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LETTER TO THE EDITOR

Premature Greying of Hairs, Premature Ageing and Predisposition to Cancer in Jajjal, Punjab: A Preliminary Observation

HALDER A

Sir,

Reproductive, developmental, and neoplastic disorders due to occupational pesticide exposure are an international issue [1],[2]. There has been increasing anxiety following several media reports concerning health-related problems such as cancer, infertility, malformation, abortion, developmental delay, etc. in Punjab, particularly in Jajjal of Bathinda [3–6]. Punjab Pollution Control Board and Post Graduate Institute of Medical Education and Research, Chandigarh, have reported through press a close association between environmental pollution and cancer in Jajjal [7],[8]. To assess the authenticity of above reports this preliminary survey was carried out.

A preliminary survey was undertaken during a documentary film production for Public Service Broadcasting Trust on the issue of pesticides (granted by the Ministry of Environment, India), to assess the authenticity of reported health effects, in particular reproductive and cancer, in Jajjal village of Bathinda, Punjab. Observations were gathered on reproductive and other health effects, using both qualitative and quantitative methods. The qualitative phase consisted of brief interviews (volunteered to provide information) in school, market, medical clinic, and club from

farmer, shop keeper, school teacher, alternative medical personnel, student, and unemployed in Bathinda (city and several villages) for any noticeable medical disorder. In the quantitative phase, data were obtained from randomly selected 15 families (from both higher and lower socioeconomic group for equal representation, i.e. random stratified) consisting of 596 individuals, from Jajjal village (most severely affected village). Information was obtained on current age, gender, age at menarche, age at puberty, infertility, time to pregnancy, sex determination, family size, contraception, abortion, malformation (particularly cryptorchidism, hypospadias, and neural tube defect), stillbirth, postnatal death, mental deficiency, age of menopause, premature greying of hairs (more than 50% greying of scalp hairs before the age of 40 years), premature ageing (more than 10 years older in appearance than corresponding chronologic age), cancer, hypertension, diabetes mellitus, joint pain, and any other significant problem. Information was also obtained on source of drinking water. Survey was assisted by village chief, school head master, and two local non-government organisations. Consent (verbal) was obtained for the use of data, including photograph and video recording for academic use and video documentary.

The age range of survey population was between <1 and 92 years. There were 330 males and 266 females, i.e. overall sex ratio of 806 (i.e. skewed). Premature greying of hairs [9] was seen in 28 individuals (4.7%) of both sexes (23 males and five females) and as early as 10 years of age ([Table/Fig 1A, B]). Premature ageing was seen in 19 males (3.2%) ([Table/Fig 2]).

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There were eight cases (four males: parotid, larynx, stomach and multiple myeloma; four females: breast, cervix in two, and bone) of death due to cancer in last 10 years. There were 118 boys between 13 and 23 years of age and 15 failed to show puberty (voice change and moustache; enlargement of external genitalia also failed in four cases); however, growth spurt was normal. There were 85 girls between the age of 13 and 20 years. All except five girls had started menstruation before completion of 15 years. There were seven cases of infertility, 10 cases of neonatal and infantile death (five males

, five female), four cases of mental sub-normality, five cases of diabetes mellitus, one case of cryptorchidism, and one case of spina bifida.

Excess of cryptorchidism, hypospadias, congenital malformation (including neural tube defect), spontaneous abortion, prenatal sex selection, infertility, early menarche, and early menopause were not observed in the preliminary surveyed population.



(A)



(B)

[Table/Fig 1] Premature greying of hairs in an 11-year-old boy (A) and a 12-year-old girl (B).



[Table/Fig 2] Premature ageing in a 44-year-old man (left). His 74-year-old uncle (right) is provided for comparison.

Premature greying of hairs, premature ageing, and increased cancer deaths were observed in the survey. Greying of hairs was due to varying degree of admixture of white and black hairs and not uniformly white as seen with albinism. Furthermore, there was no pigmentary change in skin or eyes. Greying of hairs is under-reported, as most affected individuals (adults) use hair dye to prevent social stigma, discrimination, and difficulties in marriages. Although greyness of hair in the survey was not quantified, however, it was obvious, noticeable, and appreciable. Most of the observed cases (19/29) of premature greying of hairs in the survey were from healthy school-going children, as they were not aware of discrimination later on. The perception of grey hair derives in large part from the admixture of pigmented and white hair in most cases; however, in some individuals it was from pigment dilution. It is possible that melanocytes from grey and white hair follicles can be induced to pigment in vitro [9]. Spontaneous re-pigmentation was seen in one case following migration from the village, thus indicating local

environmental factors as likely explanation. It is also supported by appearance of grey hairs in two sisters few years after marriage in the village. Hair greying may be caused by defective self-maintenance of melanocyte stem cells [10] or reactive oxygen species-mediated damage to nuclear and mitochondrial DNA or through the exposure of environmental toxicants [10].

Ageing has a variety of definitions and implications depending on one's perspective; thus, phenotypes include extremely diversified clinico-pathological conditions [11]. In this study, premature ageing was considered when an individual was apparently looking more than 10 years older than the chronological age, mainly based on greying of hairs, alopecia, skin wrinkling, and overall appearance. As the nature of the study was a preliminary survey no attempt to examine biomarkers (glucose, insulin, ATP, and reproductive hormones, in particular dehydro-epiandrosterone sulphate, reactive oxygen species, β -galactosidase, etc.) or radiologic markers (osteopenia/osteoporosis, soft-tissue calcifications, etc.) or other markers (atherosclerosis, hypogonadism, atrophy of organs, etc.) of ageing were made. Premature ageing (excluding genetic progeria syndromes) commonly refers to the unnatural acceleration of the natural ageing process primarily due to damage (faulty genome maintenance) from sun exposure, other environmental assaults (radiation, chemical toxins, metal ions, free radicals, hydrolysis, glycation, etc.) and an unhealthy lifestyle. Premature ageing was not expected before the survey. There are two major theories of ageing, i.e. evolutionary and damage based [12]. The former is natural selection and favours a genetic composition. Second theory is based on accumulated cellular damage over a time and mainly environmental. Reactive oxygen species (ROS), the by-products of cellular metabolism, have long been regarded as the principal intrinsic effector of cell damage [13]. An emerging consensus is that ageing is a consequence of macromolecular damage by ROS, which oxidise lipids, proteins, and DNA, with damage to the DNA leading to mutations and chromosomal abnormalities [14]. In some instances, this could irreversibly affect important functions of the cell without causing cell death, i.e. cell senescence. The p53 protein plays a vital role in maintaining cell cycle (cell-cycle inhibitors). A defective p53 protein leads to increased cancer susceptibility, while higher

than normal levels contribute to premature ageing [15], through apoptosis-mediated cell death and/or cell senescence.

There were eight cases of cancer death in last 10 years. This gives a frequency of 134 cancer deaths per lakh per year. This incidence is higher than expected (~50 per annum per lakh) [16],[17]. From a study [17] of house-to-house survey in Bathinda, cancer prevalence was found as 103 per lakh in Talwandi Sabo (107/85315) and cancer deaths as 52 per lakh per year. The same study [17] also reported higher level of heavy metals (viz. arsenic, cadmium, chromium, selenium, and mercury) and pesticides (viz. heptachlor, ethion, and chlorpyrifos) in drinking water, vegetables, and blood in the region. Several reports have found association of cancer with environmental pollution, viz. arsenic with leukaemia, radiation with cancer of bone/soft-tissue/blood/lymphoid tissue, and pesticide with cancers of thyroid/breast/uterus/prostate/testis/lymphoma/leukaemia [18],[19]. Lung cancer was reported with exposure to silica, asbestos, chromium, nickel, and radon [20]. Preliminary survey supports reports of excess of cancer deaths in Jajjal.

This preliminary survey finds, for the first time, many unreported health effects in Jajjal. These are premature greying of hairs and premature ageing. Survey supports reports of excess of cancer deaths. Genomic instability, cancer, and accelerated ageing (premature ageing and premature greying of hairs) are interrelated. All these health effects can be explained by one hypothesis, i.e. "derailed genomic integrity following exogenous insult". A large-scale epidemiological survey is warranted to validate the findings and if so then study to find out reason and prevention.

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