentrations of radioactive materials contained in food, people's consumption patterns, large concentrations of radioactive materials in air particulates, home ventilation systems, and respiratory flow rate [6–9]. The external dose comes from radiation exposure originating from outside the body. Exposure to external radiation is affected by the distance between the radiation source and the body. This resulted in the smaller contribution of the external dose towards the lymphocyte cells' effective dose compared to the internal dose [10].

Correlation of External Radiation Dose to Chromosome Aberrations Frequency in Lymphocyte Cells

The occurrence frequency of chromosomal abnormalities depends on the dose, energy, and type of radiation received [11]. The correlation between the probability of a stochastic effect and the dose received can be predicted using the Linear Non-Threshold Hypothesis. As the result of the analysis, there is no linearity relationship between the external radiation dose and the chromosome aberration frequency in lymphocyte cells (p-value=0.176 > 0.05). This indicates a phenomenon of radio adaptive response, in peripheral blood lymphocyte cells of people living in areas with high natural background radiation.

Ionizing radiation exposure that occurs in an area with high natural background radiation, Botteng Village, is considered as a low dose radiation exposure. The exposure occurs continuously (chronic). Exposure to low doses of radiation causes non-lethal (non-mutagenic) cell damage and is expressed in subsequent cells. It also resulted in making the cell become unstable. The characteristic of unstable cells in the presence of several delayed damages, one of them is the chromosome aberrations. The magnitude of the response and the characteristics of unstable cells depend on the linear energy transfer and radiation dose, as well as cell type and genetics. External radiation from gamma rays only causes an increase in the aberrations frequency in the 20 – 30th generation of the population after receiving exposure and then decreases towards the background [12,13].

Communities in areas with high natural background radiation receive chronic exposure to low doses of radiation. Human cells were able to recognize and respond to a very low dose of radiation exposure with several changes, including gene expression. When cells have received exposure to a low dose of radiation (adaptive dose), thus in a short time followed by subsequent radiation exposure with a larger dose (challenge dose). The chromosome aberrations frequency in these cells was lower than in cells that had not received previous low-dose radiation exposure. This shows the existence of cell resistance to exposure to higher doses of radiation in cells that have previously received low doses of exposure [12,13].

The existence of a radio adaptive response in lymphocyte cells is proved by a study conducted on residents living in areas with high natural background radiation, in Ramsar, Iran. The study was conducted on peripheral blood lymphocyte cell cultures, which were taken from

15 healthy residents of the area with high natural background radiation as the case group, and 30 healthy residents of the area with normal natural background radiation as the control group. In lymphocyte cell culture, both groups were exposed to external radiation (gamma rays) of 1.5 Gy. It shows that there is a radio adaptive response in resident lymphocyte cells in areas of high natural background radiation [14]. This is in line with the results of the Spearman Rank correlation analysis which shows that there is no relationship between external dose and the chromosome aberrations frequency in the inhabitants in Botteng Village.

Correlation of Internal Radiation Dose to Chromosome Aberrations Frequency in Lymphocyte Cells

The result of analysis there is no linearity correlation between the internal radiation dose and the chromosome aberrations frequency (p-value 0,376 > 0,05). Low flux exposure of alpha particles by the board beam does not cross every cell in the radiation environment. In the human body exposure to a low flux of alpha particles only occurs when the radionuclides contaminated the body (internal radiation). Low flux alpha particles can increase the number of mutations. In addition, it led to the accumulation of the tumor suppressor gene protein p53 (TP53) in a higher percentage of the exposed population compared to the nucleus of cells that received the low flux alpha particle 1 pathway. Thus, it is known that intracellular communication is involved in transmitting several damage signals from cells that receive exposure to cells that do not. Hence this effect can potentially increase the number of damaged cells more than those that were directly exposed to radiation. This means that the internal dose in the human body will affect the chromosome aberrations frequency [6].

Some damage as a consequence of the response that occurs in several cells not traversed by an alpha particle directly. Several studies have shown an increase in sister chromatid exchange (SCE) of cells exposed to radiation as a bystander effect. The bystander effect is an effect that occurs in cells that do not receive alpha particle exposure but receive a signal from exposed cells as a result of alpha particle exposure [15]

Theoretically, Sister Chromatid Exchange (SCE) is mediated by the release of extracellular factors and its frequency can be reduced by free radical scavengers[15,16]. radionuclides that contaminated the body through inhalation and ingestion, are materials that have unstable atoms, certain atoms can become free radical scavengers due to radiation exposure. Thus, in the up following research, it is necessary to conduct an assessment using the IC50 assay method, on food materials, drink and inhaled air. To determine the presence and effectiveness of certain ingredients that are antioxidants, aiming that those materials can be used to increase resistance to radiation. This study is in line with those efforts that will result in the improvement of public health status in areas with high natural background radiation.

Effect of Internal Radiation Dose. External Radiation Dose. and Effective Dose on Chromosome Aberrations Frequency in Lymphocyte Cells

Path analysis in structure 2 aims to see the simultaneous effect of external, internal, and effective doses of lymphocytes on the chromosome aberrations frequency. The correlation between the high dose with the probability of stochastic effects' occurrence can be predicted by using the Linear Non-Threshold Hypothesis. The stochastic effect on humans is caused by high natural background radiation exposure, initiated by a cytogenetic response identified from early biologic markers, which is one of the earliest biologic markers of chromosome aberrations exposure-response. Chromosome Aberrations can be observed through peripheral blood lymphocytes, which are the most sensitive cells to ionizing radiation. These peripheral blood lymphocyte cells also circulate throughout the body, so the damage that occurs in the peripheral blood will represent the damage that occurs in the body[17,18].

Based on the analysis, the external and internal dose of radiation has a significant effect on the chromosome aberrations frequency only through an effective dose of R2 = 0.093 and determination error ε2 = 0.952. Meaning that 9.3% of the chromosome aberrations frequency

can be predicted by external, internal, and effective radiation doses, meanwhile, 90.7% is affected by other variables outside the model.

Chronic exposure to low-dose radiation received by people living in areas with high natural background radiation can induce a radio adaptive response. This has been described by several experts.

a. Low-dose radiation can increase the immune response[19–21].

b. Low-dose radiation can reduce DNA damage below spontaneous levels and reduce the likelihood of neoplastic transformation by stimulating cellular detoxification and repair mechanisms [22–24].

c. Exposure to low doses of ionizing radiation can boost the immune system and eliminate the detrimental effects of high doses of radiation [25,26].

d. The immune system of residents in areas with high natural background radiation has been adapted to the naturally high levels of radiation by shifting from Type 1 to Type 2 response to increase anti-inflammatory[27,28].

e. The response of cells exposed to sublethal doses from DNA-damaging agents (non-mutagenic doses of chemicals or radiation), known as conditioning treatment (CT), leads to an increase in resistance to subsequent exposure by higher doses of the similar or other agents, known as challenge treatment (CR)[29–31].

Although there is a radio adaptive response and cell repair mechanism, the radiation dose contributes 9.3% to the chromosome aberrations frequency. This indicates the effects of health problems that can occur in the future. Thus, it is necessary to improve the medical record system or clinical data registry inhabitant at health facilities located in areas with high natural background radiations, to analyze health problems experienced by people in areas with high natural background radiations, in a cohort manner. Which is the utilization of data science to empower research from clinical data registry the inhabitants and next generation. Therefore, it is necessary to increase cross-sectoral collaboration between stakeholders.

Suggestions

1. For Botteng Village Inhabitants:
   a. Efforts to reduce indoor external radiation exposure to the body, including reducing materials or rocks containing radionuclide elements..

2. For Health Facilities:
   a. Improve the medical record system at health facilities located in areas with high natural background radiation to analyze health problems experienced by people in areas with high natural background radiation in a cohort.
   b. Increasing promotive and preventive efforts through The Clean and Healthy Living Behavior (PHBS) counseling program.
   c. Utilization of data science to empower research from clinical data registry the inhabitants.

3. For Further Research:
   a. It is necessary to conduct an assessment using the IC50 assay method, on food materials, drink, and inhaled air. To determine the presence and effectiveness of certain materials that are free radical scavengers (antioxidants).
   b. It is necessary to conduct an analytical assessment on factors affecting the external dose.
   c. It is necessary to conduct an analytical assessment on factors affecting the internal dose.
   d. It is necessary to conduct a big data analysis on the clinical data register for the inhabitants to discover the health effect of chronic low dose ionizing radiation exposure. Furthermore, to make a decision to improve public health more effectively.

Conclusion

On the basis of the results of the conducted research, the conclusions are as follows:

1. The average dose of external radiation is 5.49 mSv/year, the internal dose is 10.340 mSv/year, and the effective dose of lymphocyte cells is 1.918 mSv/year. The examination results of chromosome aberrations have an average value of 0.00082 from approximately 14.695 metaphase cells observed manually with a microscope.
2. There was a linear relationship between eksternal radiation dose and effective dose. The Path Coefficients P_{YX1} = 0.434 (p-value=0.000)
3. There was a linear relationship between internal radiation dose and effective dose. The Path Coefficients P_{YX2} = 0,837 (p-value=0.000)
4. The external and internal radiation dose simultaneously and significantly affects the effective dose, amounting to $R2$ = 0.901 and determination error $\varepsilon1$ = 0.315.
5. There was no direct correlation between external, internal radiation dose and chromosome aberrations frequency.
6. The external (indirect corelation = 0.132) and internal dose of radiation (indirect correlation = 0.254) has a significant effect on the chromosome aberrations frequency only through an effective dose of $R2$ = 0.093 and determination error $\varepsilon2$ = 0.952.

Ethics approval

Ethics approval from Center for Tech of Radiation Safety, Jakarta (Indonesia).

Author Contribution

EF analyzed and interpreted the path analysis model and was a major contributor in writing the manuscript. EP performed data collection and analyze data from Center for Technology of Radiation Safety, Nuclear Energy Agency of Indonesia. AS has given advice on the results of the research to be recommended to the relevant agencies and improve the writing of the manuscript to make it perfect. All authors read and approved the final manuscript.

References

1. UNSCEAR. Scientific Report: summary of low-dose radiation effects on health [Internet]. United Nations Publication. 2011. 4–14 p. Available from: http://www.unscear.org/docs/publications/2010/UNSCEAR_2010_Report.pdf
2. Ramadhani D, Syaifudin M, Nurhayati S, Tetriana D, Rahardjo T, Mailana W, et al. Assessment of DNA damage in lymphocytes of Mamuju (a high background radiation area) inhabitants using alkaline single cell gel electrophoresis. Int J Low Radiat. 2017;10(4):314.
3. Setiawan A, Pudjadi E, Laju P, Radiasi D, Di G, Pulau W, et al. Pemetaan Laju Dosis Radiasi Gamma Di Wilayah Pulau Bangka. 2013;205–11.
4. Hasan Basri IK, Yusuf D, Rahardjo T, Nurhayati S, Tetriana D, Ramadhani D, et al. Study of γ-H2AX as DNA double strand break biomarker in resident living in high natural radiation area of Mamuju, West Sulawesi. J Environ Radioact. 2017;171:212–6.
5. Udiyani PM, Setiawan MB, Subekti M, Kuntjoro S, Pane JS, Hastuti EP, et al. Assessment of dose consequences based on postulated BDBA (beyond design basic accident) A-30MWt RSG-GAS after 30-year operation. Prog Nucl Energy [Internet]. 2021;140:103927. Available from: https://doi.org/10.1016/j.pnucene.2021.103927

6. George K, Willingham V, Wu H, Gridley D, Nelson G, Cucinotta FA. Chromosome aberrations in human lymphocytes induced by 250 MeV protons: effects of dose, dose rate and shielding. Adv Sp Res. 2002 Jan 1;30(4):891–9.

7. Harty Krieg R, Hickey EE, Weber JR, Masnik MT. Nuclear Power Plants, Decommissioning of. Encycl Energy [Internet]. 2004 [cited 2022 Feb 28];409–20. Available from: https://linkinghub.elsevier.com/retrieve/pii/B012176480X004150

8. Amiro BD. Environmental Radioactivity. Encycl Phys Sci Technol [Internet]. 2003 [cited 2022 Feb 28];583–99. Available from: https://linkinghub.elsevier.com/retrieve/pii/B0122274105002283

9. Siegel MD, Bryan CR. Environmental Geochemistry of Radioactive Contamination. Treatise on Geochemistry. 2003 Dec 4;9–9:205–62.

10. Holly A. Swartz, Jessica C. Levenson and EFU. 乳鼠心肌提取 HHS Public Access. Physiol Behav. 2012;43(2):145–53.

11. Kravtsov V, Livanova A, Belyakov O, Fedortseva R. The frequency of lymphocytes containing dumbbell-shaped nuclei depends on ionizing radiation dose and correlates with appearance of chromosomal aberrations. Genome Integr. 2018;9(1):1–7.

12. Mothersill C, Seymour C. Low dose radiation mechanisms: The certainty of uncertainty. Mutat Res Toxicol Environ Mutagen. 2022 Apr 1;876–877:503451.

13. Alatas Z. Paradigma Bard Efek Radiasi Dosis Rendah. Bul Al. 2011;13(2):242258.

14. Ramachandran EN, Karuppasamy C V., Kumar VA, Soren DC, Kumar PRV, Koya PKM, et al. Radio-adaptive response in peripheral blood lymphocytes of individuals residing in high-level natural radiation areas of Kerala in the southwest coast of India. Mutagenesis. 2017;32(2):267–73.

15. Marín A, Martín M, Liñán O, Alvarenga F, López M, Fernández L, et al. Bystander effects and radiotherapy. Reports Pract Oncol Radiother. 2015;20(1):12–21.

16. Lehnert BE, Goodwin EH. Extracellular factor(s) following exposure to α particles can cause sister chromatid exchanges in normal human cells. Cancer Res. 1997;57(11):2164–71.

17. Pillon S. Actinide-Bearing Fuels and Transmutation Targets. Compr Nucl Mater. 2012;3:109–41.

18. Burakov BE. Lava-Like Materials Formed and Solidified During Chernobyl Accident. Compr Nucl Mater Second Ed. 2020 Jul 22;525–39.

19. Liu J, Zhou J, Wu M, Hu CF, Yang J, Li D, et al. Low-dose total body irradiation can enhance systemic immune related response induced by hypofractionated radiation. Front Immunol. 2019;10(FEB):1–16.

20. Hekim N, Cetin Z, Nikitaki Z, Cort A, Saygili EI. Radiation triggering immune response and inflammation. Cancer Lett. 2015 Nov 28;368(2):156–63.

21. Georgakilas AG, Pavlopoulou A, Louka M, Nikitaki Z, Vorgias CE, Bagos PG, et al. Emerging molecular networks common in ionizing radiation, immune and inflammatory responses by employing bioinformatics approaches. Cancer Lett. 2015 Nov 28;368(2):164–72.

22. Schöllnberger H, Stewart RD, Mitchel REJ, Hofmann W. An Examination of Radiation Hormesis Mechanisms Using a Multistage Carcinogenesis Model. Nonlinearity Biol Toxicol Med. 2004;2(4):154014204909002.

23. Scott BR, Belinsky SA, Leng S, Lin Y, Wilder JA, Damiani LA. Radiation-stimulated epigenetic reprogramming of adaptive-response genes in the lung: An evolutionary gift for mounting adaptive protection against lung cancer. Dose-Response. 2009;7(2):104–31.

24. Liu SZ. Biological effects of low level exposures to ionizing radiation: Theory and practice. Hum Exp Toxicol. 2010;29(4):275–81.

25. Cui J, Yang G, Pan Z, Zhao Y, Liang X, Li W, et al. Hormetic response to low-dose radiation: Focus on the immune system and its clinical implications. Int J Mol Sci. 2017;18(2).

26. Lumniczky K, Impens N, Armengol G, Candéias S, Georgakilas AG, Hornhardt S, et al. Low dose ionizing radiation effects on the immune system. Environ Int. 2021;149(June

2020).

27. Manisalidis I, Stavropoulou E, Stavropoulos A, Bezirtzoglou E. Environmental and Health Impacts of Air Pollution: A Review. Front Public Heal. 2020;8(February):1–13.

28. Borzoueisileh S, Monfared AS, Abediankenari S, Mostafazadeh A, Khosravifarsani M. The effects of residence duration in high background radiation areas on immune surveillance. J Nat Sci Biol Med [Internet]. 2013 Jan;4(1):218—222. Available from: https://europepmc.org/articles/PMC3633281

29. Venkat S, Apte SK, Chaubey RC, Chauhan PS. Radioadaptive response in human lymphocytes in vitro. J Environ Pathol Toxicol Oncol Off organ Int Soc Environ Toxicol Cancer. 2001;20(3):165–75.

30. Bannister LA, Serran ML, Mantha RR. Low-Dose Gamma Radiation Does Not Induce an Adaptive Response for Micronucleus Induction in Mouse Splenocytes. Radiat Res. 2015 Nov;184(5):533–44.

31. Komova O, Krasavin E, Nasonova E, Mel'nikova L, Shmakova N, Cunha M, et al. Relationship between radioadaptive response and individual radiosensitivity to low doses of gamma radiation: an extended study of chromosome damage in blood lymphocytes of three donors. Int J Radiat Biol. 2018 Jan;94(1):54–61.

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