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TREND AND ASSOCIATION OF MEAN GLYCATED HAEMOGLOBIN LEVELS TO PARTICULATE MATTER 2.5 (PM 2.5) IN LOW INCOME AND UPPER-MIDDLE INCOME COUNTRIES

Aisha Binti Abdul Malek[1], Jeevan K Shetty[2], Venkatesh R Naik[3]

[1]Medical Student, Perdana University-Royal College Of Surgeons In Ireland School Of Medicine (Pu-Rcsi), Perdana University, Kuala Lumpur, Malaysia.
[2]Department Of Biochemistry, Manipal University College Malaysia, Melaka, Malaysia-75150.
[3]Department Of Pathology, Perdana University-Royal College Of Surgeons In Ireland School Of Medicine (Pu-Rcsi), Perdana University, Kuala Lumpur, Malaysia

***Corresponding author:** Assoc. Prof. Dr.Venkatesh R Naik
Lead And Associate, Professor in Pathology, Pu-Rcsi School pf Medicine- Perdana University, Suite 9, 9thfloor, Wisma Chase Perdana, Changkat Semantan Damansara Heights, 50490 Kuala Lumpur, Malaysia.
Tel: +60386579534
Email: venkatesh@perdanauniversity.edu.my

ABSTRACT

Background: Diabetes Mellitus (D.M.) Incidence is constantly rising, and studies have investigated its association with air pollution in a few developed countries. However, evidence in developing countries is limited and varied. Hence, we designed a secondary data analysis research to explore the trend and also to compare and correlate mean HbA1c with PM 2.5 in LIC and UMIC.

Materials and Methods: This study is a secondary data analysis for LIC and UMIC. The mean value of HbA1c and PM 2.5 was analysed in SPSS package 23.0, and a trend was generated in a line graph. The mean values were compared using Independent T-test, and Pearson Correlation was used to correlate the parameters. Ethical approval was obtained from the university's ethical clearance committee.

Results: The result revealed that LIC has significantly higher PM 2.5, while UMIC showed a higher HbA1c. Furthermore, LIC noted a weak positive correlation (r=0.156, p-value=0.479) and UMIC had a weak negative correlation (r=-0.097, p-value=0.498) between HbA1c and PM 2.5.

Conclusion: Our findings suggested that due to economic scale and urbanization impacts, LIC and UMIC's environmental factors vary. The study indicates a higher PM 2.5 in LIC and higher HbA1c in UMIC, which may have an impact on public health, so demand targeted preventive measures.

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INTRODUCTION

Diabetes Mellitus (D.M.) is a chronic metabolic disorder that causes hyperglycemia [1]. It is caused by a deficiency in insulin hormone secretion or defective insulin action, causing inadequacy in glucose usage [1]. There are two types of D.M.; Type 1 Diabetes, usually caused by an autoimmune process that destroys islet's beta cells of the pancreas, which makes insulin hormone, resulting in absolute insulin deficiency. It is typically diagnosed in children or young adults [1]. Type 2 Diabetes Mellitus (T2DM) is caused by insulin resistance, making the cells unable to use insulin relative to need, and is usually detected in middle or older-age people [1].

Insulin deficiency and consequent hyperglycemia in both forms of D.M. can lead to serious complications like nephropathy, retinopathy, and cardiovascular or peripheral vascular diseases [1]. It is ideal for preventing such complications by controlling plasma glucose level through a healthy-eating diet, regular exercises, weight loss and adhering to prescribed medications (Metformin, Sulphonylureas, Thiazolidinedione) [1]. HbA1c (glycated haemoglobin) is used to assess 'individual's long-term glycaemic status and diagnosis of D.M. by monitoring average blood glucose concentration over the lifespan of red blood cells (2-3 months) [1,2]. The cut-off point of diabetes according to ADA's guideline is 6.5% (DCCT), with pre-diabetes: 5.7-6.4% and normal level <5.7% [2].

D.M. is persistently rising, with 463 million cases seen globally in 2019[3] and is particularly seen in developing countries with Low and Middle-Income [3]. Developing countries are countries with lower Gross Domestic Product (GDP) per capita value and are less industrialized than developed countries [4]. Countries are classified into income levels by the World Bank Organization.

The countries assessed in this study are Low-income countries (LIC) composed of 29 countries and 56 Upper-Middle Income countries (UMIC) [5]. A rise in T2DM in these countries are linked to genetics, geographical epidemiology, and environmental factors, including sedentary lifestyles, dietary, and increasing air pollution [5,6].

According to WHO, ambient air pollution leads to 4.2 million deaths annually worldwide, with LIC and MIC most affected by it [7]. One of the most harmful air pollutants is Particulate Matter 2.5 (PM 2.5) [8], which is solid and liquid particles sized 2.5 micrometres. It can be formed from natural or human-made sources (forest fires, volcanoes, solid-fuel combustions). They are small enough to penetrate the lungs and enter the bloodstream causing severe detrimental to health, leading to respiratory and cardiovascular diseases. There is also evidence of an increased risk of developing D.M. [9]. Air Quality Index (AQI) is used to measure overall air quality. It measures 5 major air pollutants: Ground-Level Ozone, Carbon Monoxide, Sulphur Dioxide, Nitrogen Dioxide, and Particulate Matters. It is divided into six categories, with values ranging from 0 to 500. The higher the value is, the more harmful the pollutants are and pose a risk to health[8].

Studies are divided in the current literature, with some showing a significant association whilst others have not found a consistent relation between air pollution and T2DM [10]. Studies done in developed countries like Canada and U.S. have shown that ambient air pollution increases the risk of T2DM in their countries; however, further studies are needed to assess and comprehend the associations in LIC and UMIC [10]. Hence, we designed a secondary data analysis to explore the trend of HbA1c and PM 2.5, and compare and correlate the mean of HbA1c with PM 2.5.

MATERIAL AND METHODS

Study design

This study is a secondary data analysis using quantitative methods to study data taken from World Bank and WHO websites. GDP per capita and PM 2.5 mean annual exposure [11] information was obtained from the World bank website, and mean Fasting Blood Glucose values were obtained from the WHO website [12]. The study was specified to data available between 2010-2018.

Study subjects (inclusion and exclusion criteria)

The data was collected for LIC and UMIC, according to the World Bank's category. Table 1 includes the list of countries used in this study [5].

Inclusion Criteria

GDP per capita (the year 2010-2018) and PM 2.5 annual exposures (year 2010-2017) value for each LIC and UMIC were taken from the World Bank Database [12]. WHO'S available mean fasting blood glucose data (2010-2014) was taken and converted to HbA1c unit [12].

Exclusion Criteria

Missing data from WHO and World Bank's database were excluded; this includes data unavailable from 2010 to 2018. Countries with unavailable data (Eritrea, North Korea, Somalia, South Sudan, Sudan, Syrian Arab Republic, American Samoa, Kosovo, Tuvalu, Venezuela and North Macedonia) were excluded.

Research methods

GDP per capita of the World Bank is calculated in U.S Dollars. GDP was calculated from the sum of gross value with all resident producers and product taxes, with the deduction of subsidies not in product values. The GDP value is then divided by countries' midyear population to get per capita for an estimated living standard [11].

PM 2.5 concentration of mean annual exposure ($\mu g/m^3$) was taken for each country. The data provided by the World Bank was measured using satellite remote sensing PM 2.5 particles along with atmospheric chemistry transport models and ground-level monitoring [11]. The limit acceptable by WHO AQG (Air Quality Guidelines) is 10 $\mu g/m^3$ annual mean or 25 $\mu g/m^3$ 24-hour mean [9].

HbA1c data used in this study was collected from WHO's database. It was given in the form of mean fasting blood glucose value [12]. Each value was converted to HbA1c by EAG/A1C Conversion Calculator provided by ADA Diabetes [13].

Statistical methods

The SPSS Statistics package version 23.0 was used to analyse the data. Values that were sorted into SPSS were represented in Mean ± S.D. according to Descriptive Statistics for GDP, PM 2.5 and HbA1c.

LIC include:		UMIC include:			
Afghanistan	Madagascar	Albania	Cuba	Iraq	Peru,
Burkina Faso,	Malawi	Argentina	Dominica	Jamaica,	Russian Federation,
Burundi	Mali	Armenia	Dominican Republic	Jordan,	Samoa,
Central African Republic	Mozambique	Azerbaijan	Ecuador	Kazakhstan,	Serbia,
Chad	Niger	Belarus	Equatorial Guinea	Lebanon,	South Africa,
Congo Dem. Rep.	Rwanda	Belize	Fiji	Libya,	St. Lucia,
Ethiopia	Sierra Leone	Bosnia And Herzegovina	Gabon	Malaysia,	St. Vincent And The Grenadines,
Gambia	Tajikistan	Botswana	Georgia	Maldives,	Suriname,
Guinea	Togo	Brazil	Grenada	Marshall Islands,	Thailand,
Guinea-Bissau	Uganda	Bulgaria	Guatemala	Mexico,	Tonga,
Haiti	Yemen Rep.	China	Guyana	Montenegro,	Turkey,
	Liberia	Colombia	Indonesia	Namibia,	Turkmenistan
		Costa Rica	Iran, Islamic Rep.,	Paraguay	

Table 1: Includes the list of countries used in this study

PM 2.5 and HbA1c trends represented using year-wise mean value were generated into the excel sheet to produce a line graph for LIC and UMIC. Then, the country-wise mean values were compared by Independent T-test. Additionally, Pearson Correlation was used to correlate HbA1c and PM 2.5 country-wise mean values. A P-value of less than 0.05 was considered statistically significant.

Ethical permission

This study used databases that were made available to the public (WHO and World Bank). Data that were not made available by the countries were not used. Ethical approval was obtained from the Universities internal review board.

RESULTS

This study examined the trend in the year-wise mean value of PM 2.5, HbA1c and GDP per capita. The mean GDP per capita for UMIC has a higher value between 6437 USD to 7354 USD from 2010-2018 (Figure 1), with slight fluctuations throughout the year. LIC's GDP per capita has shown a constant value (<1000USD) over the past eight years.

As shown in figure 2, PM 2.5 concentrations (2010-2017), LIC showed a higher PM 2.5 value than UMIC, with a notable increase in 2015. In contrast, UMIC displayed a slight decrease in PM 2.5 throughout the years. LIC countries showed a higher PM 2.5 concentration value, with a difference of around 10 $\mu g/m^3$ between the two income countries. LIC have an average of about 38 $\mu g/m^3$ with the highest value of 40.82 $\mu g/m^3$ in 2015. UMIC concentration ranged from 27.22 $\mu g/m^3$in 2010 to 23.86 $\mu g/m^3$ in 2017.

As depicted in figure 3, HbA1c values (2010-2014) UMIC instead showed a higher mean HbA1c in both genders compared to LIC annually. We have observed the data for the

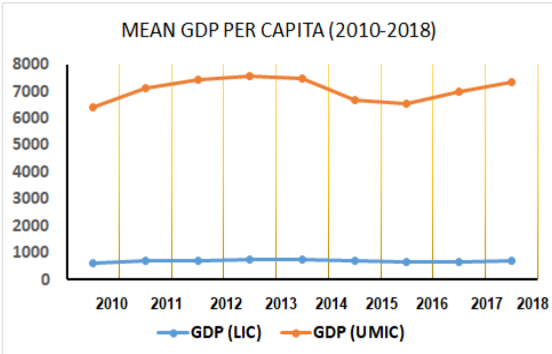

Figure 1: Showing mean GDP per capita in LIC and UMIC between 2010 to 2018.

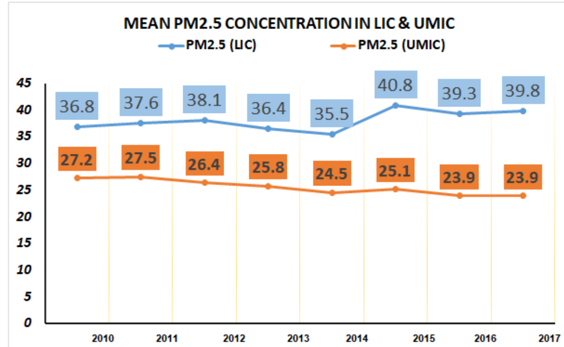

Figure 2: Shows a PM2.5 concentrations trend in LIC & UMIC from 2010 to 2017)

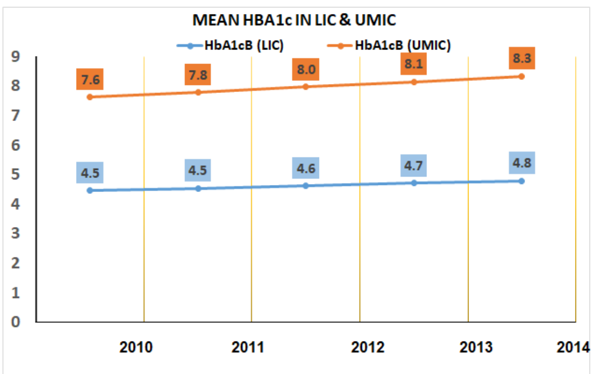

Figure 3: Shows a HbA1c trend in LIC & UMIC from 2010 to 2014

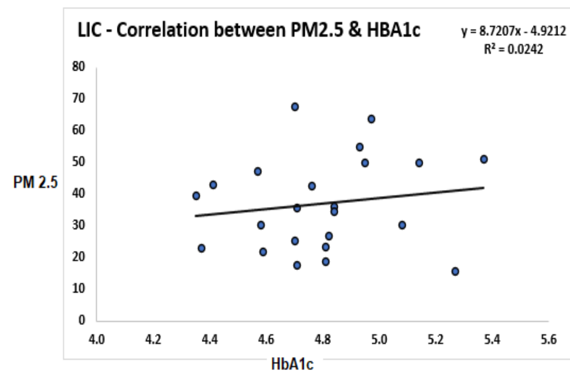

Figure 4: Graph showing the correlation between PM 2.5 and HbA1c in LIC

male and female genders individually, and there were similar values of HbA1c. UMIC countries showed a slight yearly increase of HBA1c with an average of 7-8%, whilst LIC has a lower value of around 4%.

Table 2 displays a comparison of Mean GDP per capita, PM 2.5 and HbA1c between LIC and UMIC. The GDP mean of UMIC (7060 USD) was significantly higher ($p<0.01$) than LIC (684 USD) on applying an independent t-test. The PM 2.5 mean concentration was significantly higher($p<0.01$) in LIC compared to UMIC. In contrast, the HbA1c mean was significantly higher ($p<0.01$) in UMIC compared to LIC.

We also analysed relation between PM 2.5 and HbA1c values from the year 2010-2014 using Pearson's correlation. LIC presented a positive correlation (figure-4: r=0.156, p-value=0.479) whereas UMIC displayed a negative correlation (figure-5: r=-0.097, p-value=0.498) between HbA1c and PM 2.5 concentrations.

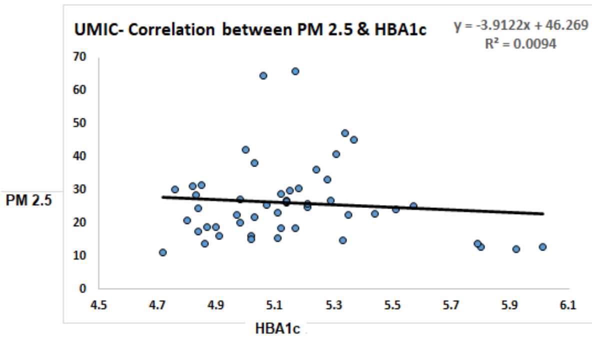

Figure 5: Graph showing the correlation between PM 2.5 and HbA1c in UMIC

	LIC (Mean ± SD)	UMIC(Mean ± SD)
GDP per capita 2010-2018	685 ± 255	7098 ± 2644**
PM2.5 2010-2017	38 ± 16*	25 ± 12
HBA1c 2010-2017	4.79 ± 0.26	5.15 ± 0.29**

** GDP per capita and HbA1c in UMIC significantly higher ($p<0.01$) on comparing with LIC

* PM2.5 Significantly higher in LIC ($p<0.01$) on comparing with UMIC by using independen

Table 2: Comparison table between LIC and UMIC for Mean GDP per capita, PM2.5 and HbA1c

DISCUSSION

A trend in low GDP per capita was observed in LIC, which impacts the living standards of the population, resulting in poor public health, environmental conditions, and education. They require constant financial assistance from governments and organizations for countries' continuous development [14]. Significantly higher PM 2.5 in LIC is mainly attributed to population growth with widespread industrialization and urbanization [15]. A study on LIC reported that low socioeconomic areas with limited political authority have high unfavourable use of cheap land to build factories and roadside communities to keep up with rapid industrialization [16]. LIC countries invest in low-cost fuels rather than expensive renewable energy to power emerging infrastructures and maintain economic growth [17]. Furthermore, a report in Sub-Saharan Africa (SSA), representing more than half of LIC, found that air pollution from biomass burnings, dust and chemical mixtures is linked to increased mortality in the population. Unpaved-roadways, industrial and old-vehicle emissions related to poverty contribute substantially to increasing pollution levels [18].

In addition, our result indicated an increasing trend of HbA1c in LIC. Thus, increased PM 2.5 is of great concern in LIC because it may increase D.M. prevalence in the long run by interfering with insulin action[19]. This is supported by previous studies, which found that inhaled PM 2.5 on entering the bloodstream may interact with organs and adipose tissue, causing a rise in oxidative stress. This damages tissue and activates inflammation, disrupting insulin signalling pathways and preventing glucose absorption, ultimately leading to insulin resistance and beta-cell dysfunction [19,20]. Besides air pollution in most LIC countries, studies have revealed that scarce resources, illiteracy, lack of funds, and inadequate healthcare facilities aggravate D.M.'s prevalence, mortality, and morbidity [21]. However, LIC still showed a significantly lower HbA1c compared to UMIC. This is seen in another SSA study wherein individuals change to urban lifestyle, consequently changing their diet, involving added refined carbohydrates and saturated fats, compared to low-income regions' nutritional availability [22]. Rural residents further engaged in frequent exercises with walking as the primary mode of transportation and rigorous agricultural labour [22].

As for UMIC, the GDP per capita trend has clearly shown a more considerable total market value, comprising a large population and leading economic growth, consisting of Brazil, China, and Russia among top upcoming global dominant suppliers [23]. Additionally, UMIC recorded lower air pollution than LIC. This verifies that higher-income countries have the resources and technology needed to control emissions and invest in renewable energy [17]. Asian countries strongly encourage public transportation or environmentally-friendly fuels usage, investing in pollution reduction equipment in the industry, and stricter regulations in biomass combustions [24]. UMIC has noted exposure reduction since 2010, with Pacific Asia showing the most progress [25].

HbA1c has a significantly higher value in UMIC and showed a weak negative correlation with PM 2.5. This indicates air pollution may not be a significant risk factor for the prevalence of T2DM in UMIC. However, other dominant risk factors of T2DM play a huge role in the increasing trend of HbA1c. We looked into environmental factors in UMIC and found an increase in living standards based on the GDP per capita. As living standards increase, there is a change in diet and physical inactivity, leading to increasing obesity and T2DM [26]. Physical inactivity is prominently high, with 25.4% in UMIC [27]. China, Brazil and Mexico are the top 10 countries with the highest D.M. cases [28]. China has shown that rapid economic development has led to an increase in a sedentary lifestyle. T2DM rate grew from 2.5% (in 1994) to 9.7% (in 2007-2008), with overweight and obese patients accounting 43% and 16.7% of T2DM cases, respectively [29]. Moreover, improved healthcare is provided with a better economic level, increasing life expectancy in chronic diseases, affecting the increased T2DM prevalence [30].

Although average PM 2.5 is low in overall UMIC, there is a wide variance of PM 2.5 concentrations in certain countries (Armenia, China, Equatorial Guinea, Gabon, Iran, Iraq, Libya and Turkey) that have PM 2.5 concentrations higher than 35 $\mu g/m^3$. Most UMIC countries showed a lower PM 2.5, which could be the reason for a weak correlation exhibited with HBA1c. This is supported by studies in China and Iran which showed a significant positive correlation between PM 2.5 and HBA1c[10]. This result may reveal that a high PM 2.5 concentration is more likely to affect T2DM than a low-polluted country.

CONCLUSION

Our study provided a trend and comparison of GDP per capita, PM 2.5, and HbA1c. The rise in PM 2.5 LIC over the years is a concern due to its ill effects on the population. This demand targeted preventive measures in LIC countries such as raising awareness, education on air pollution, reducing the use of fossil fuels, encouraging the use of renewable energy and strict enforcement of the laws to improve air quality [3,17].

Likewise, a rise in HbA1c indicates an increased prevalence of D.M. in UMIC countries which needs a targeted intervention on diet & lifestyle to prevent the increased prevalence.

LIMITATIONS

The limited availability of HbA1c data from the past ten years. The study period is not long enough to show a long-term risk of developing D.M. air pollution fluctuates annually. There is also a variance in countries with higher or lower pollution than other countries, leading to weak correlations. Furthermore, estimated HbA1c data was not available, so we used the calculated mean derived from fasting glucose. Population and assessment of exposure methods may also affect the result.

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