SIGNAL OR NOISE?

INCIDENCE OF DOWN'S SYNDROME AND OTHER GENETIC ABNORMALITIES AMONG PEOPLE EXPOSED TO HIGH NATURAL RADIATION IN THE COASTAL VILLAGES OF KERALA INDIA

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The beach sands of four villages in Kollam district of Kerala state in South India have a rich deposit of monazite, a mineral containing radio-active thorium and uranium. The deposit has been subjected to commercial use for over 7 decades. The beaches have been inhabited by over 500 years. Majority of the people are traditional fisherfolk.

International attention was focussed on these villages in 1957 when WHO convened a meeting of geneticists to take stock of the then existing knowledge of radiation induced genetic disorders among humans. At that time, little was known about the incidence of spontaneous mutation among humans. The meeting recommended to undertake detailed studies of the normal population and communities receiving higher than normal radiation. The Kerala villages were identified as ideal setting for a long term genetic epidemiological study because :

There were sufficiently large number of people living in the strip for over several generations

The mean exposure is 700 mRad per year, a situation close to that of the radiation workers

A comparable control population live in coastal villages, south and north of the monazite belt. (WHO,1957) (1)

In 1959, another WHO expert committee discussed the modalities for a long term epidemiological study in the Kerala villages. This study has not been conducted so far. (WHO,1959) (2)

A team of experts from the All India Institute of Medical Sciences (AIIMS) reported a higher prevalence of Downs Syndrome, Severe Mental Retardation and chromosomal aberrations in the study area. Scientists from the Atomic Energy Establishment of India joined issue with Kochupillai and attempted to establish that the observed higher prevalence of Downs's syndrome in the exposed population is an artefact of wrong study design. This was refuted by the original authors in the pages of Nature. (Kochupillai et.al, 1976) (3). This debate has been summarised elsewhere.(VT Padmanmabhan,1987)(4)

Inspite of this positive finding, the WHO recommended study has not been conducted so far. Official committees still estimate the risk of radiation induced genetic disorders on the basis of animal findings. (BEIR 1986, UNSCEAR 1986) (5)

The Present Study

A cross sectional epidemiolgical study was carried out by us in four monazite villages and four comparable control villages in the neighbouring district. There are 38,000 people in 7,100 households in study area and 32,000 people in 5,300 households in control area. For the exposed people, there was no sampling involved since entire households of permanent inhabitants in a geographically compact region (separated from the main land by

lagoons and backwaters) were surveyed. The control households were selected to match with the study population on social variables like caste, class, religion and occupation.

The study area is 26 km long and has a mean width of 1 km. The strip, almost an island with the Arabian sea in the west and a backwater-canal system in the east forms part of four revenue villages, which is the lowest strata of the state bureaucracy. There is also a democratically elected local government (known as Panchayat), one each for every village. On an average, a panchayat has approximately 4000 households. A panchayat is again divided into five or more wards. Each house in the state is numbered by the local self government. This house number has been used as the identification mark of the household.

The study has been conducted as per the guidelines in WHO monograph of 1959 (mentioned earlier) and standard procedure for epidemiolgoical studies.

All the inhabited households within the study area were visited by investigators from the same village. They canvassed a schedule, pretested earlier in a comparable population. The first part of schedule sought socio-economic data, information on pregnancy outcomes of all ever married women, and details of migration. This part of the data set is retrospective.

In the second part of the schedule, there were 20 questions for eliciting information regarding genetic or congenital anomalies in the household. Those households reporting positive in the congenital part were visited by a trained nurse to collect more

para medical information and details of symptoms of the patient. The nurses' reports were scrutinised by the medical investigators. In this scrutiny, certain cases of acquired disabilities like polio were eliminated. All the remaining patients were subjected to clinical examination by either of the two investigators.

Cases where conclusive diagnosis could not be offered by the medical investigators were examined by specialists in respective branches of medicine.

Chromosome studies were conducted on peripheral lymphocytes of probands suspected to be suffering from chromosomal anomalies and their parents. Other investigations conducted include urinaminogram, X rays, audiograms etc.

Dosimetry.

Though an elaborate dosimetric study using thermoluminiscent dosimeters were conducted earlier (Ayengar et.al, 1971) (6), this data could not be used since the exact boundaries of the monazite belt has not been marked. Moreover the spatial diversity of the concentration of mineral necessitated a microlevel field dosimetric survey.

The levels of gamma radiation was measured by a portable gamma counter. The counter was calibrated at the Regulation Biology Laboratory of Saitma University, Japan and at the Nuclear Physics Laboratory, Calicut University, midway during the survey. About 2070 measurements were taken from 689 points at a height of 10 cm

and 1000 cm above ground. From each square kilometer of land surface, an average of 80 measurements from 26 points were obtained.

Findings

The details of gamma radiation exposure in different Villages are given in the table No.1

Table No.1.

Details of the Dosimetric measurments at Village levels.

	10cms above ground			1000cms above ground		
Village	Mean	Maximum	Minimum	Mean	Maximum	Minimum
Alappad	460.2	3685.1	57.0	528.5	3798.9	75.9
Panmana	428.4	3704.0	77.4	466.8	3743.4	62.8
Chavara	501.8	2656.4	121.2	602.4	3401.1	122.6
Neendakara	973.2	3390.1	102.2	1140.4	4329.6	129.2

In the study area the dose readings ranges from below 100 mRads to above 3000 mRads/year with a mean of 700 millirads/year. While all the control area readings are below 100 mRads/year.

Apart from the gamma ray measurements indoor beta measurements and internal dosimetry were also done. The results will be presented later.

Congenital and Genetic anomalies

The end points under investigation includes genetic disorders and congenital anomalies, untoward pregnancy outcomes like pre-natal loss, infant and child death. This report will focus on Down's syndrome, a chromosomal abnormality.

Down's Syndrome.

19 cases of Down's Syndrome were detected in the study area as against 5 in control area. All the parents of cases in study area are permanent residents of the study area. Karyograms were done on 5 patients from study area and 6 from control area.

The prevalence of Down's syndrome in the study area is about 3 times that of the control area. In order to make the data comparable with the background incidence of other centres, birth incidence will have to be estimated by projecting the total load at birth. This is done with standard life tables. No Data on survival chances of Down's Syndrome in Kerala or India is available. So, we have used the survival statistics of Collman and Stoller, which is based on a large sample from Australia.

Out of 19 observed cases of Down's Syndrome in study area, two are above 24 yrs. Inorder to estimate the birth incidence during the past 25 years (for which a near complete data is available), only cases below age 25 have been selected. 17 observed cases in study area will be survivors of a cohort of 41 live born. In the control area, the numbers are 5 survivors and 13 live borns.

All the live births of married women during the past 25 years have been computed from the fertility history. Data on surviving cases, estimated cases born and normal live birth to all married women during the past 25 years is given in Table No 2

Table No. 2

Down's Syndrome by Birth Place Dose in mRads

	100	500	500 +	Study Total	Total
Surviving Down's	5	8	11	19	24
Down's births	13	14	27	41	54
Total births	17292	8343	11575	19918	37210
Incidence	0.73	1.66	2.36	2.07	1.44

Children with trisomies would be more susceptible to radiation injuries and those living in the high radiation areas will have a higher mortality risk (Sasaki and Tommura 1969). Poverty related death will be higher among the poorer people. These factors have not been considered in projecting the Down's Syndrome birth and hence our rates would be on the lower side.

The incidences worked out for the control area and two dose groups of study area show a positive correlatiion with dose. The mean age of Down's Syndrome patients is 14.3 in Study area and 14.6 in control area as against 26.6 and 26.0 respectively for

the general population.

Other Congenital diseases

The other congenital anomalies detected were severe and profound mental retardation, epilepsy, congenital deafness, congenital blindness, cleft lip, cerebral palsy, congenital tallipes equino varus (CTEV), congenital heart diseases and muskulo-skeletal and other anomalies. All these except congenital heart diseases and CTEV show a higher prevalence in the study population. Further analysis to study the dose effect relationship and the incidences of sentiniel anomalies etc. are being carried out.

Discussion.

There have been several surveys of Down's syndrome at birth in Indian cities. These big cities subject their people to higher dose of chemical mutagens and also X rays. (Nearly half of the modern medical facilities in India are located in big cities with less than 10% of the nation's population).

There has been three studies of birth incidence of Down's Syndrome in Kerala state. Their results are reproduced below along with the present series. (Table No. 3)

Table No. 3

Birth incidence of Down's Syndrome in Kerala

Series	Total Births	Incidence of Down's
Calicut (1975)	3,721	0.00
Trivandrum (1975)	7,167	0.84
Kollam Trivandrum.(1990)	43,600	0.48
Present series - study area	19,918	2.07
Present series - control area	17,292	0.73

Sources:

1. Calicut - N.S. Nair and Mathai N.M., 1964 (7)
2. Suguna Bai quoted in N Kocupillai et.al,1977.(8)
3. K.P. George et.al, 1989.(9)

The first two studies were conducted at teaching hospitals, while the third also included two primary health centres, the district headquarters hospital at Kollam and the Medical College of Trivandrum. More than three fourth of the births took place in the Medical college, where there are qualified paediatricians. Chances of false negatives will be very lower.

The background incidence nearly halved between the second and the third survey. During the past two decades, Kerala state recorded a sharp decline in birth rate. Births to mothers below 20 years declined from 12% in the 70 to 9% during the later half of the eighties. The decline in births to elderly mothers has been much sharper with those in age group 30-35 registering a three fold

decrease during the same period.

The estimated birth incidence for the control area is 0.73 per 1000 live births which is 50% higher than the incidence in Southern Kerala. The control incidence however, is only slightly lower than the rate observed in Trivandrum and the aggregated incidence for 6 North Indian Cities during the mid seventies. (Verma and Singh, 1975)(10) Down's Syndrome survivors included in the study were born during the past two and a half decades, when the contribution of elderly mothers was higher than that of the late eighties.

Parental Ages.

It has been well established that risk for Down's Syndrome birth increases with maternal and paternal age. The maternal ages for Down's Syndrome in the present series is 34.6 years in the study area and 33.6 years in the control area. The mean maternal age for normal births is 25 years in both areas.

Comparative statistics on maternal age for normal births in the US and Hungary are given in table No.4. The contribution of younger and elederly couples to the redproductive pool in Kerala during the 80s is considerable lower than the US and Hungary. The comparatively lower incidence observed in our control series and the general population in Kerala can be partially explained by the difference in parental age.

Table No. 4

Percentage of births by maternal age groups

Age Group	Hungary	USA	This Series			
	1980s		70-74	75-79	80-84	85-88
< 15	0.1	0.3	0.0	0.0	0.0	0
15 - 19	10.7	14.8	11.0	11.1	9.4	7.4
20 - 24	38.0	33.2	35.7	40.8	47.7	52.3
25 - 29	33.2	31.0	23.4	28.7	29.2	31.5
30 - 34	13.5	15.7	17.2	11.0	9.6	6.9
35 - 39	3.8	4.3	9.9	6.2	3.0	1.6
40+	0.68	0.71	2.7	2.3	1.1	0.3
Total	100	99.99	100	100	100	100

Conclusion.

Genetic risk of radiation has been seriously underplayed by the standard setting agencies. The US National Academy of Sciences and the UN Scientific Committee of Effects of Atomic Radiation base their risk estimates on results of animal experiments. The genetic doubling dose estimated by these official committees is 100 rems during the reproductive span. All the major studies which form the basis for working out the background incidence of genetic diseases have been conducted in cities of the Northern countries. A host of factors like the chemical mutagens in the

air, water and food, high rate of exposure to medical radiation (often unnecessary) and life style factors like use of contraceptive pills will be rendering the people in the urban industrialised milieu more susceptible to trisomies and other genetic disoders. Incidentally, while the maternal age has registered a decline in these societies, the incidence of Down's syndrome has remained constant. (Matsunaga and Fujita, 1977) (11)

A detailed prospective study of all pregnancies in Kerala radiation belt will, still yield valuable information on radiation and human genetics.

Conclusion: Le risque génétique des radiations a été gravement sous-estimé par les agences qui fixent les normes. L'académie des Sciences américaine et l'UNSCEAR basent leurs estimations du risque sur des résultats d'expérimentations animales. La dose de doublement pour ces effets génétiques estimée par ces agences officielles, à 100 rem durant la période de fertilité. Toutes les + importantes études qui forment la base des ~~l'étude~~ de recherches sur l'incidence des maladies génétiques en rapport au rayonnement naturel, ont été menées dans les villes de l'hémisphère Nord.

De nombreux facteurs, comme les mutagènes chimiques dans l'air, l'eau et l'aliment°, les hauts niveau d'exposit° aux Rad° Médicales (et inutiles) et des données de civilisation comme l'usage de la pilule contraceptive rendent les habitants des milieux urbains plus susceptibles de présenter trisomies et autres désordres génétiques. Incidemment, alors que l'âge maternel montre une diminution dans ces sociétés, l'incidence du . de Down est resté constant.

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