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Original article

# Study of certain congenital malformations due to low-level radiation exposures from high background radiation areas

P.J. JoJo [a], Mayeen Uddin Khandaker [b,i,*], S. Ben Byju [a], A. Sunil [a], Talha Bin Emran [c,d], Hamid Osman [e], Mohammed Almalki [j], Fahad A. Alhumaydhi [f], Saad Alghamdi [g], Ahmad O. Babalghith [h]

[a] Centre for Advanced Research in Physical Sciences, Department of Physics, Fatima Mata National College (Autonomous), Kollam 691001, India
[b] Centre for Applied Physics and Radiation Technologies, School of Engineering and Technology, Sunway University, Bandar Sunway, Selangor Darul Ehsan 47500, Malaysia
[c] Department of Pharmacy, BGC Trust University Bangladesh, Chittagong 4381, Bangladesh
[d] Department of Pharmacy, Faculty of Allied Health Sciences, Daffodil International University, Dhaka 1207, Bangladesh
[e] Department of Radiological Sciences, College of Applied Medical Science, Taif University, P O Box 2425, Taif 21944, Saudi Arabia
[f] Department of Medical Laboratories, College of Applied Medical Sciences, Qassim University, Buraydah 52571, Saudi Arabia
[g] Laboratory Medicine Department, Faculty of Applied Medical Sciences, Umm Al-Qura University, Makkah, Saudi Arabia
[h] Medical Genetics Department, College of Medicine, Umm Al-Qura University, Makkah, Saudi Arabia
[i] Department of General Educational Development, Faculty of Science and Information Technology, Daffodil International University, DIU Rd, Dhaka, 1341, Bangladesh
[j] Nursing Department, College of Applied Medical Sciences, Taif University, POB 11099, At Taif 21944, Saudi Arabia

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A B S T R A C T

The coastal regions of some states (Kerala, Tamil Nadu, Andhra Pradesh and Orissa) in India are known to have plenty of thorium-rich minerals, therefore possess high external gamma radiation fields, and are identified as Natural High Background Radiation Areas. There are concerns about congenital malformations due to the high background radiation prevailing in the region. Therefore, scientists find interest to study the possible biological effects of low-level exposures on the local populace who are living with generations under these extraordinary radiation fields. The present study is an attempt to find the correlation between the incidences of certain congenital malformations through a 1:3 matched case-control study. A total of 75 subjects (58 mental retardation cases and 17 Cleft lip/palate cases) along with 225 controls were selected for the investigations. Indoor and outdoor gamma dose rates were measured using a halogen-quenched GM tube-based survey meter, while the indoor inhalation dose rates were measured based on the radon and progeny measurements using the twin cup dosimeters equipped with LR-115 Type II solid-state nuclear track detectors. Conditional logistic regression analysis was used to find out the correlation between the radiation dose with congenital malformation. This study found an insignificant risk of cleft lip/palate (but not for mental retardation) from the exposures to natural high external gamma radiation fields in the study area. Therefore, the results of the investigation indicate no explicit risk of congenital malformations by the high background natural radiation prevailing in the region.



## 1. Introduction

High background radiation areas (HBRA) provide an exclusive opportunity for the study of possible biological effects of chronic exposures. The HBRAs with uranium or thorium deposits, and phosphate rock deposits are considered natural laboratories for epidemiological studies as the local population are exposed continuously to radiation since their birth. The population residing in high background regions receives radiation doses much greater than the estimated worldwide average background dose of 2.4 mSv per year for a human being (High Levels of Natural

* Corresponding author.
*E-mail addresses:* jojo@fatimacollege.net (P.J. JoJo), mu_khandaker@yahoo.com (M.U. Khandaker).

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Radiation,1993). Depending on the annual radiation dose rates in each region, the status of a region can be classified into four categories, these are low (up to 5 mSv $y^{-1}$), medium (5–20 mSv $y^{-1}$), high (20–50 mSv $y^{-1}$) and very high (>50 mSv $y^{-1}$) (Sohrabi, 1997; ICRP, 1993).

Prominent HBRA regions in India are in Kollam (Chavara and Karunagapally) along the southwest coast of Kerala, Tamilnadu (Manavalakurichi, Vayakallur, Midalam,), Orissa (Sanaeka-Sangi-Gopalpur, Bajarkot, Chatrapur, Puri and Satpara), Andrapradhesh (Bhimunipatnam, Kakinada, Pentakota, Konada-Kandivalasa-Mukumpeta-Bendicreek-Donkuru), Maharashtra (Kalbadevi, Malgund and Newre) and Ullal in Karnataka (Shanbag et al., 2005; Christa et al., 2012). The thorium-rich monazite sand available in plenty in the coastal belt of the state of Kerala extends up to 57 km from Neendakara (Kollam district) to Purakkadu (Alappuzha district) along the western coast of the country. Black-colored beach sand is found extensively in this area and contains 8–10 % of thorium and 0.3% Uranium along with their decay products (Humphrey and Khandaker, 2018). The activities of $^{238}$U, $^{232}$Th and $^{40}$K were reported to vary from 17 to 3081 Bq $kg^{-1}$, 54 to 11976 Bq $kg^{-1}$ and 67.4 to 216 Bq $kg^{-1}$, respectively, in the study area (Christa et al., 2012; Balakrishnan et al., 2021). The region has a very large population living for generations. These areas are also characterized by several differentiating factors such as geology, population density, socio-economic condition, etc. compared to the other regions in India. Therefore, scientists find interest to study the possible biological effects of chronic exposure on the local populace who are living with generations under these extraordinary radiation fields. The technical report of Natural Background Radiation Cancer Registry (1990–1999) brought out by Regional Cancer Centre, Trivandrum based on an extensive investigation of over 1,40,000 inhabitants in the region reported that the annual average dose to the population is in the range of 15–25 mGy (Gangadharan et al., 2004). In some locations on the coast, the radiation levels are as high as 70 mGy $y^{-1}$ with indoor radon concentrations up to 215 Bq $m^{-3}$ and thoron concentrations up to 92 Bq $m^{-3}$ (Eappen et al., 2000).

There have been numerous dosimetric studies in the region addressing various aspects of natural radioactivity and radiation exposure (Soniya et al., 2021; Arunima, et al., 2021). Cytogenetic studies in flora in the region and limited genetic studies in rats have also been reported (Gopal-Ayengar et al., 1970; Suntha, 1990; Monica et al., 2020). A demographic study conducted in the region proved that there are no significant differences in reproductive parameters and infant mortality between HBRAs and normal radiation areas (Ayengar et al., 1972). Similar results were obtained in studies carried out on cancer incidences (Nair et al., 2009). However, in a study of saliva samples from residents of the HBRA, an increased mitochondrial germline point mutation frequency was reported (Forester et al., 2002).

All studies related to congenital or genetic effects, on children and women of the reproductive period constitute the critical group of investigations. As already mentioned, there are reports of increased frequency of chromosomal aberrations in the lymphocytes of exposed persons. However, carcinogenic effects are not yet proven categorically. There are concerns about congenital malformations due to high background radiation prevailing in the region.

The study was carried out among individuals with either of the two easily identifiable congenital malformations. Mental retardation refers to below-average intellectual function along with insufficiencies in adaptive behavior. Cleft lip (*cheiloschisis*) is the presence of one or two vertical fissures in the upper lip, and cleft palate (*palatoschisis*) refers to an opening in the palate resulting in a faulty development of the face. Both malformations are congenital and have complex etiology and environmental determinants are considered to be involved in the pathogenesis. The present study is an attempt to find the correlation between the incidence of certain congenital malformations, namely mental retardation, and cleft lip/palate, through a 1:3 matched case-control study.

## 2. Methodology

Young individuals (<35 years old) with the specified malformations were selected as the cases for the study from both HBRAs as well as normal background radiation areas (NBRAs) following exhaustive exclusion criteria. The criteria include- age 35 years or less, born of singleton deliveries without any assisted reproductive tools having a living mother without a history of any previous stillbirth or recurrent abortions. The individual should have been living in the same residence of conception where the radiation dosimetry has to be conducted.

Three eligible age-matched controls were selected for each case from the region with a similar construction of the dwelling as well as other criteria. After selecting a case and its three controls, setting out of dosimeters was performed consecutively so as to get a concurrent estimation of radiation doses in all four dwellings. The statistical tool used was the conditional logistic regression analysis of the data obtained.

## 3. Experimental

Four panchayaths (hamlets) namely Kollam, Sakthiklangara, Neendakara and Chavara, along the coastal Kollam district in Kerala were selected for the study. Altogether 75 subjects (58 mental retardation cases and 17 Cleft lip/palate cases) along with 225 controls were selected for the investigations. Indoor and outdoor gamma dose rates were measured using a halogen-quenched Geiger Muller (GM) tube-based survey meter with a microprocessor-based digital display. All the measurements were made at a height of approximately 1 m from the ground. Measured gamma absorbed doses expressed in $\mu Gyh^{-1}$ were converted to indoor annual effective doses using a dose conversion coefficient of 0.7 Sv/Gy with an indoor occupancy factor of 0.8, and an outdoor effective dose with an occupancy factor of 0.2 (United Nations Scientific Committee on the Effects of Atomic Radiation, 2000). Indoor inhalation dose rates were determined using the radon and progeny measurements carried out with the twin cup dosimeters equipped with LR-115 Type II alpha detectors as described by Mayya et al. (1988).

The sum of the external and inhalation doses for the indoor atmosphere was used in the analysis.

Conditional logistic regression (CLR) analysis was used to find out a possible correlation between the radiation dose with the Congenital malformation. The evolved Odds Ratio (OR) was used to interpret the results. The investigation did not involve human subjects nor the collection of biological material from the study subjects. The CLR analysis of mental retardation and cleft lip/palate was carried out to evaluate the risk of mental retardation/cleft lip/palate at different dose levels adjusting for the effect of gender and maternal age at birth of the cases. Conditional logistic regression analysis was carried out using the SPSS software to determine the correlation between the parameters investigated.

## 4. Results and discussion

Although congenital malformations may be the result of one or more factors like genetic, infectious, nutritional, environmental, etc., it is often difficult to identify the exact causes. In this study, the impact of natural high background radiation areas on certain congenital malformations is evaluated. For all cases of mental

**Table 1**
The distributions of gender, maternal age at birth and total dose.

| Characteristics | Mental retardation (58) | | Cleft lip/palate (17) | | Control (225) | |
|---|---|---|---|---|---|---|
| | No. | % | No. | % | No. | % |
| Male | 36 | 62.07 | 10 | 58.82 | 122 | 54.22 |
| Female | 22 | 37.93 | 07 | 41.18 | 103 | 45.78 |
| Maternal age at birth | | | | | | |
| 20–24 years | 21 | 36.21 | 04 | 23.53 | 78 | 34.67 |
| 25–30 years | 24 | 41.38 | 10 | 58.82 | 94 | 41.78 |
| $\geq$ 31 years | 13 | 22.41 | 03 | 17.65 | 53 | 23.55 |
| Total dose group | | | | | | |
| $\leq$ 1 mSv $y^{-1}$ | 14 | 24.14 | 04 | 23.53 | 62 | 27.56 |
| 1.0 – 2.0 mSv $y^{-1}$ | 20 | 34.48 | 09 | 52.94 | 96 | 42.67 |
| 2.0 – 3.0 mSv $y^{-1}$ | 16 | 27.59 | 03 | 17.65 | 48 | 21.33 |
| > 3.0 m Sv $y^{-1}$ | 08 | 13.79 | 01 | 05.88 | 19 | 08.44 |

**Table 2**
Conditional logistic regression analysis of mental retardation and cleft lip/palate: risk at different dose levels.

| Characteristics | Mental retardation | | | Cleft lip/palate | | |
|---|---|---|---|---|---|---|
| | Odds Ratio | (95% CI) | *P-value* | Odds Ratio | (95% CI) | *P-value* |
| Female | 1 | | – | 1 | | – |
| Male | 1.25 | (1.12–1.43) | | 0 0.62 | (0.42–0.83) | |
| Maternal age at birth | | | | | | |
| 20–24 years | 1 | | 0.108 | 1 | | 0.631 |
| 25–30 years | 1.21 | (1.02–1.43) | | 1.42 | (1.10–1.89) | |
| $\geq$ 31 years | 1.31 | (1.08–1.61) | | 1.28 | (1.12–1.48) | |
| Total dose group | | | | | | |
| $\leq$ 1 mSv $y^{-1}$ | 1 | | 0.003 | 1 | | 0.842 |
| 1.0 – 2.0 mSv $y^{-1}$ | 1.18 | (1.06–1.41) | | 0.67 | (0.52–0.91) | |
| 2.0 – 3.0 mSv $y^{-1}$ | 1.24 | (1.01–1.60) | | 0.74 | (0.43–1.13) | |
| > 3.0 m Sv $y^{-1}$ | 1.32 | (1.22–1.53) | | 1.12 | (0.62–1.64) | |

retardation and Cleft lip/palate, all the sets of cases and controls were available. The distributions of gender, maternal age at birth, and total dose with their percentages are presented in Table 1.

Conditional Logistic Regression analysis of mental retardation and cleft lip/palate was carried out to find out the risk of mental retardation/cleft lip/palate at different dose levels adjusting for the effect, if any, of gender and maternal age at birth of the study subject. The results are shown in Table 2. Statistical significance of the odds ratio (OR) obtained from the logistic regression was evaluated by confidence interval (CI). The odds ratio is statistically significant at the 5 % level if the 95 % CI does not include 1 (Khan and Sempos, 1989).

The p-value tests the null hypothesis that the coefficient is equal to zero (no effect). A low p-value (<0.05) rejects the null hypothesis, and indicates that a significant difference does exist. Specifically, a p-value of $P > 0.05$ refers to not statistically significant (i.e., no significant difference does exists), $P < 0.05$ refers to statistically significant, $P < 0.001$ indicates statistically highly significant. Table 2 shows that the p-values, in all cases, are >0.05, except the p-value of 0.003 ($P < 0.05$) for the relation of mental retardation with the dose group.

The obtained p-value of 0.003 ($P < 0.05$) for the mental retardation suggests a statistically significant relation with doses. Other data suggests no dose-related trend in the risk of cleft lip/palate (P ¼ 0.842). While all the ORs estimating the risk of mental retardation at different dose levels relative to the dose level of 1 mSv $y^{-1}$ were higher than 1. Neither gender of the study subject nor maternal age at birth appeared to have any impact on the mental retardation (P ¼ 0.108) of cleft lip/palate (P ¼ 0.631).

## 5. Conclusions

There exists a global concern on the biological and health effects of chronic low-dose radiation exposure and/or congenital malformations due to high external gamma radiation fields arising from the Natural High Background Radiation Areas. This work investigated the correlation between the incidences of certain congenital malformations through a 1:3 matched case-control study. A total of 75 subjects (58 mental retardation cases and 17 Cleft lip/-palate cases) along with 225 controls were selected for the investigations. While the external gamma radiation doses were measured by employing GM tube-based survey meter, the inhalation doses were measured using the solid-state nuclear track detectors. Conditional logistic regression analysis was used to find out the correlation between the radiation doses with the congenital malformation. Neither gender of the study subject nor maternal age at birth appeared to have any impact on the risk of mental retardation and cleft lip/palate. But, in the case of mental retardation, this study observed a statistically significant relation with doses. However, detailed nested case-control studies with major congenital anomalies that are very difficult to identify/diagnose are planned to be carried out.

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