WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 12, Issue 1, 90-107. Review Article ISSN 2277– 7105

PREVENTIVE MEASURES IN PREGNANCY AGAINST HEAVY METALS

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Article Received on
07 Nov. 2022,

Revised on 27 Nov. 2022,
Accepted on 17 Dec. 2022

DOI: 10.20959/wjpr20231-26314

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ABSTRACT

Establishment of early being pregnant is the end result of complicated biochemical interactions among the decidua and blastocyst.. Any alteration on this chemical speak has the capacity to bring about negative being pregnant results inclusive of miscarriage. Sporadic miscarriage is that the commonest complication of maternity and might be caused by multiple factors. whereas the foremost common reason behind miscarriage is genetic abnormalities within the craniate. Nonchromosomalelements which have been related to miscarriage are many and encompass endocrine abnormalities, anatomic abnormalities, inherited and acquired thrombophilia, environmental exposures, immunologic factors, and others. The reason of this paper is to check the current evidence on the position of environmental toxins in reproduction and to further find scientific understanding of prenatal exposure to heavy metals among pregnant women and fetus. This review will also specialist inthe intersection of environmental issue associated with metals moreover the particular susceptibility that children may have to these environmental contaminants. Cases of miscarriage and stillbirths because of heavy metallic poisoning stay at the upward thrust in growing nations.

KEYWORDS: Sporadic miscarriage, Heavy metals, Chromosome abnormality, Endocrine disrupting chemical.

INTRODUCTION

Sporadic miscarriage or spontaneous abortion is, the loss of an embryo or fetus before 20 weeks of pregnancy, is the most common complication of pregnancy, affecting

approximately 15-20% of all clinically recognized pregnancies.[1] Successful pregnancy requires a complex interplay between immunological, hormonal, and genetic processes . A massive share of miscarriages are defined via way of means of chromosomal abnormalities of the offspring, specifically aneuploidy: chromosomal abnormalities have an effect on 50% of first trimester and 20% of 2nd trimester miscarried foetuses.[2-3] The miscarriages are the most common negative pregnancy outcome with increased emotional consequences that effect individuals and families. This can be a crucial indicator of embryotoxicity that will occur because of exposure of heavy metal.[4] This is important to bear in mind because the etiology of miscarriage varies greatly according to gestational age, with preimplantation losses, pre-fetal losses, and losses in which there are most effective rudimentary fetal stays being much more likely to be because of intrinsic fetal problems (e.g., chromosome abnormality), whereas later losses are more likely to be due to extrinsic or maternal factors.[5]

Certainly, way of life elements consisting of tobacco, smoke, cocaine and alcohol utilization are usually properly widely wide-spread as contributing reasons of miscarriage. Exposure to different chemical substances consisting of endocrine disruptors, heavy metals,consisting of arsenic, cadmium, lead etc and Environmental toxicant publicity to the pesticide DDT.[6] Moreover, early physiological condition loss and adverse physiological condition outcomes occur at higher rates in and around contaminated waste sites like landfills and in areas with potable contamination or high pollution.[7] Not simplest can environmental pollution effect the growing embryo, there may be additionally a ability for alteration of the endometrium of being pregnant, that is, the decidua. Successful implantation calls for a complicated biochemical communicate to arise among the blastocyst and decidua. Multiple industrial contaminants have the ability for endocrine disruption; these chemicals will impact the power to become pregnant and sustain a healthy physiological condition. Other environmental contaminants have additionally been implied to have a causal impact on being pregnant loss; those consist of radiation publicity, agricultural chemical substances, and business solvents.[8] Studies have shown that heavy metals like lead (Pb), cadmium (Cd), and mercury (Hg) have toxic effects on reproductive outcome and are also associated with miscarriages. Few reports disclosed that the exposure to heavy metals viz lead, cadmium, copper may promote the pregnancy implications viz, spontaneous abortions, toxemia and anemia. The toxic metals when present in the maternal blood stream may cause abnormal placental function and deviate nutrient delivary to the fetus through the indirect formation of reactive oxygen

species (ROS) and reactive nitrogen species (RNS) that cause oxidative stress by reacting with macromolecules and damaging them.[9]

When testing Associate in Nursing association between pollution exposure throughout maternity and syndrome spectrum disorder designation in youngsters, proscribing analyses to measure births created a state of affairs with 2 potential choice bias processes at play:

1) The possibility of nativity was influenced by each pollution exposure likewise as another risk issue for autism; and
2) The depletion of fetuses vulnerable to syndrome from the high exposure cluster.[10]

Using a mixture of CTD knowledge and our own applied math approach, we tend to evaluated the genes related to every chemical and tested them for enrichment with genes annotated to the CTD malady term "Spontaneous Abortion". The goals of this study were to:

1) Establish chemicals related to accumulated risk of miscarriage, supported toxicogenomic responses across multiple species (human, mouse and rat) exploitation the CTD;
2) Perceive chemical affects on precise molecular objectives and cell pathways concerned in miscarriage; and
3) Become aware of objectives/pathways typically impacted with the aid of using a couple of chemical substances, suggesting capability toxicant combos of concern for this endpoint.
4) Exposure of Endocrine-disrupting chemicals (EDCs) resulting in miscarriage.
5) Chromosomal abnormalities leading to miscarriage.
6) Exposure of high levels of heavy metals resulting in miscarriages and stillbirth.[11]

METHODOLOGY

Datasets

a. Background genes lists for human, Mouse and Rat species

We stratified our analyses by species to match chemical-gene-disease associations across many species whereas maintaining biological coherence across the various array of studies enclosed within the CTD. The symbols for all genes annotated to every species were downloaded from the Comparative Toxicogenomics info (CTD). We then verified that the annotated genes were listed as "active" for every species within the PubMed gene info. This came back a complete of forty two, 830 human, 34,321 mouse and twenty five, 150 rat genes.[12]

b. Spontaneous abortion gene listing

We downloaded CTD genes joined to the clinical term for miscarriage, "Spontaneous Abortion". This listing incorporates 121 curated human genes. Of these, 111 have acknowledged mouse homologs and 112 have famed rat homologs. All statistical tests have been carried out the usage of human, mouse or rat species facts as separate, unbiased analyses. Because CTD ailment phrases are curated the usage of a hierarchic annotation system, we additionally recognized and quantified genes belonging to additional "child" ailment phrases contained underneath the "parent" time period of "Spontaneous Abortion".[13]

c. Chemical gene lists

We decided on an optimized variety of 25 chemical substances for evaluation to permit for:

1) Evaluation of multiple, various chemical classes (e.g. metals, organophosphate pesticides, risky natural compounds, etc.); and
2) Practicableness of downstream follow up analysis of chemicals enriched with miscarriage genes.[14]

We centered our analysis on chemicals relevant to exposures within the population of greatest concern for the miscarriage terminus (i.e., pregnant women) at intervals a particular geographical location, a region with high rates of adverse physiological state outcomes and intensive contamination with Superfund chemicals. Therefore, we tend to chosen chemicals supported their presence in maternal blood/urine samples, 163 groundwater, tap water, Superfund sites or rumored usage in Puerto law. the whole list of twenty five chemicals enclosed serious metals [arsenic, cadmium, lead] ; phthalate esters [dibutyl phthalate], volatile organic compounds [perchloroethylene, chloroform and methylene group chloride], pesticides [aldrin, atrazine], phenols [triclosan and benzophenone-3], polycyclic aromatic hydrocarbons [naphthalene] and a private care product [N,N-Diethyl-meta-toluamide]. factor lists for these chemicals were downloaded for human, 1mouse and rat from the CTD web site.[15]

d. Search Methods and Selection criteria

The different search engines like PubMed, MEDLINE and Google scholar databases for studies were used for the literature collectively. The various key words like- heavy metals, pregnant mothers and foetus, reproductive problems, developmental concerns were used to download the literature. Hand looking was adopted to search out relevant literature that wasn't obtained using the regular search criteria. The search was conducted in each database

separately and then combined to pool along all the literature. The pooled search database was examined and also the duplicates were removed and appropriate limits were applied, and the database was saved for data extraction. The retained articles investigated the exposure to lead, arsenic, cadmium, chromium and mercury earlier than and in the course of being pregnant in terms of their effect on maternal and toddler wellbeing.[16]

Statistical tests

a. Enrichment trying out of chemical gene Lists and Miscarriage genes

All analyses had been carried out in R statistical software. R markdown code used to behavior analyses and to generate figures and tables is publicly to be had facilitating destiny programs of the workflow to different exposures and outcomes. We carried out univariate descriptive information on every species-unique chemical gene list. Within species, we generated 2x2 descriptive tables for genes related to every chemical through genes related to miscarriage. A minimal range of chemical-gene annotations had been required to fulfill the assumptions to behavior statistical checks for enrichment with miscarriage genes. Therefore, primarily based totally on the gene distributions for every chemical and every species, we decided on suitable enrichment check information as follows. When expected frequencies per cell were bigger than or adequate 5, enrichment was conducted on normal chi-square test for independence. once the expected frequency of genes per cell was lesser than 5 and bigger than one, we have a tendency to used the 'N-1' chi-squared take a look at. Chemicals with expected frequency but one in any cell of the 2x2 table were born from any analysis for that species. Out of the seventy two potential comparisons, we have a tendency to proceeded with twenty enrichment tests that met the chi-square or 'N-1' chi-square assumptions.[17]

b. Cross-validation of enrichment consequences

To examine the susceptibility of the miscarriage gene listing to false-advantageous consequences, we carried out move validation for enrichment trying out with miscarriage genes. We randomly permuted a thousand pseudo-chemical gene lists every of unique sizes (100, 500, a thousand, 2500, 5000 and ten thousand genes) to mirror the variety of genes related to chemical compounds in our dataset. Genes in those random lists have been then examined for enrichment with the specific miscarriage genes. We calculated the quantity of permuted exams meeting our significance criteria by probability. We have a tendency to visualize the patterns in results with a density plot of ascertained association p-values.

c. Gene Ontology enrichment evaluation of miscarriage gene list

To gain insight into specific biological functions represented within the 121 genes contained within the CTD term “Spontaneous Abortion". we diagnosed enriched Gene Ontology phrases represented through the 121 miscarriage genes. For statistical transparency, assumption trying out, and scripting reproducibility, we examined gene ontology enrichment with a normally used device (DAVID).[18] In addition, we used the REVIGO net primarily based totally platform to exclude redundant Gene Ontology phrases. The 121 miscarriage gene symbols had been used as enter for enrichment trying out in DAVID and “Homo sapiens” become used because the background or reference gene list. As similarly affirmation of our results, we additionally analyzed the miscarriage genes the usage of the gene set enrichment (“Set Analyzer”) device withinside the CTD on-line portal.[19]

d. Identification of chemical-gene institutions for enriched miscarriage Gene Ontology phrases and Gene Ontology enrichment evaluation of chemical gene lists

Based on enrichment testing results, we tend to prioritized a set of 5 chemicals that were enriched from the human chemical data (arsenic, cadmium, lead, atrazine and parathion). We visualized overlap in miscarriage genes interacting with those chemical compounds the use of a heatmap. Gene club in every of 4 selected miscarriage Gene Ontology phrases became highlighted. Although we prioritized chemical compounds that had been enriched in human, we additionally performed this evaluation for chemical compounds enriched in mouse and rat data. Finally, we performed gene ontology evaluation the usage of DAVID and the genes annotated to our prioritized chemical compounds in our order to establish biological pathways probably to be full of these chemicals.[20]

RESULT

Miscarriage is an crucial interest for reproductive epidemiology research. The gift look at evaluated a hard and fast of chemical substances detected in pregnant girls for institutions with molecular markers of miscarriage. Chemicals from more than one classes, which includes metals, pesticides, unstable natural carbons, polycyclic fragrant hydrocarbons and endocrine disrupting chemical substances affected greater miscarriage genes.[21] Our outcomes are steady with epidemiological research displaying institutions among heavy metallic exposure, environmental toxicants, endocrine disruptors and miscarriage:

1. **Environmental chemicals**

- Two of the phthalates examined had been enriched for miscarriage genes, with DBP enriched for rat and DEHP enriched for mouse. These outcomes are steady with numerous reviews in human observational research. Both DBP and DEHP ranges in maternal hair samples had been related to ignored abortion In addition, urinary ranges of the primary DEHP metabolite (monoethylhexyl phthalate) had been better in girls with ignored abortion. Several phthalates stimulate oxidative stress, irritation and epigenetic in gestational tissues and cells in culture, suggesting capacity mechanisms explaining institutions with miscarriage.[22]

- Carbon tetrachloride brought on abortion in a rat version steady with our locating that carbon tetrachloride changed into enriched with miscarriage genes.[23]

- Although epidemiological and experimental facts link the pesticides atrazine, dieldrin and parathion (enriched for miscarriage in our observe) to some detrimental pregnancy outcomes, evidence for miscarriage is mixed. For example, the spouses of personnel who used higher stages of atrazine had an elevated hazard of miscarriage. Dieldrin became associated with detrimental outcomes in pregnancy, which includes gestational excessive blood strain and modified thyroid hormone stages in wire blood. Parathion did not have an impact on the quantity of stay fetuses consistent with muddle in rats, however one little look at in pregnant women confirmed altered placental morphology in accomplice diploma uncovered cluster, an impact that could have implications for miscarriage.[24]

- Cell loss of life changed into some other pathway enriched amongst miscarriage genes. Cell loss of life and necrobiosis are systematically associated with miscarriage. Placentas from women with recurrent miscarriage have elevated stages of apoptosis in comparison to women with ordinary pregnancies. Toxic chemical materials which includes polycyclic aromatic hydrocarbons (PAHs) triggered apoptotic pathways, important to embryo loss in mice, a proposed mechanism explaining better miscarriage fees in women who smoke.[25]

2. **Endocrine disrupting chemicals**

- One of the foremost well-known EDCs is DDT, or 1,1,1-trichloro–2,20 bis(p-chorophenyl) ethane. DDT has estrogenic activity. Dichlorodiphenyldichloroethene (DDE), a metabolite of DDT, has been proven to be an androgen receptor antagonist. The reproductive repercussions of DDT use had been a couple of; those consist of a

recommended position in decline in sperm counts, growth in time to conception, or even intrauterine growth restriction. Spontaneous abortion has been correlated with DDT publicity in a couple of research. Most human research on miscarriage and DDT have correlated DDT or DDT metabolites with being pregnant outcomes. Several research have proven that there's additionally an growth in spontaneous miscarriage at better concentrations of DDE (>15 mg/L). Overall, those research constantly display an growth in spontaneous abortion in patients with higher serum ranges of DDT or DDT metabolite.[26]

- BPA [2,2-bis(4-hydroxyphyenyl) propane] is an estrogenic compound. BPA has been related to reproductive issues consisting of polycystic ovarian syndrome, endometriosis, infertility, and thyroid disease. Detectable concentrations of BPA have additionally been diagnosed in reproductive tissues consisting of follicular fluid and amniotic fluid, suggesting that exposure can arise at some stage in the time of implantation and established order of early being pregnant. Alteration of expression of genes related to implantation has been related to BPA as BPA is capable of weakly bind the estrogen receptor. As a end result of its estrogen agonist properties, an rise in expression of estrogen-regulated genes is observed with BPA. This includes genes like HOXA10, B3integrin, and ITGB3. These genes are recognised to be vital for everyday implantation. BPA has additionally been proven to effect endocrine signaling with the aid of using downregulating expression of ERa and PR. Endometrial angiogenesis is likewise impacted with the aid of using BPA with the aid of using downregulating vascular endothelial increase element expression. These gene expression data, taken together, advocate that BPA has the ability to disrupt implantation, with the ability downstream results of miscarriage, antenatal complications, or even implications in grownup fitness and disease. now no longer gathered at some stage in being pregnant for the miscarriage group. Taken along, BPA has been shown in laboratory models to extend the danger of miscarriage at the extent of each the endometrium and the aneyploidy oocyte.[27]

- Dioxin-associated pollutants inclusive of polychlorinated biphenyls (PCBs), polychlorinated dibenzo-p-dioxins, and polychlorinated dibenzofurans. These compounds can act now no longer best as estrogen agonists or antagonists however can also have androgenic properties. PCBs had been proven to inhibit meiotic spindle meeting in vitro. These chemicals conjointly hamper maturation of oocytes in vitro. Both of those

consequences have the ability to reason miscarriage. The endometrium additionally seems to be impacted through PCBs. In vitro endometrial cultures display an alteration in estrogen-responsive genes upon publicity to PCBs. Given that the PCBs such as dioxin have the ability to regulate each regular oogenesis and endometrial function. Dioxin exposure during pregnancy has been related to fetalloss, low delivery weight. With developmental syndrome related to hydronephrosis, cleft palate, and thymic atrophy.[28] Studies of exposed Vietnamese girls have shown a rise in miscarriage and premature deliveries. Larger studies have found a trend toward inflated risk of stillbirth in wives of veterans with low accumulation certain however not at high exposure levels .a bigger crosssectional study of 281 employees exposed to TCDD throughout production of Agent Orange, showed primary outcomes of increase stillbirth, spontaneous abortion, and intercourse ratio. Reproductive repercussions of PCB use now no longer best on being pregnancy complication however additionally have an impact on offspring.[29]

3. Chromosome abnormality

Studies performed on spontaneous losses have consistently shown that 50% are associated with fetal chromosome abnormalities. The true proportion of conceptions affected with aneuploidy is likely to be larger when one considers other data. Forinstance, studies of preimplantation embryos suggest that 30 to 65% of normally developing, good-quality embryos have aneuploidy in at least one cell.[30,31]

- **Autosomal trisomy**

It is the single largest category of abnormality, and molecular studies have proved that 90% of trisomies are the resultof errors in maternal meiosis. Interestingly, the relative proportions of maternal versus paternal meiotic error varies substantially among the different chromosomes with nearly 50% of XXY pregnancies being the result of paternal nondisjunction whereas less than 10% of other trisomies arise by paternal meiotic error.

It is the consequence of either dispermy or failure of extrusion of the second polar body, with the clinical manifestations being different depending on the origin of the extra set of chromosomes. As in 45X, no maternal age effect has been described.[32]

- **X-Chromosome inactivation**

Skewing

In females, one of the two X chromosomes is inactivated in early embryonic life, a process that generally occurs randomly. X chromosome inactivation skewing occurs in situations in which there is a cellular survival advantage associated with one of the two Xs remaining active. Structural abnormalities of the X chromosome or the presence of a dominantly acting lethal mutation are examples of when this might occur. A relatively recent development has been the purported association with skewed (or nonrandom) X-chromosome inactivation with miscarriage, although the possible biological basis for such an association has not been clear. Overall, it seems that this association is weak at best.[33]

- **Acquired thrombophilia**

Antiphospholipid syndrome

Antiphospholipid antibodies (aPL) are a family of autoantibodies directed against phospholipid-binding plasma proteins, the two most clinically relevant of which are the lupus anticoagulant (LA) and the anticardiolipin antibodies (aCL). The persistent presence of either of these antibodies is associated with an increased risk of second- and third-trimester pregnancy loss, 28 making it important that women with such losses be assessed for their presence. The mechanism postulated is thrombosis of placental vasculature, although pathologic findings are not always consistent with this. Treatment with heparin and aspirin in such women has been shown to have clear benefits.[34]

- **Inherited thrombophilia**

Familial deficiency of protein S and protein C as well as polymorphisms of clotting cascade proteins (factor V Leiden [FVL] and factor II G20210A) are associated with increased risk of thromboembolism, leading to the term inherited thrombophilia. Several studies have also reported associations between inherited thrombophilia and adverse pregnancy outcomes, including early loss, late loss, and stillbirth.[35]

- **Maternal age**

Many studies have documented that one of the strongest and most consistent associations with miscarriage is that of maternal age. The increase in risk that occurs between the ages of 25 and 40 years is nearly threefold and is therefore larger than almost any other known effect.

The incidence of fetal aneuploidy increases with maternal age, and this explains most of the strong association between maternal age and miscarriage. Roughly 10% of pregnancies in women 36 years and older end in miscarriages with normal karyotype compared with 3% in women under 30 years.[36]

4. Important heavy metals involved in Miscarriages and Stillbirths

Some key heavy metals like arsenic (As), cadmium (Cd), lead (Pb) and mercury (Hg) were proven to showcase endocrine disrupting homes and are termed Endocrine disrupting compounds 'EDCs' . The exposure to those significant heavy metals at some stage in being pregnant are believed to have destructive outcomes at the mom and the fetus. The heavy metals mercury, lead and cadmium are key toxicants which can be well-documented to move the placenta and to build up in fetal tissues with next deleterious outcomes. This unique institution of heavy metals were proven to regulate the sensitive maternal-fetal balance, consequently inflicting long-time period harm to the newborns.[37]

- **Lead**

There were reviews of pregnant ladies occupationally uncovered to excessive stages of lead in England and Hungary. This exposure but was connected with frequent spontaneous abortions, stillbirths, premature births, and babe deaths, compared with mothers in occupations unexposed to guide poisoning. The high concentration of the lead in physique can amendment central nervous system and brain which will coma, convulsions and even death. The survival cluster of children's is related to behavioural changes and intellectual impairment. Adults having high level of lead in their body become even the victims of urinary organ diseases and high pressure level. The low concentration lead manufacture a spectrum of injury like lead affects brain development in kids, resulting in reduced I.Q. behavioural changes like shortening of span and raised delinquent behavior and reduced instructional attainment. Lead is a recognized neurotoxin and it's miles exceedingly poisonous to the fetus with terrible effect on fetal developing and mind improvement. Lead interferes with synaptic transmissions in addition to mobile adhesion molecules ensuing in blockade of cellular migration at some stage in withinside the frightened gadget improvement. Research has shown that in physiological state and lactation in humans, lead is free from the maternal skeleton and transferred to the fetus/infant via the placenta and breast milk respectively which then ultimately have an effect on the developmental method of the primary frightened gadget withinside the new born. Lead is saved withinside the human

frame over a long time and probably modifications in metabolism throughout the storage could offer insight on specific periods throughout that lead exposure was highest. Increasing blood lead levels are often end result of raised maternal absorption in being pregnant or mobilization of lead out of maternal bone. Lead is freely transported across the placenta since maternal and twine blood lead levels. Lead levels in extraordinary booths and at extraordinary ranges of being pregnant are handiest modestly correlated, suggesting that every degree captures extraordinary elements of fetalpublicity. The vulnerability of developing organ systems, consisting of the start to environmental pollution range broadly over the route of being pregnant.[38,39]

- **Arsenic**

The principal exposure to arsenic is because of underground consuming water with its main supply the aquifers infected with arsenic. . In arsenic a excessive dose of arsenic is associated with unfavourable consequences at the developing embryo. In humans probabilities of craniate loss because of arsenic contamination has been determined. There is a marked modification in behaviour and developing brain because of neurotoxicity of arsenic. Arsenic concentration is connected with fever and diarrhoea at some point of being pregnant. The in-utero Arsenic publicity with the fetal immune repertoire and infectious consequences at some point of early childhood. The direct and indirect effects of arsenic exposure discovered that arsenic exposure is expounded to low birth weight, age and menstrual health. This is likewise related to multiplied chance of nausea and vomiting at some point of being pregnant. This successively contributes to pour biological process standing of the pregnant mothers that later consequences developmental alternate of the babies. Arsenic exposure has been related to changes in improvement pathways of the babies.[40]

- **Cadmium**

Cadmium could be a non-essential significant metal rather like arsenic, it's miles usually discovered underground amongst rocks, sediments, soils and dust. The concentration of cadmium in mothers who brought preterm babies turned into better compared to mothers who brought complete time period babies. This turned into attributed to the better attention of cadmium withinside the soil of area. The relation among the reduced beginning weight and cadmium exposure turned into discovered substantial with the aid of using a few research. The exposure to Lead and Cadmium promoted the headaches like threatened spontaneous abortion, toxemia and anemia. The low concentration of Cadmium reveled growth withinside

the contracted activity amongst pregnant women. The Cadmium might also additionally input into the infant with the aid of using manner of breast feeding that may cause differing kinds of biological process issues to them. Most of the studies found association between the cut birth weight of recent borne infants and increased cadmium concentration in maternal blood or the placenta. The adsorbable features a long half-life within the body and might adversely have an effect on kidney and bone and to growth the chance of most cancers and universal mortality endocrine disruptor have an effect on reproductive and baby improvement. An growing proof of maternal Cadmium and destructive being pregnant consequences like decreased beginning length and preterm delivery.[41]

- **Mercury**

The Minamata cases of the Japan reveled that mercury may be a neuro dangerous and causes birth defects. Mercury can cause injury to youngsters brain if mother are exposed to mercury throughout maternity. Even the smaller doses of mercury is related to low I.Q amongyoungsters. High levels of mercury exposure might be through petroleum products, fungicides, cosmetics, hair dyes, thermometers, vaccination, silver dental fillings and consumption of salt water fish. The relationship between average fish consumption as well as the type of fish consumed and levels of mercury in the blood of pregnant women were tested. The maternal blood mercury stage in past due being pregnant become absolutely associated with mercury tiers of wire blood which become nearly two times the extent observed in maternal blood. Pregnant women who consume a large number of fish may have high blood mercury levels. Neuropsychological tests found pronounced pathology within the domains of language, attention, and memory at exposure levels less than what is considered safe. The maternal Mercury levels in pregnancy is releatedwith inattentive at impulsive conduct at age 8. An association between the mercury contamination that cause serious offspring brain damage resulting from prenatal exposure to very high levels of mercury has been found. The priority for pregnant women and their foetuses is subjected to Methyl mercury as Mercury is actively transported throughout the placenta and impaired neurodevelopment as a result of fetalexposure. Human exposure to Methyl mercury (MeHg) in some areas occurchiefly due to consumption of fishes contaminated with Mercury. As Methyl mercury is transferred to the children through placenta, maternal exposition represents a risk for offspringis obvious.[42]

- **Male mediated miscarriage**

Male-mediated spontaneous abortion remains unreported in man till now, despite the fact thatthat a few information have emerged to suggest that the welding of stainless steel can be a applicable paternal exposure. Stainless steel fumes (not mild steel), incorporate hexavalent chromium, inhalation of that trigger pulmonary absorption of hexavalent chromium with autopsy findings of former chromate uncovered people confirming excessive concentrations of hexavalent chromium in several examined organs. Hexavalent chromium management in male rodent additionally impairs the viability of embryos fathered through that male. Increased chance self-reported spontaneous abortion was previously found in spouses of stainless-steel welders, compared with spouses of non-welders.[43]

CONCLUSION

Pregnancy loss both sporadic and recurrent is associated with a wide variety of potential etiologic factors. Etiology depends heavily on gestational age at which miscarriage occurs. In follow, once abnormal condition has been excluded, it's oftentimes not possible to impute a selected cause for any given miscarriage. We determined chemical gene sets (parathion, cadmium, naphthalene, carbon tetrachloride, arsenic, lead, dieldrin, and atrazine) had been notably enriched for miscarriage genes. Exposures to chemicals linked to miscarriage, and thus linked to decreased probability of live birth, may limit the inclusion of foetuses susceptible to adverse birth outcomes in epidemiology studies.

The reproductive outcomes impacted by endocrine disruptors are many, but the main target of this review paper is on miscarriage. Many research have proven a dose-based in crease in miscarriage with those endocrine. These research recommend that ladies of reproductive age must workout warning on exposure to those endocrine disruptors. Unfortunately, these compounds are ubiquitous within the environment and are often difficult to avoid. One concern with the ever present nature of those chemicals is that a lot of those studies might be confounded by the presence of multiple chemicals. Ideally, multiple endocrine disruptors would be assayed for, permitting an assessment of the actual com pound(s) causing an effect. Review also concludes that heavy metals if present in very less concentration may cause different adverse effects on pregnant women and developing fetus. The effects that are recognized include IQ deficits, attention-related behaviours, poor academic achievement, birth length, head and chest circumferences, reproductive effects, lower birth weight, negative relationship between umbilical cord blood lead (PbB) level and Bayley Mental

Development Index (MOl) at 6 and 12 months. Accumulation of Arsenic in Toenail increase the risk of fetal and infant death, high blood mercury levels effects on CNS. Arsenic in blood and urine, significant impact on fetal development, effects on neonatal neurodevelopmental. Hence measures to prevent the toxicity of heavy metals among pregnant women should be undertaken and as such if the area is suspected that it is contaminated with heavy extreme caution must be taken to avoid the consumption of any food from these areas.

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