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Trend and Association of Mean Glycated Hemoglobin Levels to Ambient Air Pollution in Lower-middle income and High-Income Countries: A Secondary Data Analysis

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ABSTRACT

Background and Aim: There are numerous studies published regarding the association between air pollutants and diabetes mellitus but limited studies on the overall trend and association of Particulate Matter 2.5 and HbA1c among lower-middle-income and high-income countries. So, this secondary data analysis is aimed to investigate the trend of Particulate Matter 2.5 and Hemoglobin A1c and evaluate the association between them in these countries.

Methods: This is secondary data analysis. The values of Particulate Matter 2.5 (years 2010-17), fasting plasma glucose (years 2010-2014), and Gross Domestic Product per capita (years 2010-18) for Lower middle income and High-Income countries were obtained from relevant sources. Hemoglobin A1c values were calculated. Countries with missing data were excluded. The Independent-Student T-test and Pearson correlation were applied to analyses the data using the SPSS-23-Trial version.

Results: The Gross Domestic Product per capita in High-income countries increased significantly in the past10 years while minimal changes were seen in Lower middle-income countries. The particulate Matter 2.5 value has decreased, and there is a slight increase in Hemoglobin A1c in both groups. There is a substantially higher Gross Domestic Product per capita in High income countries, significantly higher Particulate Matter 2.5 in Lower middle-income countries, and similar HemoglobinA1c in both income groups. There is a weak negative correlation between particulate Matter 2.5 and Hemoglobin A1c in Lower middle-income countries, while a significant positive correlation was seen in High-income countries.

Conclusion: The higher Particulate matter 2.5 in Lower middle-income countries is a concern because various studies have related the increased Particulate Matter 2.5 to increased Diabetes Mellitus prevalence. This demands the appropriate interventions in Lower middle-income group countries to reduce ambient air pollution and health planning to reduce the prevalence of Diabetes mellitus in the future.

INTRODUCTION

According to World Health Organization (WHO), 422 million people worldwide have Diabetes Mellitus (DM) and 1.6 million deaths annually as DM cause severe damage to organs, causing cardiomyopathy, retinopathy, nephropathy and neuropathy [1].

Prevalence of DM is increasing rapidly worldwide. Genetic predisposition, unbalanced diet, culture, and lack of physical activity can increase the prevalence of metabolic disorders such as T2DM [1].

DM is divided into Type 1 Diabetes Mellitus (T1 DM), Type 2 Diabetes Mellitus (T2 DM) and others.

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The most prevalent type of DM is type-2, which accounts for up to 90% of cases, followed by T1 DM [1]. T1 DM is an autoimmune condition Involving the Pancreatic-Beta cells, leading to the destruction of insulin-producing cells; T2 DM involves a combination of insulin deficiency and insulin resistance [2]. In healthcare settings, Fasting plasma Glucose (FPG), oral glucose tolerance test (OGTT) and Glycated Hemoglobin A1c (HbA1c) tests are used to diagnose and monitor DM. According to ADA (American Diabetes Association), there are four criteria for diagnosis of DM including FPG≥126mg/dl, 2h-OGTT≥200mg/dl, HgbA1C≥6.5%, and Random blood glucose ≥200mg/dl with symptoms of hyperglycemia include polyuria, polydipsia, polyphagia and weight loss.[2]. However, HbA1c has been recognized as the gold-standard of monitoring long-term glucose control. It can measure the average blood glucose concentration for the past three months without any prior fasting required [3].

The first-line management for type 2 DM is lifestyle modification (medical nutritional therapy and exercise) and metformin therapy. If T 2 DM is not controlled well in the initial stage, medications such as metformin can be used to improve the metabolic control of glucose. Good glycemic control reduces the risk of complications. The two main categories include Vascular and nonvascular. Vascular complications include macro-vascular (Cardiovascular, cerebrovascular and peripheral vascular diseases) and Microvascular (retinopathy, nephropathy and neuropathy) Nonvascular complications include gastroparesis, infections, skin changes, and hearing loss [4]. Forty over types of genetic predispositions have been identified which have a higher tendency to cause DM Obviously, polygenic etiology is not the only main risk factor of DM An unhealthy diet with obesity, sedentary lifestyle, smoking and exposure to air pollutants are the other prominent factors [5].

Air pollution is defined as a mixture of both man-made (vehicle and factory emissions) and natural source (volcanic eruptions and soil decomposition) substances [6]. These air pollutants cause detrimental effects on human health. An average of 4.2 million deaths per year is related to outdoor air pollution [7].

Air pollutants can be in solid or gaseous forms such as carbon monoxide, ammonia or particulate matter (PM)[6]. Air Quality Index (AQI) is used to quantify the amount of air pollutants based on the country's air quality standards. PM2.5 is air particles that are less than 2.5 microns and capable of entering the bloodstream and reaching all body systems. When the PM2.5 raises to 35.5 μg/m^3 it is considered unhealthy [6].

Prolonged inhalation increases the risk of respiratory and cardiovascular diseases [7]. Additionally, long-term exposure to ambient air pollution has a strong link to DM by impairing glucose metabolism, increasing inflammation and insulin resistance [8].

However, air pollution is not uniform across the world due to various geographical, economic and political factors. According to The World Bank, countries are classified into four income classes: high, upper-middle, lower-middle and low, based on countries Gross Domestic Product (GDP [9]). GDP per capita is a country's economic output divided by its population.

It's a good representation of a country's standard of living. GDP per capita less than $1,035 are known as low-income countries (LIC); from $1,036 to $4,045 GDP per capita is categorized as lower-middle-income countries (LMIC); $4,046 TO $12,535 as upper-middle-income countries (UMIC) and $12,535 or above as high-income countries (HIC) [9]. GDP per capita is defined as the average living standard per person and GDP per capita plays an important role in affecting the population's living standard [10]. As low GDP per capita countries are unable to provide quality healthcare, education and state of the art technologies to their nations, this leads to increasing health issues, high unemployment rates, and potentially polluting the environment [10].

In recent years, an increasing number of epidemiological studies have investigated the possible relation between chronic exposure to elevated PM2.5 and T2 DM [11,12,13,14]. A meta-analysis from North America and Europe showed that every increase of 10μg/m^3 in PM2.5 raised 10% risk of T2 DM [13].

A cross-sectional study by Disease Control and Prevention (CDC) reported 1% increase of HbA1c for every 10μg/m^3 of PM2.5 increase [14]. The annual mean of PM2.5 concentrations between developed and developing countries is in extreme contrast, and limited studies were conducted to compare and analyze the variation among HIC and LMIC. So, we have designed this study to analyze the trend of PM2.5 and HbA1c values in the lower-middle and high-income countries and also to compare and correlate the PM2.5 and HbA1c levels in these countries.

METHODS

Ethical Permission

All the data is available on the Global Health Repository database website and the World Bank Database website, which has open access to the public. The ethical approval was obtained from the Universities ethical committee in compliance with the Helsinki Declaration.

Study Design

The study was conducted in PURCSI school of Medicine, Kuala Lumpur, Malaysia, between January to June 2020. The study employed a secondary data analysis from freely available data from the Global health observatory (GHO) from lower-middle (LMIC) and high-income countries (HIC).

The GHO data repository is WHO's gateway to health-related statistics for its 194 Member States. It provides access to over 1000 indicators on priority health topics, including mortality and burden of diseases [15]. Data on GDP per capita and PM2.5 of LMIC and HIC were collected from the World Bank database [9]. Fasting plasma glucose data were obtained from the Global Health Observatory (GHO) database [15]. A total of 49 LMIC and 54 HIC data were included based on the inclusion-exclusion criteria.

The list of countries in LMIC group were: Algeria, Congo, Kiribati, Nepal, Angola, Côte D'Ivoire, Kyrgyzstan, Nicaragua, Bangladesh, Djibouti, Lao People's Democratic, Republic, Nigeria, Benin, Egypt, Lesotho, Pakistan, Bhutan, El Salvador, Mauritania, Papua New Guinea, Bolivia, Eswatini, Moldova, Philippines, Cabo Verde, Ghana, Micronesia (Federated States), Sao Tome and Principe, Cambodia, Honduras, Mongolia, Senegal, Cameroon, India, Morocco, Solomon Islands, Comoros, Kenya, Myanmar, Sri Lanka.

The List of HIC included in the study are: Andorra, Finland, Malta, Slovenia, Antigua and Barbuda, France, Mauritius, Spain, Australia, Germany, Netherlands, Sweden, Bahamas, Greece, New Zealand, Switzerland, Bahrain, Hungary, Norway, Trinidad and Tobago, Barbados, Iceland, Oman, United Arab Emirates, Belgium, Ireland, Panama, United Kingdom, Brunei Darussalam, Israel, Poland, United States, Canada, Italy, Portugal, Uruguay, Chile, Japan, Qatar, Croatia, Republic of Korea, Romania, Cyprus, Kuwait, Saudi Arabia, Czech Republic, Latvia, Seychelles, Denmark, Lithuania, Singapore, Estonia, Luxembourg, Slovak Republic.

Study Subjects

Inclusion criteria

The GDP, PM2.5 and HbA1c data obtained from the World bank Database and the global health Observatory for both LMIC and HIC were included. The GDP data was available for the years 2010-2018, PM2.5 data for the years 2010-2017 and HbA1c data was from the years 2010-2014. However, data for correlation of the Objectives was collected until 2014. Exclusion Criteria:

The following countries with missing data were excluded from the study. For HIC, it was Aruba, Bermuda, Cayman Islands, Channel Islands, Faroe Islands, Guam, Monaco, Nauru, Palau, San Marino, ST Kitts and Turks and Caicos Islands, and for LMIC, they were West Bank and Gaza strip.

Research Methods

The GHO database only provided the mean FPG values, so we converted the mean FPG into HbA1c by using the FPG/HbA1c conversion calculator provided by the American Diabetes Association [16].

The PM2.5 concentrations can be measured by infrared, BAM and laser diffraction and detected through the sensor devices [17]. The levels of PM2.5 below 12 μg/m^3 are considered healthy, 12.1-35.4μg/m3 is moderate and above 35.5μg/m3 is unhealthy [6].

Statistical Methods

All data collected was keyed into the IBM SPSS 23 system for further data analysis. The descriptive data were expressed in mean ± SD. Microsoft Excel was used to draw the trend and correlation graph. Independent Student t-test was used to compare mean HbA1c and PM2.5 between LMIC and HIC. Furthermore, Pearson correlation was used to correlate the relationship between PM2.5 and HbA1c in both groups. The p-value of less than 0.05 was considered statistically significant.

RESULTS

The trend of mean GDP per capita, HbA1c and PM2.5 levels in lower-middle and high-income countries

Our study evaluated the trend of mean GDP per capita, HbA1c and PM2.5 in 49 LMIC and 54 HIC.

As depicted in figure1, the mean GDP per capita trend in both LMIC and HIC for the period of 8 years (2010-2018). LMIC countries mean GDP per capita had very minimal changes. In contrast, HIC displayed the increased GDP for 2010-2014 followed by a dip (2015-2016) and a steady increase in GDP in these countries for the last few years.

The mean PM2.5 values for both groups of countries from the year 2010-2017 is illustrated in figure 2. There was little variation seen for the overall mean PM2.5 level as the mean PM2.5 value fluctuated throughout the years, but had declined slightly comparing 2010 to the year 2017 for LMIC and HIC. The mean HbA1c level for both groups from 2010-2014 is shown in figure 3. Mean HbA1c of HIC remained stable for the first four years, followed by a rise in 2014. However, the mean HbA1c for LMIC increased constantly throughout the years.

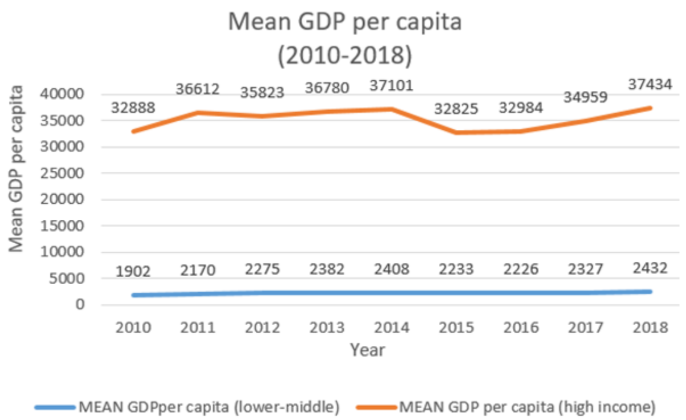

FIGURE 1. The Mean Gross Domestic Product (GDP) trend in both Lower-Middle and High-Income countries for the period 2010 -2018.

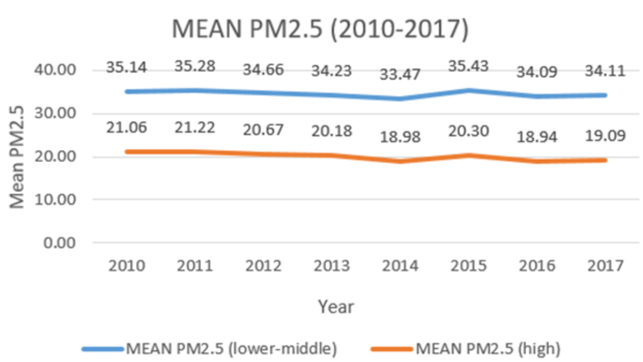

FIGURE 2. Mean Particulate Matter (PM) 2.5 values from both Lower-Middle Income and High-Income countries for the period from 2010 to 2017.

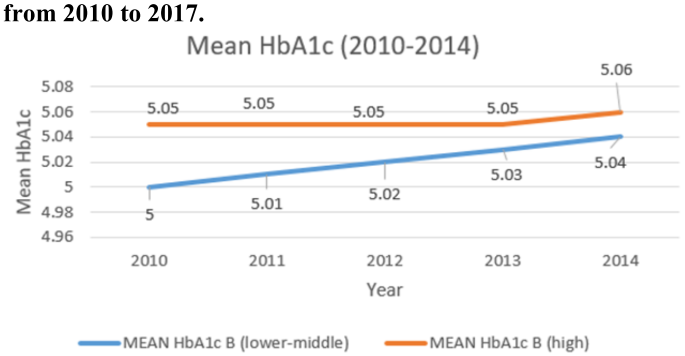

FIGURE 3. mean Hemoglobin A1c levels for both Lower-middle Income countries and High-income countries for the period from 2010 to 2014.

TABLE 1. Comparison of the mean of HbA1c and PM2.5 in lower-middle and high-income countries

	LMIC	HIC	P-Value
GDP per capita (2010-2018)	2262±1023	35267±21658	<0.001
PM2.5 (2010-2017)	34.6±19.3	20.1±17.0	<0.001
HBA1c (2010-2014)	5.02±0.33	5.05±0.26	0.129

HIC: High Income Countries; LMIC: Low-Middle Income Counties

The mean GDP was significantly higher ($p<0.001$) in HIC than LMIC on applying Independent Student T-test. In contrast, mean PM2.5 values were significantly higher ($p<0.001$) in LMIC than HIC on using Independent Student T-test. However, there was no significant difference in mean HbA1c was observed between HIC and LMIC

Correlation of the mean of HbA1c and PM2.5 in lower-middle and high-income countries

On applying Pearson correlation, negative correlation ($r=0.079$ & $p=0.60$) was observed between PM2.5 and HbA1c in LMIC, whereas a significant positive correlation was observed in HIC ($r=0.571$ & $p<0.01$, as shown in Table 1).

DISCUSSION

The relationship between the prevalence of DM and air pollution has been studied in many regions worldwide. Most of the studies indicated a positive association between air pollution and DM [13]. Since the LMIC and HIC countries differ in many ways, no studies describe the pattern of HBA1c and PM2.5 and their relation. So, the present study aimed to explore the trend of HBA1c and PM 2.5 and evaluate the relationship between them in LMIC and HIC.

Results showed that the trend of mean GDP per capita in HIC increased in the last few years. This may be mainly due to economic growth, technological advancement, and better education in these nations. high-income [18]. Thus, GDP per capita was significantly higher in HIC. At the same time, the trend of PM2.5 from 2010-2017 is in a downward trajectory compared to the initial years. This may be due to developed countries' economic ability in promoting and encouraging usage of renewable fuels, natural sources, and public transportation [19]. While the mean HbA1c remained stable throughout the first 4-years, we could relate this to promoting community awareness and health-planning measures towards reducing the prevalence of non-communicable and health-style diseases prevalence [20]. Hence, the slight increasing trend of HbA1c levels in HIC could be due to economic development, which led to lifestyle changes such as physical inactivity, stress and overconsumption of highly processed foods and foods containing artificial preservatives. These factors may impact the rise in HbA1c levels in populations that cause metabolic dysfunction in the long run and eventually could increase DM prevalence [20].

Furthermore, a statistically significant positive association was found between PM2.5 and HbA1c in HIC. Exposure to high levels of PM2.5 was reported to be one of the contributing factors for the increased prevalence of DM by many case studies [8,11,12,13,14, 21,22]. A cross-sectional study by Korean National Health analyzed that high exposure to air pollutants resulted in increased oxidation stress leading to inflammation and glucose metabolism disruption [8].

Similarly, a cohort study in Hong Kong and Canada also showed that long-term exposure to PM2.5 increased the risk of DM [21,22] Our study showed HbA1c rose, thus, interventions like increasing awareness, alternate energy sources etc., should be implemented to lower the PM2.5 level because PM2.5 is a significant factor impacting the person's glycemic status. This has been related to enhanced Exposure to PM2.5 which enhances inflammatory mediators such as TNF-α and IL-6, leading to a pro-inflammatory, insulin-resistant state, and abnormal insulin signalling in the vasculature, leading to increased susceptibility to the development of T2DM [23]. Furthermore, a varied mixture of air pollutants had been shown to affect HbA1c in different degrees too.

A study conducted in the United States showed that when PM2.5 with a combination of arsenic or sulphate elements was associated with a higher risk of T2DM than PM2.5 that contained only carbon elements. Thus, different chemical mixture affects the risks of T2DM differently [24].

In contrast, LMIC showed a slow growth rate of GDP per capita for the past 10 years due to poorly developed infrastructure, unequal income distribution across countries and lack of appropriate funding [25]. The PM2.5 level was reduced minimally in LMIC due to weak enforcement of environmental policies such as restriction on open burning by the government to ensure annual average air pollutants maintain at standard levels set by WHO [26].

However, PM2.5 was statistically higher in LMIC than HIC due to high population, industrialization, inefficient policy by authorities, and insufficient resources across LMIC [27]. The HbA1c was marginally raised in LMIC throughout the past few years. Additionally, there was a weak negative correlation between PM2.5 and HbA1c in LMIC. Thus, the rise in HbA1c could be possibly due to higher PM2.5 in LMIC because PM2.5 was considered as one of the risk factors for the increased prevalence of DM. Previous studies have shown that excessive PM2.5 triggers an inflammatory process by releasing inflammatory factors and reducing insulin sensitivity, thus, escalating the risk of DM [5,28].

However, improvement of socio-economic status in LMIC could be the factor too as it induced lifestyles alterations especially in Middle-East and North-Africa, having a more sedentary and unhealthy lifestyle which could have contributed to rise in HbA1c in the overall population [29].

Limitations

There are few limitations of the study like the availability of only four years' data for HBA1c and unavailability for the remaining years (2014-20). Non-uniform collection of data from different demography within each country group so the PM 2.5 values do not directly reflect across the nation but rather a region. This is mainly due to the lack of air-quality stations, so some polluted areas may not have the infrastructure to measure the PM 2.5 level.

In addition, using data from a limited number of years for both HBA1c and PM2.5 and the lack of study participant details from each country might have impacted the findings, so it is a hindrance to generalize these findings. We recommend further studies with 20-30 years of data from these countries with complete details of study participants, setting and compounding factors for comprehensive

CONCLUSION

DM is a muti-etiology non-communicable disease, and elevated PM2.5 is a global hazard. Several studies have reported that PM2.5 is a risk factor for the increased prevalence of DM More standardized and specific studies are needed to establish the link and in-depth association between PM2.5 and HbA1c to invent and innovate the appropriate future health plan.

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CONFLICT OF INTEREST

All authors declare no conflicts of interest.

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