

Studies on Endosulfan Pesticide Induced Health Complications on Human Populations: A Review

¹Ashok Patil, ²Jai Prabhakar S C

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Author's Affiliations: ¹Research Scholar, ICSSR Fellow, Department of studies in Anthropology, Karnatak University, Dharwad580003, Karnataka, India, ²Assistant Professor, Centre for Multi-disciplinary Development Research, Dharwad580004, Karnataka, India.

Corresponding Author: Jai Prabhakar S C, Assistant Professor, Centre for Multi-disciplinary Development Research, Dharwad 580004, Karnataka, India.

Email: anthroprabhakar@gmail.com

Abstract

India is an agrarian country where agriculture provides a principle means of livelihood for about 60% of the country's population. In many developing countries, agriculture forms the major economic output is dependence on cheaper crop protection agents like pesticides for the greater field. This leads to the probability of the persistence of pesticide residue in various ecosystems. In India, the use of synthetic pesticides has started in 1948. Among the various pesticides, Endosulfan belongs to the organochlorine group under the cyclodiene subgroup of organochlorine insecticides. It was introduced in the year 1950 and emerged as a leading chemical used against a broad spectrum of insects and mites in agriculture and allied sectors as a pesticide. It is one of the Stockholm listed persistent organochlorine pesticides, which was widely used in India against various pests of agriculture and plantation crops. Its low solubility limits are biodegradation in the water and soil. It is acutely toxic and has been implicated in many cases of poisoning, fatalities, and chronic effects including cancer and impacts on hormonal systems, etc. Indian history has witnessed many tragic events related to pesticides and other hazardous chemical usages by taking into account health conditions. The hazardous toxic chemical compound of Endosulfan resulted in many health complications on human beings, animals, and the environment. It calls for the interventions as many studies emphasizing the need for special attention from the government agencies and voluntary organizations to improve the overall health status of the Endosulfan pesticide affected victims.

Keywords: Endosulfan; Organochlorine; Hazardous; Disorders; Toxic chemicals; Rehabilitation; Health complications.

Introduction

In India, agriculture is the largest economic sector provides a principal means of the primary source of livelihood for about 58% of the country's population and contributes about 22% of the GDP and the share of agriculture and allied sectors in Gross Value Added (GVA) of India at current prices stood at 17.8 % in the financial year of 2020.

Economic Survey of India 2020-21 report stated that in the financial year of 2020 and the total food grain production in the country was recorded at 296.65 million tonnes up by 11.44 million tonnes compared with 285.21 million tonnes in the 2019 financial year (APEDA, 2021). The total agricultural area coverage under food grains in

2007-2008 was about 124.10 million hectares, which recorded a crop production statistic of 230.67 million tonnes. In this target achievement, plant protection plays a major role especially against various pests, and over recent years, there was a considerable increase in plant-protecting chemicals like pesticides due to an increase in cultivable areas and fast-changing cropping patterns. Since 2000 BC, human beings have the knowledge of pesticides and they have used this pesticide to protect their crops and it is extensively used in the Indian agricultural sector and the USA in crops such as cotton, potatoes, tomatoes, mangoes, cashews, etc. and but the use of pesticide in the USA is gradually being phased out. Endosulfan is one of the extremely effective insecticides and one of the most toxic chemical pesticides on the global market and is responsible for fatal pesticide poisoning incidents around the world (Pan Magazine, 2006). At the global level, the average pesticide consumption is about 0.5 Kg per hectare in India and occupies a tenth place.

In India, there are about 125 basic pesticide producing industries and 500 formulation industries among the formulations produced, and in total production, the dusting powder has the 85% of the share and according to the central insecticide board [section of 9(3) of the insecticides acts 1968, amended on 20th August 2014] where 246 pesticides were registered for use in India and of which 13 are restricted for usage. Among the registered pesticides, insecticides consumption covers about 69.39%, fungicides 19.06%, herbicides 16.75%, and others by 2.80% (Shetty et al, 2008). In a developing country like India where agriculture forms the major economic output, dependence on cheaper crop protection agents, as pesticides are more usage, therefore the probability of persistence of pesticide residue in various ecosystems would be more in a country like India and witnessed in many tragic events related to pesticide usage. The usage of synthetic pesticides has started in India in 1948 and production started in 1952 with the setting up of the BHC production plant at Rishra in Kolkata and the Dichloro Diphenyl Trichloroethane (DDT) and Benzene Hexachloride (BHC) are the first used chemical pesticide. In India, organophosphates have found the least application as an organochlorine pesticide (regarding the type of usage, insecticides) come first, which is followed by herbicides and fungicides. On a global level market, herbicides are the leading one that comes about 50% and in its consumption is 15%. Pesticides are organic chemical compounds that have more applications in the field of agriculture and its allied sectors. This insecticide has a wide range of applications against various crop pests used in the agricultural

sectors. Endosulfan pesticide is an organochlorine insecticide belonging to the cyclodiene group and it is extensively used in the agricultural sector to protect crops (Li et al., 2009). Among the various organochlorine pesticides, Endosulfan is the most extensively used insecticide in India. Endosulfan pesticide was first introduced in 1950. Endosulfan chemical emerged as a leading pesticide in broadspectrum extensively used to control insects and mites in agriculture and its allied sectors (Harikrishnan et al. (2004); Greeshma (2017). and third largest selling insecticide worldwide (George et al, 2012). Endosulfan pesticides are a contact insecticide and acaricide registered for use on a wide variety of fruits, cereal grains, cotton, vegetables, ornamental shrubs, vines, and ornamentals, etc. in agriculture (PubChem, 2021). Endosulfan is sold under the trade name of Thiodan®, which is a mixture of 70% Endosulfan- α (Endosulfan I) and 30% Endosulfan- β (Endosulfan II) (Richard et al., 2010). Endosulfan is available in two different formulations 35% Emulsifiable Concentrate (EC) and wettable powder as Endosulfan, Thiodan, Thionex, Endosan, Farmoz, Nufarm, etc. The IUPAC name of the Endosulfan is (1,2,3,4,7,7-hexachlorobicyclo-2,2,1-heptene-2,3-bis-hydroxy methane-5,6-sulfite) is a mixture of two stereoisomers of α and β Endosulfan, in the ratio of 7:3. It is extensively used throughout the world to control the pests on different crops (Verma et al., 2011). The Endosulfan sulphate is the main degradation product of both isomers with equal toxicity and is itself more persistent in the environment than its parent compounds. It has a distinct odor similar to turpentine. The solubility of Endosulfan in water is 0.33 mg/L and with half-life is a period of more than a hundred years and is broken down by hydrolysis, photolysis, and biodegradation. (Greeshma, et al. (2017). Endosulfan diol, Endosulfan lactone, Endosulfan ether, etc are some of the other byproducts of the Endosulfan pesticide and are depended on the formulation concentration. Although the Endosulfan isomers are fairly resistant to photolysis, the breakdown products are susceptible and on plant surfaces rapidly degrades to their metabolites. It is fairly immobile in soil and is highly persistent (Endosulfandioli, Endosulfan sulfate, and Endosulfan lactone) (Greeshma, et al., 2017) and considering the level of toxicity nature the Environment protection agency (EPA) of the USA and the European Union classifies Endosulfan as category Ib-highly hazardous and WHO also classifies as category II-moderately hazardous. Industrial Toxicological Research Centre, Lucknow classifies Endosulfan as extremely hazardous (Anon, 1989). The classification is mainly based on the LD50 value

for acute toxicity generated by the producer company (Paul et al, 1995).

In India, the toxic remains of the Endosulfan were detected in air, sediments of the soil, surface and groundwater, aquatic water, sediments and water in Ghana (Mensah et al, 2011), and shallow groundwater in Pakistan, river water in China (Jabbar, et al, 1999), lagoons in Spain (Hongliang et al, 2012) ground and well waters in the Philippines (Cerejeira et al, 2003) and coastal, estuarine, river sediments in Israel, soil and water in Benin, Malawi, Nigeria and from drinking, ground, surface, and marine waters in South Africa (Fatokia et al, 2004), sediments of the soil in Benin, Nigeria, Sudan, and Zambia, sediments in Benin and Nigeria, vegetation in Madagascar, Zambia and Ghana, Paddy fields in Mediterranean, water from remote mountain lakes in Europe and river and seawater in South East Asia, etc (Poza et al, 2004). The persistence of Endosulfan in the environment in different two stereoisomers and also depends on the medium it gets deposited and within two stereoisomers, β Endosulfan isomer is more persistent than stereoisomers of α Endosulfan isomer (Greeshma, et. al. (2017). Endosulfan is one of the highly persistent hazardous, harmful organic pollutants. It is banned from use and manufacture under the Stockholm Convention (EHA, 2007).

Observed Health Complications of Endosulfan Usage

Endosulfan is extremely hazardous and toxic nature impacted more adversely on the environment, humans, domestic and wild animals. World health organization has estimated the worldwide annual production of Endosulfan to be about 9,000 metric tonnes (t) in the early 1980s. From 1980 to 1989, worldwide consumption averaged about 10,500 tonnes per year, and for the 1990s use increased to 12,800 tonnes per year (WHO, 1984) and the harmful, hazardous toxic nature is responsible for many fatal pesticide poisoning incidents around the world and the adverse impacts made it ban by many NGO's and agencies (Pan magazine, 2006). It is also a xenoestrogen a synthetic substance that imitates or enhances the effect of estrogens and it can act as an endocrine disruptor, causing reproductive and developmental damage in both humans and on animals and found to act as an aromatase inhibitor (Anderson, et, al. 2002). The many research studies were done on where Endosulfan chemicals can cause cancer is about consumers' intake of Endosulfan from residues on food. The food and agriculture organization of the United Nations has concluded that the long term exposure from food

is unlikely to present a public health concern, but short term exposure can exceed acute reference doses (WHO, 2006). The clinical signs of acute exposure to chemical pesticides include hyperactivity, salivation, respiratory distress, tremors, hunching convulsions, nausea, unconsciousness, permanent brain damage, coma, and death (WHO, 2004). In subcontinent India, incidences many hazardous and harmful toxic chemical disasters. Bhopal gas disaster in 1984, a fire in an oil well in Andhra Pradesh in 2003, a vapor cloud explosion in HPCL, Vishakhapatnam in 1997, an explosion in the IPCL gas cracker complex, Nagothane, Maharashtra in 1990 and other 20 major chemical accidents have been reported in MAH units during 2002–2006 (Trivedi, et, al. 2014) are some of the major. The supreme court of India passed an interim order on May 13, 2011, which banned the production, distribution, and use of Endosulfan.

Findings from the Various Research Studies

Many researchers from varied disciplines have conducted studies around the world on pesticide usage. Pesticides are used to control the harmful insects which harm crops. Many adverse impacts from these toxic chemicals on human beings, animals, and the environment are noticed in varying degrees across the globe. Many of these studies call for the need for the greater assessment of Endosulfan victims from other lesser known parts of the country. *Suresh Tet. al., (2019)* conducted a study on the impact of Endosulfan, an organochlorine pesticide, which is a broad spectrum contact insecticide widely used in pest control. Bleeding on probing was present in all the participants. Micrognathia, Macroglossia, and Fissured tongue were the main features observed in the study. The overall oral health status was found to be unsatisfactory due to the disabilities of the Endosulfan. *Heong et. al. (1994)* highlighted the excessive usage of insecticides in the rice fields of the Philippines and Vietnam to control the harmful insects which affected the crops. The majority of pesticide applications by rice farmers in the Mekong Delta, Vietnam, and Leyte, Philippines, were insecticides. The research has shown that leaf feeder control generally does not increase yields, a large proportion of insecticides currently used may be unnecessary. *Harriet et. al. (2012)* studied the persistence of organochlorine pesticide residue in the sediment and water from the Densu river basin of Ghana. The evaluation was based on the levels of distribution of organochlorine pesticides residues in the aquatic ecosystem of the Densu River and the three sediment samples in different locations to identify the varying levels of pesticide concentration in

water. The results indicated significant differences for most organochlorine pesticide residue in the samples of the sediments from the various locations and some of the organochlorine chemical pesticides levels detected in the water samples were relatively high as per the values set by WHO and Australia. *Khan (2012)* studied the Impact of Endosulfan on human beings, marine life, and the environment the study discussed the nature of hazards and toxicity of the Endosulfan pesticide and on oxidative stress and its biodegradation. The study found that the major health complications on human organs like the ovary, enzymes, hormones, DNA damage, and apoptosis. *Harikumaret. al. (2014)* conducted a study to explore the persistence of Endosulfan pesticide residues in selected areas of Kasaragod district, Kerala. The study found that the persistence of Endosulfan in the sediments showed variations depending upon the climatic conditions and physicochemical characteristics such as pH, organic matter content, and particle size of the soil in the selected area. *Karataset. al. (2006)* study was conducted to know the nature of health complications from Endosulfan poisoning cases in 23 students. Primary symptoms noticed such as nausea and vomiting in 17 patients (73.9 percent), Seizures in 5 patients (21.7 percent), and Dizziness in 1 patient (4.3 percent) for different periods for several days and all patients were treated symptomatically by intravenous diazepam for controlling seizures. The health problems caused by Endosulfan poisoning can be suspected in the presence of primary central nervous system (CNS) manifestations including seizures, with or without clinical or laboratory evidence of other organ dysfunction such as liver failure. *Alonso et. al. (2020)* considered the impact of hazardous chemical pesticide Endosulfan on the ecosystem of marine water and the toxic contamination in air, soil, marine, and groundwater. The toxic and harmful to beneficial non target invertebrates, aquatic life, and even humans upon consumption. Endosulfan is a dangerous pesticide since it biomagnifies quickly in the food chain. The anticipated outcome results suggested a low pesticide concentration activates the acute response in Physella acute by affecting detoxification and stress responses and altering endoplasmic reticulum function and lipid metabolism. Furthermore, the newly identified genes extend the number of processes and cellular locations that can be analysed in this organism. *Dayakar et. al. (2015)* assessed the health complications from Endosulfan pesticide caused severe neurobehavioral disorders, congenital malformations in female subjects, and the abnormalities related to the reproductive system of males. The results showed that there was no

abnormality in terms of extra oral appearance and oral mucosal characterizes none of the study subjects had either enamel hypoplasia (Dental fluorosis). The overall periodontal status among the studied subjects was considerably poor and the 5 subjects were not recorded because of <15 years of age and 5 subjects had a score of one which implies bleeding on probing, 2 subjects each had a score of three and four stating pocket depth 4-5 mm and more than 6 mm, respectively and seven subjects had a score of one of loss of attachment which implies 0-3 mm attachment loss and six subjects with score 2 which implies attachment loss of 4-5 mm. In many of the observed subjects were suffering from major medical problems such as mental retardation and the overall health status of the affected victims was reported to be poor. *Moses et. al. (2010)* study was conducted to know the acute intentional toxicity produced by the Endosulfan and other organochlorines chemical substances. The clinical features, course, and outcomes among patients with acute Endosulfan poisoning requiring admission to the hospital for 8 years (1999-2007) were reviewed among 34 patients, hospitalized during this study period for alleged organochlorine poisoning. During the study, 16 patients with Endosulfan poisoning were identified. The majority (75%) received initial treatment at a primary or secondary centre. Neurological toxicity predominated, particularly low sensorium (81%) and generalized seizures (75%), including status epilepticus (33%). Hepatic transaminase elevation, azotemia, metabolic acidosis, and leukocytosis, and other features are observed. The study showed that there was a need for mechanical ventilation in 69% and vasoactive agents in 19%. In hospital mortality of 19% was observed that there were no gross neurological sequelae at discharge. In three other patients who presented with organochlorine poisoning, the compounds ingested were lindane, endrin, and dicofol (n = 1 each). The course and outcomes in these patients were unremarkable and all three patients survived and Endosulfan is capable of high lethality and significant morbidity. The commonest manifestations were neurological although additional organ dysfunctions were also observed. *Patocka et. al. (2016)* made a study on the destructive nature of Endosulfan pesticides. The destructive chemical properties of Endosulfan resulted in more health complications on female hormone estrogen, liver tissue injury, reproductive complications, and other developmental injuries. The persistent lipophilic compound is one of the most abundant organochlorine chemical pesticides. In the environment and capable of undergoing long range transport to remote locations such as the Arctic and usually, these chemical compounds are insoluble in water for

several years, but are readily adheres to clay particles and persists in the soil, water deposits and due to extreme toxicity nature of Endosulfan considerably increased the health risks on human beings and when these chemical contaminants are swallowed accidentally from food, water and in suicidal poisoning cases. *Sunita (2017)* stated that the impact of harmful pesticide Endosulfan on the health of the affected victims. Endosulfan pesticide was sprayed aerially on cashew farms for 20 years by the Government of Karnataka with the help of Karnataka Cashew Development Corporation to kill Tea mosquitoes in the cashew's forms between 1980 and 2000. Use of Endosulfan pesticide in agricultural fields as pest control resulted in severe health complications such as fatal anomalies, genetic disorders, severe mental problems, infertility of primary and secondary, damage to eyesight, cancer, physical disability, endocrine disorders, kidney problems, and other major health problems in the year 2011. But initially, no compensation has been paid to the affected victims and there is not enough rehabilitation centre for facilities, a day-care centre for treatments, care, and caretaker for the affected victims. The concerning state government authority gives a monthly pension of Rs 3,000 for those affected and bears with more than 60% physical disability and Rs 1,500 for those with 25-59% physical disability, but the requirement is far more with concern to their health complications, day to day problems facing by the victim's family and on caretaking expenditure like hospital and social. *Sharma et. al. (2019)* conducted a study to know the level of Endosulfan among the women in Talwandi Sabo Block of Southern Punjab a cotton belt of Malwa region, India and owing to the pesticide beneficiary of north India. The assessment was made to identify the levels of Endosulfan in the blood samples of women working in agricultural activities such as cotton picking, dilution of chemical pesticide concentrates and home storage, cloth washing work, etc. The levels of Endosulfan metabolites in the twenty active female workers were done with the help of a gas chromatograph an electron capture detector device and the mean of the level of the presence of Endosulfan toxic contaminations in the tested population are recorded and observed and is found to be 2.22 ppb. Detection of even very low concentrations of Endosulfan residues signifies its continued access to the women population. *Sharma et. al. (2011)* study conducted to know the High anion gap refractory metabolic acidosis as a critical presentation of Endosulfan poisoning. The study observed the characteristic clinical signs following acute exposure are indicative of CNS disturbances and overstimulation. Mortality and morbidity rates were high and there is no specific antidote.

The pulmonary toxicity associated with Endosulfan poisoning has been reported. The major symptoms from Endosulfan poisoning were due to the involvement of the CNS and severe metabolic acidosis and suspected unknown poisoning in the presence of primary CNS manifestations and other organ dysfunctions such as liver failure and high anion gap metabolic acidosis in tropical nations like India. *Embrandiriet. al. (2012)* a study conducted to know the frequency of prevalence of health problems in residents of the Endosulfan affected areas of Kasaragod district, Kerala. After the ban on the use of Endosulfan in agricultural fields by government agencies in Kerala by Plantation Corporation of Kerala and the epidemiological study on the health effects of Endosulfan spraying on cashew plantations in Kasaragod. The researcher analysed the interviews of thousands of Endosulfan affected victims. In the observed samples that in 0-30 age group victim's samples, were recorded the highest cases of mental retardation with 79.5% male and 74.1% females and also, in the 0-14 years age group 46% males and 42.5% females had congenital anomalies whereas, in the 15-30 years of age group 30.4% males and 31.7% female cases were recorded as with the case of cancer, 39.2% had mostly lung, throat or prostate cancer, whereas, 35.4% females had breast, ovarian or blood cancer. *Venkateswarlu et. al. (2000)* study was conducted to know the clinical profile of Endosulfan poisoning and also to identify any biochemical parameters which indicate clinical or subclinical dysfunction of organs so that the offending agent can be easily identified in a given case of poisoning and the appropriate treatment. In the present case history, 44 individuals who consumed food that was accidentally contaminated by Endosulfan chemicals in a rural area were considered as the subjects of the study and except for the one who died. The rest of the 43 individuals were examined by the authors. The detailed case histories regarding the item of food taken and quantity consumed were recorded and they estimated and calculated the routine biochemical parameters like CBC, blood urea, serum creatinine, serum electrolytes, LFT, S Calcium, S Phosphorus. In total patients, 14 were admitted into this hospital and seven of the patients were available for follow-up, abnormal laboratory parameters initially were repeated and the anticipated outcome results in examining the patients revealed that vital signs were stable and there was no jaundice and the CNS examination showed varying grades of altered sensorium, normalized pupils briskly reacting to light, normal oculocephalic reflex and were no lateralizing signs like hemiparesis. Planters were bilateral extensors,

signs of meningeal irritation. The complete blood counts, blood sugar, urea, serum creatinine, serum electrolytes were all normal in these cases and liver function tests in the form of SGPT, SGOT was abnormal and serum bilirubin levels were normal. The values of SGOT and SGPT returned to normal at the end of six weeks during treatment and a post-mortem examination carried out on the individual who died due to status epilepticus confirmed that the death was due to asphyxia and the study concludes that the health complications from the Endosulfan poisoning can be suspected by the primary CNS manifestations with or without clinical or laboratory evidence of other organ dysfunction like liver, kidney, and muscle. *Pathaket.al. (2008)* conducted a study is Humans are exposed to various environmental chemicals such as organochlorine pesticide residues, heavy metals, polychlorinatedbiphenyls (PCBs), etc. There is a paucity of data regarding the present blood levels of organochlorine residues in the North Indian population concerning reproductive health. The present study was designed to analyze the levels of organochlorine pesticide residues in maternal and cord blood samples of normal healthy women with full-term pregnancy to gain insight into the current status of pesticide burden in newborns. Hexachlorocyclohexane (HCH) contributed maximum towards the total organochlorine residues present in maternal and cord blood followed by Endosulfan, pp' DDE, and pp' DDT being the least. This is also the first report indicating Endosulfan levels in this population. The data indicated a transfer rate of 60-70% of these pesticides from mothers to newborns and this high rate of transfer of pesticides is of great concern as it may adversely affect the growth and development of the newborn. *Gude et. al. (2012)* study conducted on Endosulfan toxicity could precipitate gargantuan jeopardy and may result in irreversible and fatal damage. The spectrum of involvement may range from mild nausea, vomiting, and anxiety to intractable seizures and multiorgan damage resulting in death. A case of Endosulfan poisoning complicated by multi organ dysfunction, cardiac arrest, and death were also reported. Endosulfan poisoning is a devastating catastrophe with very high mortality and there is no antidote available, aggressive supportive treatment remains the mainstay of management.

Conclusion

Pesticides are hazardous toxic chemical compounds that resulted in many health complications on human beings, animals, and the environment. Endosulfan is an organochlorine insecticide widely used in the agricultural fields as

an insect controller and one of the acute neurotoxic chemical compounds that accounted for numerous severe poisonings and fatality cases in human beings as well as animals. The review of multiple studies found that the hazardous chemical Endosulfan caused several adverse health complications in the daily life of poor people. The government intervention is far from satisfactory levels, as many other studies emphasize the need for special attention from the government and other non-governmental organizations to improve the overall health status of the Endosulfan affected victims.

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