Effects of Occupational Chemicals Exposure on Diabetes Mellitus: A Review

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

Review Article

ABSTRACT

Diabetes mellitus is a disease caused by the disorder in carbohydrate metabolism and it is characterized by impairment in insulin production by the body cells. Beta cells located within clusters of cells in the pancreas are responsible for the secretion of insulin whose role in the body is to stimulate cells to take up and metabolize glucose. Dysfunction of beta cells re usually found in people with diabetes mellitus and this results in reduced glucose uptake/metabolism by the cells. This work centers on a comprehensive review of possible relationships between occupational exposure to specific chemical substances or industrial activities and diabetes mellitus-related outcomes, including alterations in glucose homeostasis and diabetes mellitus incidence/prevalence or mortality. Many occupational chemicals have been seen to have adverse effects on diabetes mellitus. Such chemicals include metals like cadmium and arsenic, hydrocarbons like benzene, methane and organophosphates. Studies revealed that different concentrations of heavy metals increase the risk of diabetes mellitus. Exposure to toxic metals like cadmium due to uncontrolled pollution and industrialization increases defect in glucose uptake and other problems. Study on

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occupational chemical exposure disclosed that exposure to 0.84-mg/kg of cadmium in model organisms accelerated the concentration of   blood glucose. Study also revealed that exposure of diabetic mice to volatile benzene-increases insulin resistance in the liver and skeletal muscle. Exposure to perfluorinated alkyl substances (PFAS) which are used in fire-fighting foam, textiles, kitchen ware, and food packaging material have been shown to be associated with diabetes in an elderly population, backing the view that perfluorinated alkyl substances can alter glucose metabolism in humans and induce Type 2 diabetes mellitus. Moreso, in this review, the complications associated with diabetics exposed to industrial chemicals is discussed and management highlighted.

1. INTRODUCTION

Diabetes mellitus is a disease caused by the disorder in carbohydrate metabolism and it is characterized by impairment in insulin production by the body cells [1]. Beta cells located within clusters of cells in the pancreas are responsible for the secretion of insulin whose role in the body is to stimulate cells to take up and metabolize glucose. Dysfunction of beta cells re usually found in people with diabetes mellitus and this results in reduced glucose uptake/metabolism by the cells [1].

Retinopathy, nephropathy and neuropathy, among other complications are some of the long-term complications of diabetes mellitus and also people with this disease have high tendency of suffering from other disease conditions like obesity, heart disease, peripheral arterial and cerebrovascular disease, erectile dysfunction, and fatty liver disease [2]. Thirst, polyuria, blurring of vision, and weight loss are some of the characteristic symptoms of diabetes.

Research carried out revealed that about 13.6 million people in African continent counts have diabetes and also   Sub-saharan Africa which is the African Region of IDF have about 7 million people living with diabetes [3]. The number of people living with diabetes in this African   is predicted to increase by   2025 and may reach 15 million.

The pathophysiology of this disease is not well understood, although the disease epidemiology and inheritance pattern shows that the disorder originate from genetic and lifestyle risk factors, such intake of excessive calories, excessive weight and obesity, love as well as cigarette smoking [4]. Most epidemiological studies have linked diabetes mellitus to environmental contaminants [5,6,7] (Howard *et al.*, 2011; Kuo *et al.*, 2013). Information on how occupational chemicals affect the pathogenesis and clinical history of the diabetes mellitus is still lacking. A number of studies has been carried out to know whether heavy metals such as Chromium (Cr), Arsenic (As), lead (Pb), Iron (Fe) and Nickel (Ni) could be involved in diabetes related outcome in industries where these metals are being used.

Therefore, the present review aims to give a comprehensive review of the possible relationship between occupational exposure to specific chemical substances or industrial activities and diabetes mellitus-related outcomes, including alterations in glucose homeostasis, diabetes mellitus incidence/prevalence or mortality, with a specific focus on the biological plausibility, dose–response relationship and temporality.

2. EPIDEMIOLOGY AND GLOBAL BURDEN OF DIABETES

Diabetes is a global disease, occurring in both rural parts of low and middle countries. The number of people with diabetes worldwide was estimated to about 422 million adults as at 2014 [2].

About 1.1 million children and adolescents aged 14-19 years were estimated to have type 1 diabetes mellitus by the International Diabetes Federation. Study performed   by the IDF in 2017, prove that without proper action taken to reduce the diabetes increase, there will be at least 629 million people living with diabetes by 2045 [8]. Studies shows that about 4 million death year is caused by hyperglycemia in and the international Diabetes Federation estimates that the yearly global health care spending on diabetes among adults was US$850 billion in 2017 [8].

2.1 Aetiology of Diabetes

Beta cells dysfunction or destruction is main cause of diabetes mellitus (Figs. 1 and 2). A

decline in the function or the complete destruction of B-cells can also be caused by other underlying factors [9]. Genetic predisposition and abnormalities, epigenetics processes, insulin resistance, auto-immunity, concurrent illnesses and inflammation are some of the underlying factors that can cause beta cells dysfunction.

Diabetes aetiology differs no depending on the genetic makeup, family history, ethnicity, health and environmental factors.

3. CLASSIFICATION OF DIABETES MELLITUS

Classification system helps health care professionals choose appropriate treatments are choosed by experts [2]. According to WHO Classification, the types of diabetes mellitus include:

3.1 Type 1 Diabetes

There are no data available on Type 1 diabetes mellitus trends, globally but there is an increase in the incidence of type 1 diabetes mellitus in childhood between 3% and 4%, annually, in high-income countries [10]. Type 1 diabetes mellitus affect both males and females. Type 1 diabetes mellitus prognosis is difficult in countries with limited access to insulin [2]. T1DM symptoms occur rapidly in children, although it may also occur in adults. Ketoacidosis is usually presented as the first sign of manifestation of this disease, especially in children and adolescents [11].

Moderate hyperglycemia which can change rapidly to severe hyperglycemia and/or Ketoacidosis in the presence of infection or other stress may be seen in other patients [2]. Immune-mediated process with beta cell autoantibodies against glutamic acid decarboxylase, islet antigen-2 , ZnT8 transporter or insulin, and associations with genes controlling immune responses have been seen in 70% - 90% of people with type 1 diabetes mellitus at diagnosis [12]. The specific pathogenesis in those without immune features is unclear although some may have monogenic forms of diabetes.

Type 1 diabetes symptoms can appear suddenly and may include thirstiness, frequent urination, blurred vision, weight loss, fatigue, hunger and bed-wetting in children.
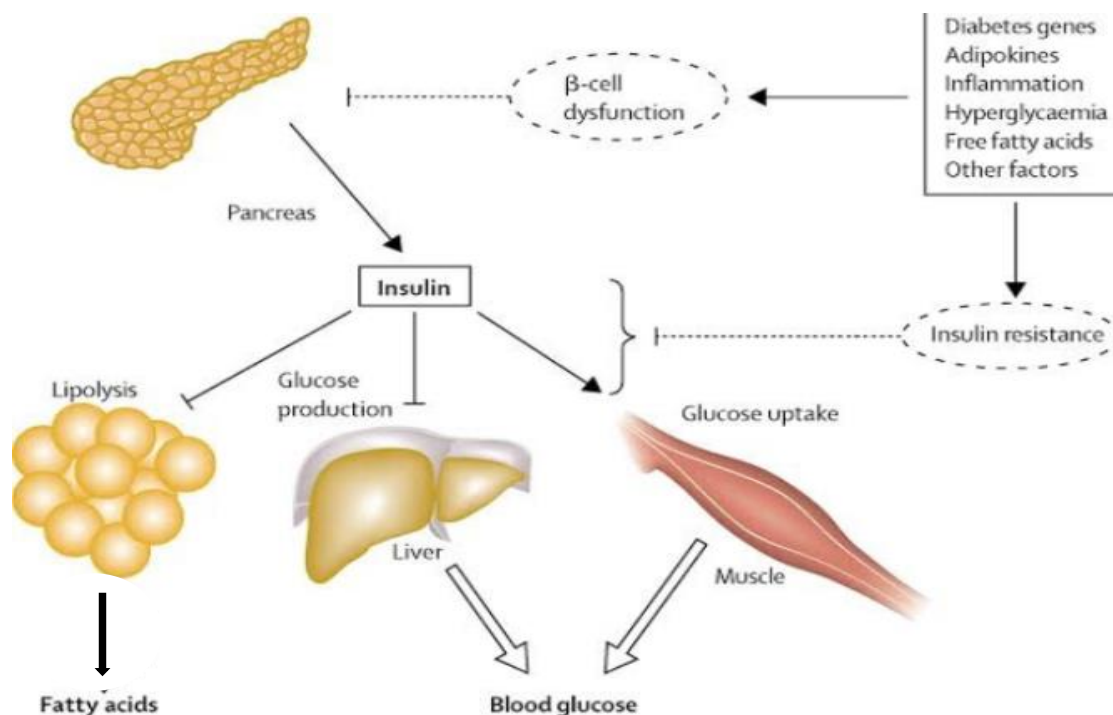

Fig. 1. Diagram showing the causes of Diabetes mellitus
Source: Kara,[1]

3.2 Type 2 Diabetes Mellitus

About 90% - 95% of diabetes affecting humans is the type 2 diabetes mellitus, being high in low and middle Income countries [2]. Type 2 diabetes is a serious world health problem, arising in relation to cultural, economic, social and dietary changes such as highly processed foods and sugar– sweetened beverages, consumption increase , reduced physical activity, obesity, unhealthy lifestyle patterns, fetal malnutrition, and hyperglycemia exposure during pregnancy [2]. Adults are more susceptible to T2DM, although greater number of children and adolescents are also affected [13].

Insulin is seen in most people with this disease and in the onset of this disease, there is increase in absolute insulin levels with resistance to the action of insulin [14]. Obesity/ overweight is common among people with T2DM and this either causes or increase insulin resistance [15]. Treatment with insulin is not required in people with type 2 diabetes, although it may be required to lower blood glucose to avert chronic complications.

Age, obesity, unhealthy lifestyles and prior gestational diabetes are some factors that can increase of developing type 2 diabetes mellitus. The frequency of T2DM also varies between different racial and ethnic subgroups, especially in young and middle-aged people [2]. Some symptoms of T2DM include blurred vision, fatigue, thirstiness, numbness in the hands and feet, slow healing of cuts or sores and weight loss.

3.3 Hybrid Forms of Diabetes

Proposal of new categories of diseases is due to efforts made in differentiating T1DM from T2DM , and this hybrid form of diabetes are the slowly evolving immune-mediated diabetes and ketosis prone T2DM [16].

3.4 Slowly Evolving Immune-Mediated Diabetes

This hybrid form of diabetes is common in adults, having pancreatic autoantibodies that can react with non-specific cytoplasmic antigens in islet cells, Glutamic acid decarboxylase, protein tyrosine phosphatase A-2, insulin, or ZnT8 [2]. The latent autoimmune diabetes in adults was it's common name [2]. Insulin therapy is not needed in people with this type of diabetes at diagnosis.

Lifestyle modification and oral was an initial way of controlling this type of diabetes but now progress to use of insulin more rapidly than people with typical T2DM [17]. The symptoms of this type diabetes is similar to other form: polydipsia (excessive thirst), polyuria and often blurred vision.

3.5 Ketosis-prone Type 2

A young African-American was the first to identify this hybrid form of diabetes [18] and it has become a new clinical entity [19]. This type of diabetes has diversely been delineated has a form of T1DM or T2DM [2]. Some advocate that people classified with idiopathic or type 1 B diabetes of T1DM or T2DM Should be reclassified as having ketosis-prone type 2 diabetes [17]. Specific epidemiologic, Clinical, and metabolic features of diabetes onset and natural history of impairment in insulin secretion and action can be used to differentiate ketosis-prone T2DM from T1DM and classical T2DM [2].

4. OTHER SPECIFIC FORMS OF DIABETES

4.1 Monogenic Diabetes

Molecular genetics has been defined by WHO so that they can help identify specific subtypes of diabetes. Subgroups that are genetically have been disclosed through this advances, resulting in new genetics identification [2]. Genetic diagnosis which is an outstanding advance can result in improved treatment outcomes for some people [2] Classification of monogenic subtypes of diabetes is based on the uses of gene symbol of the mutated gene followed by the clinical syndrome (Hattersey *et al.*, 2009). For example, a child diagnosed with neonatal diabetes (PNDM) due to a mutation in KCNJ11 is labeled as having KCNJ11 PNDM. If there is a clinical diagnosis of PNDM but a gene mutation had neither been looked for nor found, then the person would be categorized as PNDM only [2].

4.2 Monogenic Defects of β-cell Function

Maturity-onset diabetes of the young (MODY), permanent neonatal diabetes (PNDM), transient neonatal diabetes (TNDM) and genetic syndrome are clinical indications of monogenic defects in beta cell function, linking insulin-deficient diabetes with specific clinical characteristics [20]. MODY which is an inherited early-onset familial diabetes that is not dependent on insulin and

results from β-cell dysfunction was clinically discovered [21].

Mutations in the gluco-kinase gene result in the commonest genetic subtypes and hepato-nucear factor gene (HNF1A MODY and HNF4A MODY) [22]. Glucose-kinase gene MODY results in life-long mild fasting hyperglycemia that deteriorates with age. Micro-vascular complications are rarely developed by these people and pharmacological treatment for hyperglycemia are not required [23].

Progressive and marked hyperglycemia with a high risk of microvascular and macrovascular complications is the hallmark of HNF1A MODY [2]. People with this subtype are sensitive to the hypoglycemic effects of sulfonylureas [23], allowing people with insulin-treated HNF1A to be successfully transferred to sulphonylureas [24].

4.3 Monogenic Defects of Insulin Action

Monogenic causes of insulin resistance are not common when compared to monogenic β-cell defects [2]. They are typically present with characteristic features of insulin resistance in the absence of obesity, including hyperinsulinemia, acanthosis nigricans, polycystic ovarian disease and Jul [25]. Diabetes starts when the β-cells fails to equilibrate for the insulin resistance [2].

Mutations in the insulin receptor give rise to several clinical manifestations and degrees of hyperglycemia [26]. The two pediatric syndrome that have mutations in the insulin receptor gene with extreme insulin resistance, dymorphism, severe intrauterine and mortality [27]. Insulin resistance is a feature associated with lipid storage disorders and it is characterized by lipodystrophy [27]. Familial partial lipodystrophy is a persistent condition characterized by limb lipoatrophy in young adult life, associated with hyperlipidemia and insulin resistant diabetes [2]. Mutations in the LMNA gene coding for nuclear Amin A/C are the commonest risk factor [28]. PPARG mutations also result in a partial lipodystrophy which is usually associated with severe insulin resistance, early onset T2DM and hypertension [29].

4.4 Diseases of the Exocrine Pancreas

Diseases which damage the pancreas can cause diabetes [2]. Pancreatitis, trauma, infection, pancreatic cancer and pancreatectomy are some of these [30]. Pancreatic damage must be severe for diabetes to occur. Adenocarcinomas involving little portion of the pancreas have been linked with diabetes [2]. This involves mechanism other than simple reduction in β-cell mass [31]. Both exocrine pancreatic failure and reduced insulin secretion are seen in cystic fibrosis, resulting in diabetes, although the relationship between these two defects is not clear [32].

4.5 Endocrine Disorders

Many hormones like growth hormone, cortisol, glucagon, epinephrine are capable of disrupting the action of insulin. Diseases such as acromegaly, Cushing's syndrome glucagonoma and pheochromocytoma which occur due to excessive secretion of these hormones can cause diabetes [33]. Hyperglycemia occurring due to these conditions be corrected when the condition causing excessive increase/raise in the hormone is treated successfully [2].

4.6 Drug or Chemical-Induced Diabetes

Corticosteroids, Beta-blockers, Thiazide diuretics, Antipsychotics, Statin, Pyrinuron, Pentamidine, Interferon-Alpha, Nicotinic acid and Dilantin are some drugs that can affect insulin secretion/action [2]. Due to insulin resistance or β-cell dysfunction in people, this drug can cause diabetes [34]. Pyrinuron (a rat poison) and pentamidine are some toxins which can destroy pancreatic β-cells permanently [35].

4.7 Infection-related Diabetes

Destruction of β-cell have been linked with virus, causing Type1 Diabetes Mellitus (T1DM), but their manner of causes remained uncertain [2]. People with congenital rubella also have diabetes [36]. Type 1 diabetes mellitus have been seen to be induced by Coxsackie B and viruses such as cytomegaovirus, Adenovirus and mumps [37].

4.8 Uncommon Specific Forms of Immune-Mediated Diabetes

Specific immune diseases are linked with diabetes and they have distinct causes to those that lead to T1DM [2]. Symptoms of hypoglycemia are usually seen in people immune mediated diabetes. An autoimmune disorder of the central nervous system, the stiff man syndrome is characterized by axial muscles stiffness with painful spasms [38]. High titres of

Glutamic acid decarboxylase (GAD65) autoantibodies are found in people with this form of diabetes and about half will develop diabetes [2]. It has been reported that people who received interfon- alpha can develop diabetes which is linked with islet cell autoantibodies and, in some cases, severe deficiency of insulin [39].

Receptor of insulin autoantibodies have ability to initiate diabetes by binding to the receptor, thereby decreasing the binding of insulin to target tissues [40]. Hypoglycemia can also occur when the insulin receptor autoantibodies act as an insulin agonist after binding to the receptor [2]. Patents with systemic lupus, erythematosus and other autoimmune diseases may also have insulin receptor autoantibodies [41]. Acanthosis negricans are usually found in people with insulin receptor autoantibodies these type of syndrome is termed type B insulin resistance.

5. SYMPTOMS AND HEALTH CONSQUENCES OF DIABETES

According to WHO, some general symptoms of diabetes mellitus include:

- Frequent urination
- Thirstiness
- Loss of weight
- Hunger
- Blurred vision
- Numbness or tingling of hands or
- Feet damage
- Skin damage
- Delayed wound or sore healing
- Infections

6. HEALTH CONSEQUENCES OF DIABETES

- **Cardiovascular disease:** This is the commonest and leading cause of diabetes, globally. Damage to blood vessels and the nerves that control the heart. Can occur due to high blood sugar [42]. A two to three fold increased risk of heart attacks and strokes are seen in adults with diabetes [2]. Cardiovascular problems, such as coronary artery disease with chest pain (angina), heart attack, stroke and narrowing of arteries (atherosclerosis) are also seen in diabetic patients.
- **Nervous damage (neuropathy):** Excess sugar can damage capillaries that nurture the nerves, especially in the leg, resulting in tingling, numbness, burning or altered pain sensation [43]. A person can lose all sense of feeling in the affected limbs, if not treated. Nausea, vomiting, diarrhea or constipation (Diabetes ketoacidosis) can occur due to damage of nerves associated with digestion. Erectile dysfunction in men can also occur due to neuropathy [43].
- **Kidney damage (nephropathy):** Damage to the tiny blood vessels in the kidney can result in diabetes and kidney failure or kidney disease can occur due to strong damage [44]. Tissue scarring, urine protein loss and severe kidney disease which can require dialysis or kidney transplant can occur due to nephropathy (Hossam, 2015).
- **Retinopathy:** Damage to blood vessels in the retina of the eye (diabetic retinopathy) can occur due to diabetes, resulting in vision loss. Other serious vision conditions, such as cataracts and glaucoma can also occur [44].
- **Foot damage and Skin conditions:** The risk of various foot complications can be increased due to damage of nerves in the feet or poor blood flow to the feet, resulting in cuts and blisters development with serious infections, if not treated [44]. Also the skin can be prone to diseases such as bacterial and fungal infections due to diabetes. Some skin rashes is usually found in the skin of a person suffering diabetes and this rashes are collectively known as diabetic dermadromes (Hossam,2015).
- **Alzheimer's disease:** Alzheimer's disease is a brain disorder, characterized by brain changes, resulting deposition of certainproteins [43]. The risk of dementia, such as Alzheimer's disease may increase due to type 2 diabetes.

7. SOME OCCUPATIONAL CHEMICALS AND DIABETES MELLITUS

Occupational or industrial chemicals are chemicals use in industries for production purposes. Exposure to most of these chemicals is seen to have some health impact. Some of the occupational chemicals which may have effects on diabetes include metallic compounds, hydrocarbons compounds and other compounds.

7.1 Diabetes Mellitus and Metallic Compounds

Naturally, heavy metals are existing metallic elements whose atomic weights and densities

are high [45]. Over a hundred milligrams of a macro metals such magnesium are required in our everyday diet while less than 100 ppm of macronutrients like manganese, cop-per, nickel, zinc, and iron are required [46]. These metals are important in several physiological and biochemical processes in the body [47,48]. Most studies suggest that uncertainty in the quantity of these metals results in significant side effects on health like that of pancreatic islets, which lead to the occurrence of diabetes. (Planchart *et al.*, 2018) [49]. Heavy metals like cadmium, (Ni), mercury, arsenic, and lead exert toxic effects on human health [50,51]. These metals have been seen to affect patient with Type 2 Diabetes Mellitus, impairing glucose uptake and glucose regulation [52].

In many studies, the length to which heavy metals affect diabetic patients have been measured. (Anam *et al.*,2021). The results reveal that a different concentration of heavy metals increases the risk of diabetes mellitus (Planchart *et al.,* 2018). Exposure to toxic metals like Pb, Ni, Cd, and Hg due to uncontrolled pollution and industrialization increases defect in glucose uptake disturbance and other problems (Anam *et al.*,2021).

7.2 Cadmium

Cadmium is one of the heavy metals which is soft and silver-white, being very toxic. (Anam *et al.*,2021). Naturally, cadmium is present in air, water, and soil and overly distributed in the earth's crust. Industrially, it is used in alloy, pigments, and batteries production. Because of its toxicity, it is not commonly used in developed countries. (Anam *et al.*, 2021). In an experiment carried out, it was seen that exposure to 0.84-mg/kg of Cd in model organisms remarkably accelerated the concentration of blood glucose (Bell *et al.*, 2003). Remarkable escalation in glucose and serum concentration decrease in experimental animals as compared to control animals after exposure was observed [53].

Moreover, the precise mechanism of action and effect of cadmium on secretion, production, utilization of Insulin and blood glucose regulation is not known because only view reports have been made on the link of cadmium and diabetes until now [54]. Many studies carried out recognized cadmium's contribution in glucose trans-porter-4 (GLUT4) down regulation and the increased alteration of pancreatic beta cells in diabetes [54]. Diabetes associated with exposure to cadmium was seen in rat adipocytes (Anam *et al.*, 2021).There was an observation in Decreased GLUT4 protein and mRNA expression was also observed as well as low glucose tolerance in experimental rats [55]. Accumulation of Cadmium metal causes several dysfunctions like cell degeneration or necrosis and weak degranulation in pancreatic β cells as shown by many experimental studies.
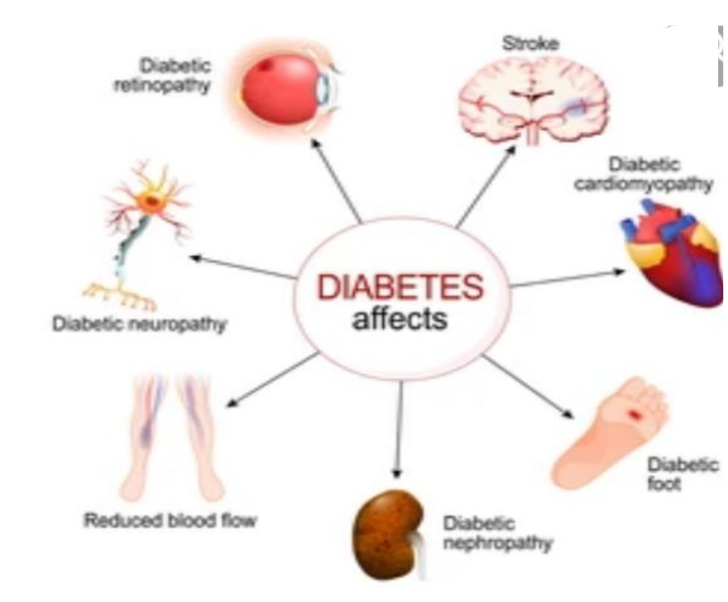

Fig. 2. Diagram showing the health Consequences of diabetes mellitus
Source: Hossam, (2015)

7.3 Arsenic

Arsenic (As,) a chemical element occurring naturally and distributed widely in the earth's crust (NIH, 2016). Its level in the environment differs, found commonly in water, air and soil. Organic arsenic which contain carbon and inorganic arsenic which is highly toxic are the two types of arsenic. (NIH, 2016). Smelters and glass workers used arsenic during production and it is used in production of arsenic containing pesticides [56]. The link between Arsenic exposure and different diabetes mellitus outcome have been investigated by most research studies [57]. Drinking water from private wells can be contaminated by arsenic especially throughout South East-Asia and Latin-America [58]. There are no epidemiological studies investigating associations between arsenic exposure and T1DM development. Immune system in humans and animal models were seen to be impaired due to exposure to arsenic [58], alteration of gut microbiome diversity, metabolic profiles of microbiomes   well as inhibition of   glucose stimulated insulin release in mice were also observed [59].

7.4 Diabetes Mellitus and Hydrocarbons

Organic molecules that consist mainly carbon and hydrogen atoms are termed Hydrocarbons. Hydrocarbons can be aromatic or aliphatic. Hydrocarbons with closed ring structures are called aromatic hydrocarbons while those with linear chain structures are called aliphatic hydrocarbons [60]. Both types of hydrocarbons can undergo modification by replacing the hydrogen atoms with halogens, thereby changing their physical and chemical properties [61]. Hydrocarbons found in industries are used mainly as solvents, raw material in plastics/rubber production, as fire extinguisher, metal cleaning agents, fumigants and Insecticides [62].

7.5 Diabetes Mellitus and Aromatic Compounds Aromatic

Hydrocarbons are Hydrocarbons with a closed ring structure. Examples of aromatic hydrocarbons are Benzene, Napthalene, Phenanthrene, Methylbenzene, Trinitrotoluene and O-dihydroxybenzene.

7.6 Benzene

It is the commonest complex aromatic hydrocarbon. The bonding nature of Benzene was first discovered by August Kekulé in the 19thcentury. Benzene is an organic hydrocarbon which is colourless and has a molecular structure C_6H_6 (Fig. 4). Benzene is mainly used as solvent in industries and it is widely used in production of various polymers, resins and synthetic fibers [63]. Studies have been carried out to investigate the mortality rate of diabetes mellitus in relation to benzene exposure during the production, processing, recovering, loading and unloading of benzene contained materials [64]. Disturbance of glucose homeostasis and glucose intolerance is seen in experimental models exposed to benzene.

Study revealed that exposure of diabetic mice to volatile benzene-increases insulin resistance in the liver and skeletal muscle. This is due to Nuclear factor Kappa (Nf-kb) activation, Macrophage inflammatory protein (Mip-1α) expression, and Suppressor of cytokine signaling 1-mediated inhibition of Akt-phosphorylation, thereby inhibiting insulin receptor substrate(Ir-2)phosphorylation [65].

7.7 Methane

Methane is a colourless and odourless gas which exists in nature abundantly, and it is a produced as a result of activities carried out by humans. The simplest member of the paraffin sequence of hydrocarbons is methane and is seen to be one of the most potent of the greenhouse gases with a chemical formula is CH_4 (Fig. 4.). Methane is water soluble, burning at ease in air to form CO_2 and water vapour. Methane is produced naturally by an anaerobic decomposition of vegetable matter under water by bacteria. Methane is a the major constituent of natural gas and also exist as the component of flammable gas together with coal steam [66].
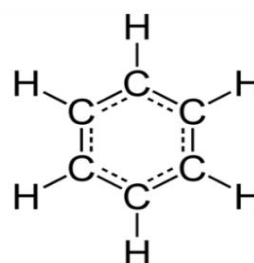

Fig. 3. Structure of benzene
Source: Bahadar et al., [63]

According to experimental studies, it was shown that subjects producing methane have higher increase in the levels of their glucose when an oral glucose test was carried out compared to

non-methane producing subjects but there was no outstanding difference in the insulin resistance of subjects producing methane [67]. This suggest that subjects with increase levels of methane in the intestine may also have impaired glucose tolerance increase when affected with a high carbohydrate load, and may have high tendency of developing hyperglycemia [67].

Fig. 4.Structure of methane
Source: Britannica, [63]

7.8 Diabetes Mellitus and Other Occupational Chemicals

Other widely used industrially chemicals include Polychlorinated Biphenyls (PCBs), Tetrachlorodibenzo-p-dioxin (TCDD), Triclosan, etc.

7.9 Polychlorinated Biphenyls (PCBs)

One of the man-made organic chemicals that contain carbon, hydrogen and chlorine atoms is the polychlorinated Biphenyls (Fig. 5). Dielectric and coolant fluids in electrical equipment are polychlorinated biphenyls. In a study conducted on pregnant women who were diabetic (primarily type 1), Increase in the serum levels PCBs were linked with diabetes [7]. Another epidemiological study, however, showed inverse link between an increased PCB-135 or p.p`DDE serum level during pregnancy and development of Type 1 diabetes mellitus in the child, but this was not statistically significant [68]. Studies carried out revealed that employees working in factories were PCB are produced had higher anti-glutamic acid decarboxylase (anti-GAD) antibodies prevalence in their serum compared to controls, supporting the polychlorinated biphenyls effects on autoimmunity [69].

In studies conducted on animals exposed to persistent organic pollutants, an increase in insulin resistance was seen, indicating T2DM development [70] and the link between serum PCB levels and T2DM in humans have been shown by numerous studies [5]. Dioxins and dioxin like PCBs act via the aryl hydrocarbon receptor (AhR) and can cause Oxidative stress, apoptosis, and increased inflammation can be caused by dioxins and dioxin like PCBs which act via the aryl hydrocarbon receptor, during metabolization/detoxification of the chemical [71].
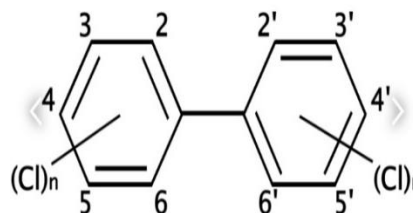

Fig. 5. Structure of polychlorinated biphenyls
Source: Longnecker et al., [7]

7.10 7,8-Tetrachlorodibenzo-pdioxin (TCDD)

7,8Tetrachlorodibenzo-p-dioxin (TCDD) is a chemical with a chemical formula $C_{12}H_4Cl_4O_2$ (Fig. 6) and it is a byproduct formed during the manufacture of materials that require the use of chlorinated and during the combustion of chlorinated chemical products. It has been used in widely in herbicide production [72]. Exposure of humans to this chemical is mainly through Intake of marine food and result in the exposure of humans to this chemical, due to accumulation of the chemical in fatty tissue in the food chain.

Toxicity to insulin-secreting cells (INS-1E) of rat pancreatic beta cells, despite survival and ultrastructure via activation of the aryl hydrocarbon receptor was seen in a study carried out [73]. Also, many experimental studies have shown an impairment in glucose-stimulated secretion of insulin from the islets via the AhR signaling pathway in mice exposed to TCDD [74]. TCDD exert adverse effects on beta cells by stimulating continuous insulin release resulting in beta cell exhaustion in an INS-1 rat beta-cell line [75, 103-108].
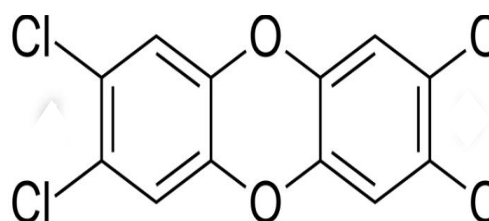

Fig. 6. Structure of 7,8-Tetrachlorodibenzo-p-dioxin (TCDD)
Source: Holsapple et al., [72]

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7.11 Polybrominated Diphenyl Ethers

Polybrominateddiphenyl ethers (PDBE) are chemicals used as retardants of flames in building materials, textiles, furnishings, and electronics. Ingestion of food and inhalation of air contaminated with polybrominated diphenyl ethers results in exposure of humans to this chemicals. Studies carried out on mice shown hyperglycemia induction, decreased insulin, increased glutathione and superoxide dismutase levels in the serum and increased TNFα levels in the serum on exposure of mice to the chemical, probably via oxidative induction [76, 96-102].

7.12 Perfluorinatedakyl Substance

Perfluorinatedalkyl substances (PFAS) are substances having attractive lipid and water repelling properties, used as fire extinguishing foam, textiles, kitchen ware, and food packaging materials. Human are exposed to PFAS primarily through diet via marine food and game. Epidemiological study reported that increased serum level of the perfluorononanoic acid (PFNA) in human adolescents is associated with decreased blood insulin and beta-cell function [77-81]. In elderly population, increase PFAS level in the serum is linked with diabetes and studies shown that PFAS can alter glucose metabolism in humans and induce T2DM (Kind *et al.*, 2014) [82-88, 109-110].

7.13 Management Approach to Chemical Exposure

Some of the management approach to reduce the effects of occupational chemicals on diabetic include [89-95]:

- Use of protective cover such as gloves, masks, etc. to reduce contact with the chemicals
- Washing of hands with soap and warm water after using the chemicals
- Keep the work area ventilated
- Read the instructions for how to use the chemical properly.

8. SUMMARY

In this research work, it was interesting to know that some occupational chemicals can increase the risk of diabetes mellitus. In a study carried out on pregnant women with diabetes (primarily type 1), Polychlorinated Biphenyl serum levels were linked with Type 1 diabetes mellitus.

Exposure to cadmium which is an heavy metal shows an escalation in glucose and serum concentration decrease in experimental animals compared to control animals. Hyperglycemia, decreased insulin, increased glutathione, and superoxide dismutase levels in the serum, increased TNFα levels in the serum, through the induction of oxidative damage was seen in experimental mice exposed to polybrominated diphenyl.

9. CONCLUSION

Some occupational have been seen to have adverse effects on diabetes mellitus. These occupational chemicals could be metals, hydrocarbons or other compounds. These chemicals exert their effects via different mechanisms.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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