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Organochlorine Pesticides in Human Placenta: A Threat for Prenates

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Abstract: Organic substances that are persistent, bioaccumulative and possess toxic characteristics which are likely to cause adverse effects on human health and environment are called PBTs (Persistent, Bioaccumulative, Toxic substances). Depending on their mobility in the environment, PBTs could be of local, regional or of global concern. Subclass of PBTs, so called as POPs (**P**ersistent **O**rganic **P**ollutants) is group of compounds, which are prone to long-range atmospheric transport and deposition. Organochlorine pesticides (OCPs) belong to the category of POPs and are extremely and extensively persistent and toxic compounds. OCPs are the main culprits of the environmental pollution because of their long persistence in the environment and their ability to become concentrated along the food chain reaching higher concentration at higher trophic level. Since, men is located at the top of the food chain, he receives and accumulates OCPs residues that vegetables and animals have stored up in various periods of development. Being lipophilic in nature, they may accumulate in the fat rich tissues and fluids of humans and animals. A number of OCPs used in different national programmes seem to be accessible to human beings through different routes of exposure, with digestive tract being the main. After the absorption, OCPs are circulated in the blood and then distributed to different organs and tissues where they get accumulated in accordance to the fat content of the tissues. Placenta serving as a barrier between mother and baby for large number of endogenous and exogenous substances contains appreciable content of fat and hence can serve as a carrier for lipophilic xenobiotics, including OCPs. There are many reports from India and all over the world giving an idea about the concentration of detectable OCPs in the placenta of a woman, but no such report is available from Pink City of India, Jaipur. A study was, therefore conducted in the Jaipur, Pink city of India and capital of Rajasthan to assess the OCPs residues in the placental tissue of women, using gas liquid chromatography. The results revealed the presence of isomers of HCH, heptachlor, DDT and its metabolites and Aldrin in the samples analyzed. In the present findings, concentration of Aldrin, total HCH, total heptachlor and total DDT were found 122.2, 170.6, 1058.6 and 99.9 ppb respectively in placental tissue. The data is further stratified with respect to dietary habits, age, different habits of pesticide use, weight and parity. The OCPs residues present in the placenta indicate the pesticide burden in the human population, which in turn is a risk to human health. Secondly, this may be considered as an indication of the transfer of these chemicals from maternal to fetal circulation across the placenta which may pose various problems of management of prenatal health.

Key-words: Placenta, Organochlorine, Contamination, Residues, Gas Chromatograph, Prenates

Introduction

The large-scale use of persistent organochlorine pesticides in modern agriculture has caused serious concern because of their residual presence in the environment. Pesticides can be defined as any substance or mixture of substances deliberately added to the environment and intended for preventing, destroying, repelling, or mitigating pests. Pesticides may be more specifically identified as insecticides (insects), herbicides (weeds), fungicides (fungi and molds), rodenticides (rodents), acaricides (mites), molluscides (snails and other mollusks), miticides (mites), larvicides (larvae), and pediculocides (lice). In addition, for regulatory purposes, plant growth regulators, repellants, and attractants (pheromones) often also fall in this broad classification of chemicals. Pesticides are not always selective for their intended target species, and adverse health effects can occur in non-target species, including humans.

Persistent organic pollutants (POPs) are chemical substances that resist to environmental, chemical, physical and biological degradation; because of their characteristic persistence, they are transported through air, water and migratory species across international boundaries and deposited far from their place of release, where they accumulate in terrestrial and aquatic ecosystems [1]. POP inputs in the environment can be distinguished in primary and

secondary sources. Primary sources are those with direct fluxes into the environment and secondary sources are already contaminated environmental compartments that can release POPs in a time subsequent to their use or production [2], [3]. Due to their extensive distribution, tendency to bioaccumulate, and potential harmful effects such as immunotoxicity, neurotoxicity, developmental toxicity, carcinogenicity, mutagenicity, and endocrine disruption potentials, POPs have drawn scientific and political concern during the last decades [4]. POPs undergo long–range transport (LRT), meaning that they are transported to areas that are remote if compared to the source regions. The group consisting of intentionally and unintentionally produced compounds of POPs includes two types of important compounds: halogenated hydrocarbons and polycyclic aromatic hydrocarbons. Organochlorines family are the most important and persistent groups of all the halogenated hydrocarbons, including organochlorine pesticides (OCPs), polychlorinated biphenyls (PCBs), polychlorinated dibenzop-dioxins/furans (PCDD/F) which are in the first group of 12 POPs whose production and emission is to be reduced or eliminated in all over the world according to Stockholm Convention[5]. The organochlorine insecticides include the chlorinated ethane derivatives, such as DDT and its analogs; the cyclodienes, such as chlordane, aldrin, dieldrin, heptachlor, endrin, and toxaphene; the hexachlorocyclohexanes, such as lindane; and the caged structures mirex and chlordecone.

The large-scale use of long lasting OCPs in modern agriculture has caused serious concern due to the presence of their residues in the environment. Besides combating insect pests, insecticides also get accumulated in many parts of the ecosystem and exert toxic effects on organism including human. Human are exposed to these hazardous chemicals through consumption of contaminated food or through occupational exposure. The occupational exposure could be during manufacture and formulation of pesticides and their distribution in field condition during application of pesticides. Presence of these compounds in human adipose tissues [6], human milk [7] and maternal serum [8] are reported from various part of the world. Increasing incidence of cancer, chronic kidney diseases, suppression of the immune system, sterility in male and females, endocrine disruption, neurological disorders, have been attributed to chronic pesticide poisoning [9]. OCPs, such as Hexachlorocyclohexane (HCH) and DDT account for two-thirds of the total consumption in India [10] for agriculture and public health purposes respectively. Currently, there are about 165 pesticides registered for use in India, of which 40% are organochlorines [11]. The consumption pattern of these chemicals in India differs from the rest of the world.

However, food chain studies have demonstrated that bioaccumulation in food chains is not solely a lipid–water partitioning process [12]. Dietary accumulation or biomagnification can cause additional bioaccumulation, resulting in an increase in chemical concentration with increasing trophic level in food chains (i.e. trophic magnification) [13]- [15].

At least 70% of the pesticides handled by the Indian farmer have been declared “excessively toxic” by world health organization. Unfortunately, pesticides are big money often banned in their country of origin stocks are dumped on eager to purchase developing nations. It is a known fact that one quarter of all pesticides exported by the United State are not registered for use in the US. They include cancelled or suspended pesticides because they may cause cancer or otherwise endanger human or the environment. A pesticide action group in Paraguay remarks, “We do not understand how industrialized countries, producer of pesticides, they do not consume, can allow export to less developed countries, perhaps we are more resistant human being” (Hindustan Times 3.11.90)

The problems would further aggravate in the coming year, as many pesticides mainly organochlorines being lipophilic and non-biodegradable due to their great chemical solubility. Low aqueous solubility and high fat soluble character became concentrated and magnified as they move up in the food chain [16]. Since man in at the top of the food chain he receives and accumulates insecticide residues that vegetables and animals have stored up in various periods of development [17], [18] thus poisoning a challenge to the ecologists and toxicologists. It has been well established that pesticides, particularly the chlorinated hydrocarbons directly affect the fetuses and neonates

as they get transferred through placenta and mother milk respectively. This has been confirmed in all the mammalian species that have been examined including humans [19].

More frightening studies have indicated that we have largely over looked the darker side of these chemicals as OCPs are reported to be carcinogenic [20], [21] mutagenic [21],[22] teratogenic [22],[23] immunosuppressive [24],[25] create endocrine dysfunction such as hypothyroidism or high estrogenic activity [26],[27] disturb reproductive processes [28],[29] growth depressants [30],[31] induces several psychogenic and neurogenic abnormalities in adult stages [32],[33], and are associated with abortions, premature deliveries, still births and infants with low birth weights [34]-[37]. OCPs have been in use in India nearly for a half century now. Even after having clear cut evidence suggesting that these chemicals have the ability to eliminate entire species from the planet, the annual consumption of pesticides in India is about 85,000 tonnes of which OCPs comprise the bulk [38].Therefore, today OCPs are perhaps the most ubiquitous of the potentially harmful chemicals encountered in the environment and are still widely detected in humans despite the considerable decline in environmental concentrations [39].

Placenta serving as a barrier between mother and baby for large number of endogenous and exogenous substances contains appreciable content of fat and hence can serve as a carrier for lipophilic xenobiotics, including organochlorine pesticides. Placenta has already been reported to carry the organochlorine pesticides and there is only one report in Indian context from Lucknow [40]. Since there is no such report from Jaipur, pink city of India and capital of Rajasthan, therefore it was planned to carry out systematic study on placental transfer of pesticides in human beings. In the present study obstetrical material - placenta was used for biological monitoring of pesticides which besides indicating quantitative and qualitative trends in residue deposits and distribution in pregnant women of the general population, also gives an assessment of the vulnerability of the progeny to these environmental toxins.

Materials and Methods

101 pregnant women admitted to Zanana Hospital and Mahila Chikitsalya: attached to the Deptt. of obstetrics & Gynecology. S.M.S. Medical College, Jaipur (India) and two private hospitals "Sanjeevani Hospital" and " Meera Hospital", Bani Park, Jaipur are Included in the present study. In general they had no history of any occupational or accidental exposure to pesticides. However, they were asked to fill up a questionnaire giving information relevant to the pesticide residue accumulation such as age, dietary habits, area of residence, parity, social status, accidental or occupational exposure to pesticides etc. according to WHO methodology [41].

Sample Collection

A fraction of placental tissue was collected at the time delivery, into the acetone washed aluminum foil and stored at -10 degree Celsius till analyzed, generally within 48 hours.

Extraction of Pesticide from Samples

Pesticides were extracted and separated from samples by liquid partition and column chromatography so that they could be analyzed by Gas Liquid Chromatography (GLC) and Thin Layer Chromatography (TLC) procedures. All reagents and chemicals used were of analytical grade and checked for any pesticide contamination. Specimens of placenta were extracted and cleaned by florosil column as per the methodology given by Bush and his coworkers with little modifications according to the prevailing laboratory conditions [42].

Quantitative Estimation

Quantitative estimation of pesticide residues in all the extracts was done by HP 5890 series II gas chromatograph (GC) equipped with Ni 63 Electron capture detector (ECD) coupled to HP 3396A integrator. Glass coiled column (1.43 m x 4 mm L x I.D) was packed with Solid Support, Chromosorb 100/120 mesh size along with the Liquid phase: 1.5% OV-14±1.95% OV-210 .Purified nitrogen (IOLAR-1) gas was used as the carrier gas and a known volume of sample was injected in the column with the help of the 10 µl Hamilton syringe. Different peaks of the samples were identified by comparing their retention times with those of standards. Quantitation of the samples were done by the data obtained from the integrator and were based on peak areas. Standards were obtained

from Environmental Protection agency (EPA) U.S.A.

Recovery Analysis and Confirmation of Pesticide residues

Recovery analysis was done by fortification experiments and the percentage recovery was 95–98%.TLC was used for confirming the identity of the OCPs already detected by the GC. The pesticides for which the GC was standardized and were estimated were Aldrin, isomers of HCH (α, β & γ), metabolites of heptachlor (Heptachlor & Heptachlor epoxide) and DDT (DDE, DDD and DDT).

Statistical Analysis

The calculations are based on biological statistics and values are expressed as mean± standard error (S.E.).The difference in the pesticide residue levels between different groups was analyzed with the help of student t test. Significance between the residue levels of different groups was judged at 5 % and 1% levels

Observations

Table 1: Concentration of OCPs in the placenta of 101 women (ppb).

S. No.	OCPs detected	Range (Mean ± S.E.)
1.	∝-HCH	1.0-472.0(n=95) 82.1±9.94
2.	γ-HCH	1.0-780.0(n=77) 37.4 ±10.35
3.	β-HCH	ND 1879.0(n=64) 91.7 ±29.68
4.	Heptachlor	5.0-4616.0(n=59) 809.3 ±114.66
5.	Aldrin	1.0-758.0(n=81) 122.2 ±16.02
6.	Heptachlor epoxide	9.0-6751.0(n=56) 769.8 ± 146.94
7.	DDE	2.0-3766.0(n=87) 98.6 ±43.32
8.	DDD	ND-256.0(n=26) 62.9 ± 14.97
9.	DDT	ND -868.0 (n=64) 55.5 ± 16.13
10.	Σ HCH	2.0-1981.0(n=99) 170.6±25.70
11.	Σ Heptachlor	5.0-7194.0(n=82) 1058.6±132.55
12.	Σ DDT	1.0-4181.0(n=97) 99.9± 14.70

Table.2: Stratification of OCPs residue data in human placenta with respect to dietary habit, parity pesticide use, weight categories and age categories. (ppb)

S.No	OCPs detected	Dietary habits		Age Categories		Pesticide use	
		Veg.	Non Veg.	17-24 Yrs	25-34 Yrs	Pesticide used	Pesticide not used
		45 Cases Mean ± S.E.	56 Cases Mean ± S.E.	55 Cases Mean ± S.E.	46 Cases Mean ± S.E.	45 Cases Mean ± S.E.	56 Cases Mean ± S.E.
1.	∝-HCH	72.1±11.14 (n=41)	90.9±15.11 (n=54)	81.8±14.45 (n=48)	73.1±12.83 (n=46)	100.4±17.77 (n=41)	73.7±11.44 (n=53)
2.	γ-HCH	32.2±5.64 (n=30)	40.7±16.75 (n=47)	52.1±19.62 (n=39)	19.4±3.33 (n=35)	55.4±21.33 (n=36)	21.6±3.77 (n=41)
3.	β-HCH	57.5±11.25 (n=31)	123.6±56.07 (n=33)	69.4±11.96 (n=35)	105.2±65.20 (n=28)	153.7±62.69 (n=29)	40.29±9.53 (n=34)
4.	Heptachlor	724.4±196.81 (n=26)	859.9±135.38 (n=33)	733.5±122.77 (n=32)	872.1±195.0 (n=28)	988.6±142.15 (n=26)	773.4±182.00 (n=32)
5.	Aldrin	142.5±33.84 (n=32)	121.9±20.26 (n=49)	115.8±20.87 (n=40)	125.1±25.03 (n=39)	154.8±27.62 (n=38)	91.8±16.42# (n=44)
6.	Heptachlor epoxide	749.6±169.07 (n=20)	754.1±208.95 (n=36)	1056.8±259.54 (n=27)	516.6±135.79 (n=29)	614.9±132.43 (n=27)	914.6±252.88 (n=29)
7.	DDE	36.6±5.94 (n=38)	145.8±76.23 (n=49)	129.5±82.72 (n=45)	58.21±13.85 (n=41)	158.6±95.12 (n=39)	50.63±11.35 (n=46)
8.	DDD	65.9±22.87 (n=10)	35.0±11.78 (n=15)	39.2±15.89 (n=14)	74.9±21.59 (n=11)	24.1±11.83 (n=08)	80.5±19.73 (n=18)
9.	DDT	44.3±14.70 (n=30)	65.5±27.35 (n=34)	34.7±12.39 (n=33)	75.1±29.02 (n=32)	90.8±35.08 (n=27)	30.3±9.15 (n=37)
10.	Σ HCH	132.3±18.76 (n=43)	193.2±42.74 (n=56)	155.2±27.19 (n=53)	182.8±46.43 (n=45)	241.1±52.46 (n=44)	108.6±15.20* (n=55)
11.	Σ Heptachlor	953.3±171.21 (n=36)	1327.0±240.71 (n=45)	1164.8±196.76 (n=43)	1174.4±243.25 (n=38)	10140.2±145.38 (n=37)	1058.28±221.5 (n=45)
12.	Σ DDT	80.3±17.29 (n=43)	187.4±77.97 (n=54)	147.8±79.49 (n=52)	130.4±27.55 (n=43)	206.4±96.99 (n=43)	89.1±16.79 (n=54)

Table-2 Contd:

S. No.	OCPs detected	Weight Categories		Parity	
		45-55 Kg	56-75 Kg	primiparous	multiparous
		56 Cases Mean ± S.E.	45 Cases Mean ± S.E.	30 Cases Mean ± S.E.	71 Cases Mean ± S.E.
1.	∝-HCH	69.0±11.63 (n=52)	85.5±13.73 (n=43)	7103±16.91 (n=29)	86.0±12.25 (n=66)
2.	γ-HCH	33.11±5.61 (n=43)	42.8±22.31 (n=34)	54.7±31.18 (n=24)	29.5±4388 (n=53)
3.	β-HCH	67.9±13.10 (n=37)	124.3±67.60 (n=27)	60.8±15.02 (n=19)	104.6±41.64 (n=45)
4.	Heptachlor	882.3±162.56 (n=37)	554.8±100.73 (n=21)	777.8±136.70 (n=22)	801.10±161.26 (n=37)
5.	Aldrin	139.17±21.76 (n=45)	101.1±23.35 (n=36)	98.0±23.24 (n=25)	133.2±20.62± (n=56)
6.	Heptachlor epoxide	960.4±262.51 (n=26)	625.3±151.08 (n=29)	652.9±142.35 (n=23)	845.0±221.09 (n=34)
7.	DDE	54.6±19.79 (n=15)	74.2±22.51 (n=11)	199.0±145.94 (n=25)	49.5±9.62 (n=62)
8.	DDD	136.9±76.16 (n=49)	49.2±11.35 (n=38)	67.7±27.50 (n=7)	61.2±17.83 (n=19)
9.	DDT	68.4±27.50 (n=34)	40.9±14.12 (n=30)	49.0±20.53 (n=20)	58.6±21.52 (n=44)
10.	Σ HCH	159.2±23.41 (n=56)	172.1±39.60 (n=42)	151.9±39.96 (n=30)	171.2±32.90 (n=68)
11.	Σ Heptachlor	759.9±136.75 (n=46)	1319.7±218.07* (n=36)	938.1±173.05 (n=27)	1142.4±214.75 (n=54)
12.	Σ DDT	185.1±79.34 (n=53)	90.6±17.99 (n=43)	240. ±145.10 (n=28)	101.0±19.22 (n=66)

* Statistically Significant (P<.01)
\# Statistically Significant (P<.05)

Table.3: Amount of OCPs excreted through human placenta with respect to dietary habit, parity pesticide use, weight categories and age categories. (ppb)

S. No.	OCPs detected	Dietary habits		Age		Pesticide use		Weight		Parity	
		Veg.	Non. Veg.	17-24 Yrs.	25-34 Yrs.	Pesticide Used	Pesticide Not Used	45-55 kg.	56-75 Kg.	Primi-Parous	Multi-Parous
1.	∝-HCH	72.1	90.9	81.8	73.1	100.4	73.7	69.0	85.5	71.3	86.0
2.	γ-HCH	32.2	40.7	52.1	19.4	55.4	21.6	33.1	42.8	54.7	29.5
3.	β-HCH	57.5	123.6	69.4	105.2	153.7	40.29	67.9	124.3	60.8	104.6
4.	Heptachlor	724.4	859.9	733.5	872.14	988.6	773.4	882.3	554.8	777.8	801.1
5.	Aldrin	142.5	121.9	115.8	125.1	154.84	91.8	139.17	101.1	98.0	133.2
6.	Heptachlor epoxide	749.6	754.1	1056.8	516.6	614.9	914.6	960.4	625.3	652.9	845.0
7.	DDE	36.6	145.8	129.5	58.21	158.6	50.63	136.9	49.2	199.0	49.5
8.	DDD	65.9	35.0	39.0	74.9	24.1	80.5	54.6	74.2	67.7	61.2
9.	DDT	44.6	65.5	34.7	75.1	90.1	30.3	68.4	40.9	49.0	58.6
10.	Σ HCH	132.3	193.2	155.2	182.8	241.1	108.2	159.2	172.1	151.9	171.2
11.	Σ Heptachlor	953.3	1327.0	1164.8	1174.4	1140.2	1058.2	759.9	1319.7	938.1	1142.4
12.	Σ DDT	80.3	187.4	147.8	130.4	206.4	89.1	185.1	90.6	240.3	101.0

Σ HCH-total HCH
Σ Heptachlor-Total Heptachlor
Σ DDT-Total DDT
n-no of positive samples
ND-not detected

Table 4: Percentage metabolism of DDT, estimated as DDD and DDE (ppb).

S. No	Specimen	Metabolite of DDT	Vegetarian	Non Vegetarian	17-24 Yrs.	25-34 Yrs.	Pesticide Not used	Pesticide Used	45-55 Kg.	56-75 Kg	Primi-parous	Multi-parous
1.	Maternal Blood	DDE	43.9	77.7	70.1	58.9	64.0	66.8	82.2	44.9	56.9	65.7
		DDD	25.8	103.7	28.3	105.7	94.0	45.5	22.1	122.7	22.0	92.2
2.	Cord Blood	DDE	38.7	50.6	37.9	54.7	47.8	40.8	45.7	43.1	44.2	47.9
		DDD	72.6	226.1	52.4	278.0	15.8	214.0	201.7	51.9	56.9	201.6
3.	Placenta	DDE	36.6	145.8	129.5	58.21	158.6	50.63	136.9	49.2	199.0	49.5
		DDD	65.9	35.0	39.2	74.9	24.1	80.5	54.6	74.2	67.7	61.2

Results

1. Concentrations of OCPs in the placental tissue of women are included in the **Table.1.** In the present findings concentration of Aldrin, total HCH, total heptachlor and total DDT were found to be 122.2, 170.6, 1058.6

and 99.9 ppb respectively in the placental tissue of women **(Table.1).**

2. An attempt has been made to find out the effects of dietary habit, age, parity, weight, habits of pesticide use and weeks of gestation period on the accumulation and excretion of via placental tissue **(Table.2).**
   - Significantly high concentrations of OCPs were found in the placental tissue of women with non-vegetarian dietary habits.
   - A general trend of high residue accumulation in the placenta of women of higher age group was observed when compared with the women of lower age group. But the difference was statistically non-significant between the two groups.
   - Higher accumulation of pesticides was found in the placental tissue of the women who has used pesticides in comparison of women who has not used pesticides at all.
   - A general trend of high residue accumulation was observed in the placental tissues of women of high weight category in comparison of women of low weight category.
   - In the present findings, parity also influenced the accumulation of OCPs in the placental tissue. On comparing the residue deposits of primiparous and multiparous females no statistically significant difference could be observed between the above two groups. But general trend of high residue levels was observed in the placenta of multiparous females.
3. Computation has also been done on quantitative removal of detected pesticides through placenta at the time of delivery. To have a better understanding on excretion of lipophilic pesticide residues through placenta, impact of dietary habits, age, habits of pesticide use, parity and weight has also been studied **(Table.3).**
4. Efforts were also made to find out whether placenta could serve as a site of biodegradation of detected pesticides by computing the percent concentration of their metabolites in blood and placental tissue. However no significant conclusion could be drawn. Some in vitro study is, therefore, needed to this regard **(Table.4).**

DISCUSSION

The frequency of distribution of the OCPs detected in the placenta of 101 women are incorporated in the Table.1. In the present study concentration of total DDT and total HCH came out to be 99.9 and 170.6 ppb respectively. These values are quite higher in comparison to the values reported from Lucknow in which concentration were 56.2 and 45.4 ppb respectively by Saxena and his colleagues in 1981[43].

Besides, India there are many reports from all over the world giving an idea about the concentration of detectable OCPs in placental tissue. Selby and his colleagues (1969) reported contamination of human placental tissue with certain OCPs from Louisiana [44]. Concentrations reported were 24.07, 1.19 and 2.12 ppb for total DDT, total HCH and total heptachlor respectively. In the present study, values for the above pesticides came out to be 99.9, 170.6 and 1056.6 ppb respectively which are quite higher in comparison to the above reported value from Louisiana. Polishuk and his colleagues (1970) reported concentration of 67.8 ppb of total DDT and 7.8 ppb of total HCH in the placental tissue from Jerusalem, Israel which is quite low in comparison of our findings[45]. In a report from Miami, Florida, O' Leary and his colleagues (1970) reported concentration of 37.9 ppb of DDT and 21.80 ppb of DDE in the placental tissue [46].In our findings the values came out to be 55.5 and 98.6 ppb respectively which are quite high in comparison to the above mentioned values. Eckenhausen and his colleagues (1981) reported contamination of placental tissue with 14.0 ppb of DDE, 0.5 ppb of p, p' DDD, 1.1 ppb of p, p' DDT, 0.8 ppb of a-HCH and 2.7 ppb of ß-HCH. In our findings the values for the above pesticides came out to be 98.6, 62.9, 55.5, 37.4, and 91.7 ppb respectively which are again quite higher in comparison to the above reported values [47].

With the help of reported case histories of the subjects,

efforts were made to find out the possible impact of age, dietary habit, parity, weight and pesticide use in the field and house hold of the mother on the distribution and accumulation pattern of pesticides in the mother and thereby on the degree of their transfer to the fetus.

(a) Effect of dietary habits on the accumulation of pesticide residues in the placental tissue. Dietary habits of the mother were found to play an important role in the body burden of lipophilic pesticide residues. Interestingly higher concentrations of OCPs were found in the placenta of women with non-vegetarian dietary habits than in those with vegetarian dietary habits but no statistical significant difference was found. The significant difference in the levels of pesticides in the two groups may result from high DDT and BHC values in mutton, eggs and chicken which are common in non-vegetarian meals[48],[49]. The results of our findings are in accordance with the results reported by Siddiqui in 1982 from Lucknow. He reported that residue levels of HCH, p,p-' DDD, Aldrin, p,p'-DDE in mothers blood, cord blood and placenta were significantly higher in the mothers with non-vegetarian habits.

(b) Effect of age on the accumulation of pesticide residues in the placental tissue.

Mother's age has also been reported to influence accumulation of OCPs in her circulating blood and its subsequent transfer to the fetus. Siddiqui in the year 1982 divided pregnant women in the two groups, one of age, 18-25 years and second was of 26-34 years. On Statistical evaluation of the data, he observed that in placenta, the difference in the values for total HCH, Lindane, p, p'-DDE and p, p' -DDT were statistically significant for two different age groups [50]. Therefore, an attempt has also been made to divide the subjects into two different age groups 17-24 and 25-34 and to compare the difference in the residue levels of pesticides. A general trend of high residue accumulation in the placenta of Women of higher age group was observed when compared with the women of lower age group. But the differences were statistically non-significant between two groups of dissimilar ages. The greater accumulation of pesticides in the higher age group women might be due to the fact that a longer life span of mothers may cause a greater accumulation of pesticides in them and subsequently may result in comparatively higher transfer of pesticides to the developing embryo. Alternatively a differential rate of absorption, distribution and detoxification of pesticides in two age groups may partly be responsible for higher accumulation of pesticides in mothers of other group, as the activity of drug metabolizing enzymes of the liver may decrease after a certain period, with subsequent increase in age. In a survey study conducted by Selby and his colleagues in the year 1969 in Louisiana Parish, they concluded that no marked differences were observed among age because the population group sampled was fairly homogenous with similar environmental sources of exposure to the chlorinated hydrocarbon pesticides [44].

(c) Effect of use of pesticide on the accumulation of pesticides in maternal blood, cord blood and placental tissue.

Another aspect of the study is to consider, the use of pesticides by the pregnant women to get rid of pests at household and in agricultural field. Therefore, the subjects were divided into two categories, out of which one group has been using pesticides (non-persistent type) for different work at household and in fields, while other group was not using pesticides at all. Higher accumulation of OCPs was found in the placental tissue in the group of women who had used pesticides for various purposes. Statistically higher residue levels were found in the placental tissue of the women for Aldrin and total HCH who had been using pesticide for different purposes.

(d) Effect of weight facto on the accumulation of pesticides in maternal blood, cord blood and placental tissue.

An attempt has also been made to find out the influence of weight of the mothers on the accumulation of OCPs in her blood and its subsequent transfer to the fetus, since, OCPs are lipophilic in nature, and they may accumulate in fat rich tissues of the body in alarming concentrations. Therefore, it was expected that the mothers in the high weight category will have high pesticide residue accumulation in comparison of the women of low weight category. From the table.2, it is clear that women of high weight category have a tendency to accumulate more pesticides than the women with low weight in the placental tissue. Statistically higher accumulation

could be observed only in the case of total HCH (1319.7 ppb against 759.9 ppb) in the placental tissue of a woman of high weight category.

(e) Effect of parity on the accumulation on pesticides in maternal blood, cord blood and placental tissue.

Parity might also influence the accumulation of OCPs. Therefore, the subjects were divided into two groups primiparous and multiparous, on comparing the residue deposits of these two different groups, no significant difference could be observed. But a general trend of high residue levels could be observed in maternal blood, cord blood, and placenta of multiparous females in comparison to primiparous.

This can be due to the fact that the multiparous females were of higher age group in comparison of primiparous females. Therefore, age can be a factor which might have resulted in greater accumulation of pesticides in multiparous females in comparison of primiparous females [50]. But in the present study age factor is not found to effect the accumulation of pesticide residues in the tissues of women. Therefore, findings of the present study suggests that other factors such as, dietary habits, use of pesticides and weight might influence the accumulation of chlorinated hydrocarbons in the placental tissues.

Computation has been done on quantitative removal of detected pesticides through placenta at the time of delivery. To have a better understanding on excretion of lipophilic pesticide residues through placenta, impact of dietary habits, age, weight, parity an Pesticide use habits of mothers has also been studied as shown in the table.3. Effect of dietary habit indicated the non-vegetarian mothers excrete relatively higher amount of OCPs as compared to vegetarian mothers. Amount of total DDT thrown along with placenta at the time of delivery was found to be 187.4 ppb in non-vegetarian mothers in comparison of 80.3 ppb in vegetarian mothers. Concentration of total HCH was 193.2 and 132.3 ppb respectively in non- vegetarian and vegetarian mothers. Concentration of total heptachlor was found to be 1327.0 ppb in non-vegetarian mothers and 953.3 ppb in vegetarian mothers. It is obvious from the results that a longer life span of mothers not only results in greater accumulation of pesticides but also in the greater excretion through placenta at the time of delivery. Mothers of age group 17-24 excreted 155.2 ppb of total HCH and mothers of age group 25-34 years excreted 182.8 ppb of total HCH. The excretion of total heptachlor in higher age group was 1174.4 ppb in comparison of lower age group in which it was 1164.8 ppb. Accumulation of DDT was found to be 75.1 ppb and 34.7 ppb in higher and lower age groups respectively. Results revealed that weight of mothers also affects the accumulation of pesticide residues in the body. Mothers of weight category 56-75 kg accumulated 172. 1 ppb of total HCH in comparison of mothers of weight category 45-55 kg accumulated 159 2 ppb. Concentrations of DDD were 74.2 ppb and 54.6 ppb in higher and lower weight categories respectively. Concentrations of total heptachlor in the high and low weight categories were 1319.7 ppb and 938.1 ppb respectively. Parity also seems to affect the accumulation of pesticides in the mother. Multiparous females accumulated more pesticides than primiparous females. Concentration of total HCH and total heptachlor in the placenta of multiparous females were 171.2 ppb and 1142.4 ppb respectively. Primiparous females had the concentration of 1 51.9 ppb and 938.1 ppb respectively.

The placenta is increasingly recognized not simply as a relatively inert membrane system that serves to separate the fetal circulation from the maternal circulation and mediate the transfer of nutrients and gases between the two, but rather as containing a rich variety of enzyme systems and as being extremely active metabolically [51].

Therefore, efforts were made to find out whether placenta could serve as a site of biodegradation of detected pesticides by computing percent concentration of their metabolites in blood and placental tissue as shown in the Table.4. However, no significant conclusion could be drawn. Some in vitro study is therefore, needed to this regard.

CONCLUSION

It is quite clear from the foregoing discussion, that in all over the world Indian mothers have got the highest body burden of organochlorine pesticides. This is because in the third world countries such as India, because of the cost - benefit ratio OCPs are still the major pesticides used in agriculture and public health sector. This is in accordance with the findings of Dale and his coworkers (1965) that the Indians have got the

highest body burden of organochlorine pesticides [52].

The present study directly reflects the national scene of magnitude of pesticide pollution which signifies the distribution and accumulation of non-biodegradable lipophilic pesticides in pregnant women on one side and subsequently the vulnerability of the successive generation from its very inception in the womb of the mother on other side. The so called "placental barrier" which separates the maternal compartment from the fetal compartment must be regarded as an epithelial membrane of lipoid character, i.e. a lipid sieve through which lipophilic non-polar substances are able to penetrate according to their concentration gradient and degree of lipophilicity. A physiological state like pregnancy, no doubt helps mother in fighting against the increasing burden of environmental pollutants like persistent organochlorine pesticides. During the state as evident from the present investigation, the mothers appreciably reduce their body burden of pesticides at the expense of intoxication of their own developing baby in the womb through placental transfer throughout the gestational period. A small fraction of total burden of the body gets reduced when placenta is disposed off, after child birth. Starvation stress caused an increase in the fetal concentrations of DDT and its metabolites calls for a strict regulation in time to take meals and a balance between calorific intake and energy requirement of the mother during pregnancy to avoid mobilization of fat depots resulting into mobilization of stored residues [53].

It can be concluded that the magnitude of pesticide pollution is quite high enough to contaminate the food and environment and the toxicant reach the human body through various sources mainly by absorption from the gastrointestinal tract through contaminated food chain. From there, they are further circulated in blood, stored milk and placental tissue of the women. Pesticide body burden also reduced in mothers during parturition as pesticides stored in the placenta are shed off during the delivery. Mothers also shed off the body burden of the pesticides during lactation as pesticides are also secreted along with milk resulting in sufficient neonatal intake. Since, the pesticides are reported to be carcinogenic, mutagenic, teratogenic, immunosuppressive, induces endocrine dysfunction and high estrogenic activity, disturb the reproductive processes, growth depressants, induces several psychogenic and neurogenic abnormalities in adult stages and are also reported to be associated with abortions, premature deliveries, still births, low birth weight consequences are obvious on the mother and the developing baby. It poses various problems of management of neonatal nutrition and health. It calls for suggestions like special care in nutrition and in the environment of mother throughout the life and especially during pregnancy and lactation. It would be advisable for a woman to avoid the consumption of fatty food stuffs and heavily polluted working environment. It is also advisable for a woman to avoid the use of insecticides for household purposes. It also reflects that there is an urgent need to develop less/non persistent and more/total biodegradable pesticides and other means by which we can to reduce the environmental pollution by the pesticides which is not only posing risk to human health but also a big peril our future generations

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REFERENCES

1. UNEP, 2001. Stockholm Convention on Persistent Organic Pollutants (POPs).
2. Hung, H., Kallenborn, R., Breivik, K., Su, Y.S., Brorstrom-Lunden, E.,Olafsdottir, K., Thorlacius, J.M., Leppanen, S., Bossi, R., Skov, H., Mano,S., Patton, G.W., Stern, G., Sverko, E., Fellin, P., 2010. Atmospheric monitoring of organic pollutants in the arctic under the Arctic Monitoring and Assessment Programme (AMAP): 1993-2006. Science of the Total Environment 408, 2854-2873.
3. UNEP/AMAP, 2011. Climate Change and POPs: Predicting the Impacts.Report of the UNEP/AMAP Expert Group, http://library.arcticportal.org/1214/.
4. WHO, 2003. Health risks of persistent organic pollutants from long-rangetransboundary air pollution, The Netherlands, 274 pp.
5. Çok, I., Mazmanci, B., Mazmanci, M. A., Turgut, C., Henkelmann, B., & Schramm, K. W. (2012). Analysis of human milk to assess

exposure to PAHs, PCBs and organochlorine pesticides in the vicinity Mediterranean city Mersin, Turkey. Environment international, 40, 63-69.
6. Alawi MA, Tamimi S, Jaghabir M. (1999) Storage of organochlorine pesticides in human adipose tissues of jordanian males and females. Chemosphere 38(12):2865–2873
7. Behrooz RD, Esmaili Sari A, Bahramifar N, Ghasempouri SM. (2009):Organochlorine pesticide and polychlorinated biphenyl residues in human milk from the Southern Coast of Caspian Sea, Iran. Chemosphere 74:931–937
8. Bloom MS, Buck-Louis GM, Schisterman EF, Kostyniak PJ, Vena JE.(2009): Changes in maternal serum chlorinated pesticide concentrations across critical windows of human reproduction and development. Environ Res 109:93–100.
9. Hosie, S., Loff, S., Witt, K., Niessen, K., & Waag, K. L. (2000). Is there a correlation between organochlorine compounds and undescended testes? European Journal of Pediatric Surgery, 10(05), 304-309.
10. Kumari A, Sinha RK, Gopal K, Prasad K (2001) Dietary intake of persistent organochlorine residues through Gangetic fishes in India. Int J Ecol Environ Sci 27:117–120.
11. FAO (2005) Proceedings of the Asia regional Workshop. Regional Office for Asia and the Pacific, Bangkok.
12. Gobas FAPC. A model for predicting the bioaccumulation of hydrophobic organic chemicals in aquatic food-webs: application to Lake Ontario. Ecol Model 1993; 69:1–17.
13. Gobas, F. A., Muir, D. C., & Mackay, D. (1988). Dynamics of dietary bioaccumulation and faecal elimination of hydrophobic organic chemicals in fish. Chemosphere, 17(5), 943-962.
14. Sharpe, S., & Mackay, D. (2000). A framework for evaluating bioaccumulation in food webs. Environmental science & technology, 34(12), 2373-2379.
15. Kelly, B. C., Gobas, F. A., & McLachlan, M. S. (2004): Intestinal absorption and biomagnification of organic contaminants in fish, wildlife, and humans. Environmental Toxicology and Chemistry: An International Journal, 23(10), 2324-2336.
16. Cremlyn, R. (1978): Pesticides, preparation and mode of action". Chichester. John Wiley.
17. Hornabrook, R. W., Dyment, P. G., Gomes, E. D., & Wiseman, J. S. (1972). DDT residues in human milk from New Guinea natives. Medical journal of Australia, 1(25), 1297-1300.
18. Lara, W. H., and Barreto, H.H.C. (1982): Residues de pesticidas organoclorados en leite humano Sao Paulo, Brasil 1979-81. Rev. Inst. Adolfo. Lirty. 42, 45-52.
19. Zhang, X., Wu, X., Lei, B., Jing, Y., Zhang, X., Fang, X., & Yu, Y. (2018). Transplacental transfer characteristics of organochlorine pesticides in paired maternal and cord sera, and placentas and possible influencing factors. Environmental Pollution, 233, 446-454.
20. Mathur, V., Bhatnagar, P., Sharma, R. G., Acharya, V., & Sexana, R. (2002):Breast cancer incidence and exposure to pesticides among women originating from Jaipur. Environment international, 28(5), 331-336.
21. Ingber,S.Z., Buser,M.C., Pohl,H.R., Abadin,H.G., Murray, H.E.,Scinicariello.F.(2013): DDT/DDE and breast cancer: a meta-analysis. Regul Toxicol Pharmacol., vol. 67, no. 3, pp. 421-33.
22. Yaduvanshi. S.K, Srivastava.N, F. Marotta.F, S. Jain.S and H. Yadav.H.(2012): Evaluation of micronuclei induction capacity and mutagenicity of organochlorine and organophosphate pesticides, Drug Metab Lett., vol. 6, no. 3, pp. 187-97.
23. Agency for Toxic Substances and Diseases Registry (ATSDR)/US Public Health Service, Toxicological Profile for 4,4'-DDT, 4,4'-DDE, 4, 4'-DDD (Update). ATSDR. Atlanta, GA.1994.
24. Repetto.R and Baliga.S.S.(1997): Pesticides and Immunosuppression: The Risks to Public Health," Health Policy Plan., vol. 12, no. 2,

pp.97-106.
25. Corsinia.E., Sokootib.M., Gallia.C.L., Morettoc.A and Colosiob.C. (2013):Pesticide induced immunotoxicity in humans: A comprehensive review of the existing evidence,Toxicology. vol. 307, pp. 123–135, May.
26. Dewailly.E., Ayotte.P., Bruneau.S., Gingras.S., Belles-Isles. M and Roy.R.(2000): Susceptibility to infections and immune status in Inuit infants exposed to organochlorines, Environ Health Perspect., vol.108, no.3, 205–211, March.
27. Rathore. M., Bhatnagar. P., Mathur. D and Saxena. G.N.(2002): Burden of organochlorine pesticides in blood and its effect on thyroid hormones in women," Sci Total Environ., vol. 295, no. 1–3, pp. 207–215, August.
28. Pant.N., Kumar.R., Mathur.N., Srivastava.S.P.,Saxena. D.K and Gujrati.V.R.(2007): Chlorinated pesticide concentration in semen of fertile and infertile men and correlation with sperm quality" Environ Toxicol and Pharmacol., vol. 23, no. 2, pp. 135–139, March.
29. Tiemann.U. (2008): In vivo and in vitro affects of the organochlorine pesticides DDT, TCPM, methoxychlor, and lindane on the female reproductive tract of mammals: A review, Reproductive Toxicology., vol.25, no. 3, pp. 316–326, April.
30. Colborn.T., Vom Saal. F.S., Soto A.M (1993): Developmental Effects of Endocrine-Disrupting Chemicals in Wildlife and Human," Environ. Health. Perspect, vol. 101, no. 5, pp.378-384, October.
31. Mercier. M (1981): Criteria (Dose Effect Relationships) for Organochlorine Pesticides Report, Published for the Committee of the European Communities by Pergamon Press.
32. Mactutus, C.F and Tilson, H.A (1986): Psychogenic and neurogenic abnormalities after perinatal insecticide exposure. In: Hand book of behavioral teratology. Ed. by Edward, P.R. and Charles, V.V. Plenum Press, NY, 335-91.
33. Van Wendel de Joode.B., Wesseling.C., Kromhout.H., Monge. P., García. M and Mergler. D. (2001): Chronic nervous-system effects of long-term occupational exposure to DDT, Lancet, vol. 357, no. 9261, pp. 1014–1016, March.
34. Saxena, M.C., Siddiqui, M.K.J., Seth, T.D and Krishnamurti, C.R. (1981): Organochlorine pesticides in specimens from women undergoing abortion, premature and full term delivery. J. of Anal. Toxicol.5, Jan/ Feb.
35. Saxena, M.C., Siddiqui, M.K.J., Bhargava, A.K., Seth, T.D., Krishnamurti, C.R and Kutty, D. (1980): Role of chlorinated hydrocarbon pesticides in abortions and premature labour. Toxicology. 17. 323-31
36. Tyagi.V., Garg.N., Mustafa. M.D., Banerjee, B.D and Guleria. K. (2015): Organochlorine pesticide levels in maternal blood and placental tissue with reference to preterm birth: A recent trend in North Indian population, Environ Monit Assess., vol.187, no. 7, pp. 471, July.
37. Chen.Q., Zheng.T., Bassig.B.,Cheng.Y., Leaderer.B., Lin.S., Holford.T., Qiu.J., Zhang.Y., Shi.K., Zhu.Y., Niu.J., Li.Y., Guo.Y.H., Huand.X and Jin.Y.(2014):Prenatal Exposure to Polycyclic Aromatic Hydrocarbons and Birth Weight in China," Open Journal of Air Pollution, vol.3, pp. 100-110.
38. India Environment Portal Knowledge for change, 30/10/1998.
39. Dewan, P., Jain, V., Gupta, P., & Banerjee, B. D. (2013). Organochlorine pesticide residues in maternal blood, cord blood, placenta, and breastmilk and their relation to birth size. Chemosphere, 90(5), 1704-1710.
40. Siddiqui, M. K. J. (1982). Biochemical studies on tissues accumulating pesticides (Doctoral dissertation, Ph. D. Thesis submitted to the University of Lucknow, India).
41. WHO/EURO. (1991): "WHO Protocol for Second Round of Exposure Studies: Levels of PCBs and PCDFs in human milk".
42. Bush. B., Snow.J and Koblintz,R.(1984):

Polychlorobiphenyl (PCB) congeners, P',p'-DDE and hexachlorobenzene in maternal and fetal cord blood from mothers in Upstate, New York. Arch. Environ. Contm. Toxicol. 13, 517-27.

43. Saxena, M. C., Siddiqui, M. K. J., Bhargava, A. K., Murti, C. K., & Kutty, D. (1981). Placental transfer of pesticides in humans. Archives of toxicology, 48(2), 127-134.
44. Selby L.A., Newell, K.M., Hauser, G.A and Junker, G. (1969): Comparison of chlorinated hydrocarbon pesticides in maternal blood and placental tissues. Environ. Res. 2,247-55.
45. Polishuk, Z.W., Wassermann, M., Wassermann, D., Groner, Y., Lazarovici, S and Tomatis, L. (1970): Effects of pregnancy on the storage of organochlorine insecticide. Arch. Environ. Hlth. 20, 215 -17.
46. O'Leary, J. A., Davies, J. E., Edmundson, W. F., & Reich, G. A. (1970). Transplacental passage of pesticides. American journal of obstetrics and gynecology, 107(1), 65-68.
47. Eckenhausen, F.W., Bennett, D., Beynon, K.I and Elgar, K.E (1981): Organochlorine pesticide concentrations in prenatal samples from mothers and babies. Arch. Environ. Hith. 36, 81-92.
48. Lakshminarayana, V and Krishna Menon, P. (1972): Insecticide residues in food stuffs. Annual Report of the Central Plant Protection Training Institute, Hyderabad.
49. Saxena, M.C., Siddiqui, M.K.J., Bhargawa, A.K., Krishnamurti, C.R and Kutty, D. (1981): Placental transfer of pesticides in humans. Arch. Toxicol. 48, 127-34.
50. Siddiqui, M. K. J. (1982). Biochemical studies on tissues accumulating pesticides (Doctoral dissertation, Ph. D. Thesis submitted to the University of Lucknow, India).
51. Juchau, M. R. (1982). The role of the placenta in developmental toxicology. In Developmental toxicology (pp. 187-209). Springer, Boston, MA.
52. Dale. W.E., Copeland, M.F., Hyes, W.J. (1965): Chlorinated insecticide in the body fat of people in India. Bull. World. Hith. org. 33,471 - 77.
53. Matsmura, F. (1976): In: Toxicology of Insecticides. 291.