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Effect of environmental air pollution on type 2 diabetes mellitus

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Abstract. – OBJECTIVE: Air pollution is a novel risk factor for insulin resistance and occurrence of type 2 diabetes mellitus (T2DM), but the evidence is limited and diverse. Therefore, the aim of this study was to assess the effect of environmental air pollution on incidence of type 2 diabetes mellitus.

METHODS: In this study, we identified 102 published studies through a systematic data base search including ISI-Web of Science, EMBASE and PubMed. We searched the related literature by using the key terms including diabetes mellitus, air pollution, occupational and environmental pollution, gaseous, NO_2, particulate matter pollutants $PM_{2.5}$, and PM_{10}. Studies in which diabetes mellitus, insulin resistance, air pollution, occupational and environmental pollution was discussed were included in the study. No confines on publication status, study design or language of publication were considered. Descriptive and quantitative information were extracted from the selected literature. Finally we included 21 publications and remaining studies were excluded.

RESULTS: Air pollution is a leading cause of insulin resistance and incidence of type 2 diabetes mellitus. The association between air pollution and diabetes is stronger for traffic associated pollutants, gaseous, nitrogen dioxide, tobacco smoke and particulate matter.

CONCLUSIONS: Exposure to air pollutants is significantly associated with increased risk of type 2 diabetes mellitus. It is suggested that, environmental protection officials must take high priority steps to minimize the air pollution, hence to decrease the incidence of type 2 diabetes mellitus.

Key Words:
Air pollution, Type 2 diabetes mellitus, Environmental pollutants.

Introduction

Diabetes mellitus is a life-long disease and swiftly increasing in all age groups and both genders. It involves various physiological functions, organs and multiple systems[1] and is associated with wide ranging and devastating health complications[2]. New figures have broken all the previous prevalence records as shown by the recent release of the International Diabetes Federation's 6th edition of the Diabetes Atlas, which indicated that global prevalence of diabetes is 8.3% which means that 382 million adults are diabetics, and the number is expected to rise to 592 million by 2035. IDF also estimated that as many as 183 million people are unaware that they have diabetes[3].

Air pollution is a leading environmental risk factor that contributes to the development of a wide range of acute and chronic respiratory and coronary artery diseases. Current literature indicates that air pollutants may contribute to impaired glucose metabolism, occurrence of insulin resistance and type 2 diabetes mellitus[4,5]. The suggested mechanism includes oxidative stress and low grade inflammation[6,7] which results in impairment of insulin signaling[8] and causes diabetes mellitus. It has also recently been hypothesized that long-term exposure to air pollution is a risk factor for type 2 diabetes[4,9-11] but still the association remains unclear due to the conflicting results. Therefore, the present study aimed to assess the effect of environmental air pollution on incidence of type 2 diabetes mellitus.

Research Methodology

Selection of Studies

The present study was conducted in the Department of Physiology, College of Medicine, King Saud University, Riyadh, Saudi Arabia. In this study, we identified 102 published studies through a systematic database searches including ISI-Web of Science, PubMed and Em-

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base. We searched the related literature by using the key terms including air pollution, type 2 diabetes mellitus, environmental pollution, diabetes risk, $PM_{2.5}$, PM_{10}, and NO_2. In addition, we also entered the keywords in the Google Scholar search engine and after getting any related article, we re-entered the title of that article in the ISI-Web of Science and PubMed to verify for any missing article. The title and abstract of the studies were evaluated to determine eligibility for the documents. All studies in which insulin resistance, diabetes mellitus and air pollution were discussed were considered eligible for inclusion. No limitations on publication status, study design or language of publication were imposed. We reviewed 102 papers; finally, we included 21 studies and remaining studies were excluded from the study.

Inclusion and Exclusion Criteria

The inclusion criteria was cohort studies; cross sectional studies, systematic review; studies which estimated the effect of long-term exposure to air pollution, including $PM_{2.5}$, PM_{10}, and NO_2, on risk of type 2 diabetes; studies which reported relative risks for type 2 diabetes and air pollutants were included. The studies published in non ISI indexed journals, without usable data or of low quality were excluded.

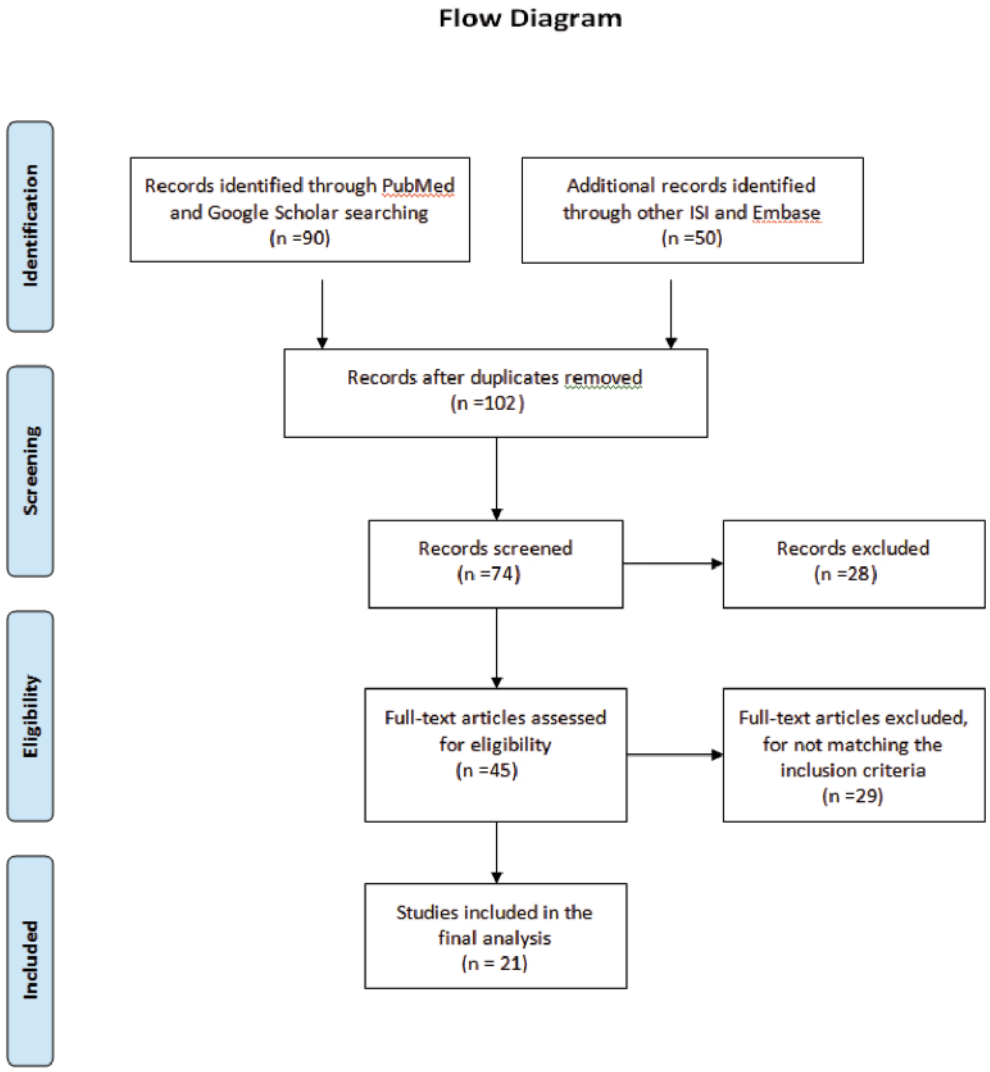

Figure 1.

Table I. Effect of various types of air pollutants and their association with insulin resistance and type 2 diabetes mellitus.

Authors name and year	Type of study	Pollutants	Effect
Liu et al, 2014[6]	Cross sectional	$PM_{2.5}$	Abnormalities in glucose homeostasis, inflammation, insulin resistance and type 2 diabetes mellitus.
Park and Wang 2014[12]	Systematic review	$PM_{2.5}$	Type 2 diabetes mellitus
Wang et al, 2014[13]	Systematic review	$PM_{2.5}$ NO_2	Type 2 diabetes mellitus
Balti et al, 2014[14]	Systematic review	NO_2, $PM_{2.5}$	Type 2 diabetes mellitus
Janghorbani et al, 2014[15]	Systemic review	Gases $PM_{2.5}$	Type 2 diabetes mellitus
Eze et al, 2014[16]	Cross sectional	$PM_{2.5}$ NO_2	Type 2 diabetes mellitus
Pope et al, 2014[17]	Cohort	$PM_{2.5}$	Contribute to cardio-metabolic disorders
Thiering et al, 2013[18]	Cross sectional	NO_2, $PM_{2.5}$	Insulin resistance and type 2 diabetes mellitus
Xu et al, 2011[8]	Cross sectional	$PM_{2.5}$	inflammation, impaired glucose tolerance, insulin resistance, mitochondrial alteration, and type 2 diabetes mellitus.
Teichert et al, 2014[19]	Cohort study	NO_2, NO_x	Impaired glucose metabolism
Coogan et al, 2012[20]	Cohort study	$PM_{2.5}$ NO_2,	Risk of type 2 diabetes mellitus

PM = particulate matter with aerodynamic diameter; NO_2 = Nitrogen dioxide; NO_x = Nitrous Oxide

Data Extraction and Quality Assessment

Findings were extracted independently by two investigators; the results were determined by using a standardized form including a full description of the study characteristics.

Results

Table I demonstrates the effect of various types of air pollutants and their association of type 2 diabetes mellitus. There is a strong association between diabetes mellitus and particulate material $PM_{2.5}$, PM_{10}, Nitrogen dioxide (NO_2) and gases. The air pollutants can cause inflammation, abnormalities in glucose homeostasis, insulin resistance, mitochondrial alteration and development of type 2 diabetes mellitus.

Discussion

Air pollution is the introduction of chemical, particulate matter and biological materials that may cause damage to natural environment and harm to living organisms. The group of molecules and pollutants identified as hormonal disruptors and insulin resistance is highly heterogeneous, including dust, fumes, synthetic chemicals, industrial solvents, lubricants, plastics, pesticides and fungicides.

Air pollution is an important risk factor for global burden of wide range of diseases, can cause various respiratory and cardiovascular problems but, more recently, it has also been reported that air pollution may cause insulin resistance and diabetes mellitus[4-5].

Liu et al[6] reported that high concentration of ambient particulate matter $PM_{2.5}$ exposure impairs energy metabolism, abnormalities in glucose homeostasis, increased inflammation in insulin responsive organs, brown adipose tissue inflammation and results in imbalance in circulating leptin/adiponectin levels. These results provide deep insights into the mechanisms adjoining air pollution mediated insulin resistance and type 2 diabetes mellitus.

Wang et al[13] reported that, long-term exposure to high levels of air pollutants is significantly associated with elevated risk of type 2 diabetes mellitus. Belti et al[14] determined the effects of air pollutants on the occurrence of diabetes mellitus. They found that the overall effect on diabetes occurrence was significant for NO_2 and $PM_{2.5}$. Available evidence supports a potential association of air pollutants with an increased risk for type 2 diabetes mellitus. Park and Wang[12] conducted a systematic review of the epidemiologic studies on the association of air pollution with T2DM. They demonstrated that air pollution is a new risk factor for type 2 diabetes mellitus (T2DM).

Eze et al[16] found that long term air pollution exposure is associated with diabetes mellitus. PM_{10} appears to be an important risk marker of air pollution relevant to diabetes. Janghorbani et al[15] demonstrated that exposure to air pollution

and diabetes was stronger for gaseous pollutants than for particulate matter. The author suggests that exposure to air pollution may be a risk factor for diabetes and increases susceptibility of people with diabetes to air pollution. Pope et al[17] demonstrated that long-term exposure to fine particulate matter ($PM_{2.5}$) air pollution contributes to risk of development or exacerbation of cardiometabolic disorders, increasing risk of coronary artery disease and cardio-metabolic disease mortality.

People in urban areas are more likely to be exposed to polluted air which is believed to be a factor in lung function impairment. Lee at al[21] examined urban/rural differences in the prevalence and associated factors with type 2 diabetes mellitus (T2DM). The crude and age standardized prevalence of T2DM was 15.4% and 14.5%, and 11.7% and 8.6% in urban and rural districts respectively. T2DM was more prevalent in urban than in rural population.

There are multiple factors involved in the contamination of the environment including cigarette smoking. Active smoking has been considered a risk factor for type 2 diabetes mellitus. Cho et al[22] reported that environmental tobacco smoke exposure is a significant risk factor for the development of type 2 diabetes with dose-response relationship. Brook et al (2008)[9] studied the relationship between diabetes mellitus and exposures to traffic pollution among more than 7600 men and women in two Canadian cities using nitrogen dioxide (NO_2). Their findings showed a statistically significant increase in DM among women with each increase in 1-ppb exposure to NO_2. It has been also reported that an average particulate matter (PM) less than 10 μm in aerodynamic diameter exposure was significantly higher for children diagnosed with DM compared with controls[23].

Researchers investigated the relationship between air pollution exposure and new-onset of type 2 diabetes using information from the prospective study on the influence of air pollution on lung. They observed that exposure to traffic-related air pollution and higher levels of complement C3 in the blood were associated with increased diabetes risk. They reported that the women living within 100 m of a busy roadway had more than double the risk of diabetes for women in the same group who did not live near a busy roadway. Overall, the researchers observed significant associations with PM and NO_2 exposure with diabetes mellitus. It has also been reported that the environmental toxins including arsenic and dioxin may have some relationship to an increased risk for diabetes mellitus[24]. Recent reports shows high prevalence of diabetes among urban population, however, there are very few studies comparing the urban, peri-urban and rural prevalence rates of diabetes and their risk factors. The lowest prevalence of self-reported diabetes was recorded in rural (3.1%) followed by peri-urban/slum (3.2%) and the highest in urban areas (7.3%). It shows that the prevalence of diabetes is higher in urban, moderate in peri-urban and lowest in rural areas. The most probable cause of this association is environmental pollution in urban areas, hence type 2 diabetes is more common in urban areas compared to rural areas.

The possible mechanism for the adverse effect of air pollution on incidence of type 2 diabetes mellitus is insulin resistance. Both experimental and epidemiologic studies suggest that environmental exposures to air pollutants can increase the risk of insulin resistance, which may lead to a link between air pollution and type 2 diabetes mellitus. Moreover, inflammation is another potential mechanism explaining the associations reported in the literature in the pathogenesis underlying the association between air pollution and type 2 diabetes.

Thiering et al[18] examined the associations between long-term exposure to traffic-related air pollution and type 2 diabetes mellitus. The level of insulin resistance was greater in children with higher exposure to air pollution. Insulin resistance increased by 17.0% and 18.7% for increase in ambient NO_2 and particulate matter ≤ 10 μm in diameter respectively. Recent literature suggests that exposure to traffic related air pollution influences the development and progression of cardio-metabolic diseases possibly via systemic oxidative stress and low-grade inflammation[7]. These underlying biological mechanisms are also involved in the pathogenesis of type 2 diabetes mellitus, particularly in the progression of insulin resistance[7].

It has also been shown in animal model studies that exposure to particulate matter 2.5 μm or less in diameter ($PM_{2.5}$) for 24 weeks exaggerates the insulin resistance, visceral inflammation and adiposity[10]. Exposure for a duration of 10 months leads to oxidative stress, decreased mitochondrial count in visceral adipose depots and decreased mitochondrial size in inter-scapular adipose depots[8]. Adverse effects have been found to be associated with indoor air pollution exposure, be-

tween environmental tobacco smoke and type 2 diabetes mellitus incidence and susceptibility among adults[25] and adolescents[26]. It thus seems biologically plausible that air pollution may be a risk factor for insulin resistance and type 2 diabetes mellitus.

There are few limitations of the present study. There was a lack of individual participant's data, no specific pollutant content concentration and lack of literature from the developing world. Large sample sized longitudinal studies are needed to provide a more precise assessment of the adverse effects of long-term exposure to air pollution on type 2 diabetes risk. Further data from both experimental and epidemiologic studies are needed to provide a better conclusion with more insights into the adverse effect of air pollution on type 2 diabetes risk.

Conclusions

Exposure to air pollutants is significantly associated with increased risk of type 2 diabetes mellitus. Long-term exposure to air pollutants induces inflammatory response in the lung and visceral adipose tissue, insulin resistance and ultimately causes type 2 diabetes mellitus. These findings suggest an important public health impact on human populations. It is suggested that, health officials must develop policies to minimize air pollution to decrease the incidence of diabetes mellitus.

Acknowledgements

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Conflict of Interest

The Authors declare that they have no conflict of interests.

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