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Fine particulate matter constituents and infant mortality in Africa: A multicountry study

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ABSTRACT

Background: Few studies have investigated the association between exposure to fine particulate matter ($PM_{2.5}$) and infant mortality in developing countries, especially for the health effects of specific $PM_{2.5}$ constituents.
Objective: We aimed to examine the association of long-term exposure to specific $PM_{2.5}$ constituents with infant mortality in 15 African countries from 2005 to 2015.
Methods: Based on the Demographic and Health Surveys (DHS) dataset, we included birth history records from 15 countries in Africa and conducted a multicountry cross-sectional study to examine the associations between specific $PM_{2.5}$ constituents and infant mortality. We estimated annual residential exposure using satellite-derived $PM_{2.5}$ for mass and a chemical transport model (GEOS-Chem) for its six constituents, including organic matter (OM), black carbon (BC), sulfate (SO_4^{2-}), nitrate (NO_3^-), ammonium (NH_4^+), and soil dust (DUST). Multivariable logistic regression analysis was employed by fitting single-constituent models, the constituent-$PM_{2.5}$ models, and the constituent-residual models. We also conducted stratified analyses by potential effect modifiers and examined the specific associations for each country.
Results: We found positive and significant associations between $PM_{2.5}$ total mass and most of its constituents with infant mortality. In the single-constituent model, for an IQR increase in pollutant concentrations, the odds ratio (OR) of infant mortality was 1.03 (95 %CI; 1.01, 1.06) for $PM_{2.5}$ total mass, and was 1.04 (95 %CI: 1.02, 1.06), 1.04 (95 %CI: 1.02, 1.05), 1.02 (95 %CI: 1.00, 1.03), 1.04 (1.01, 1.06) for BC, OM, SO_4^{2-}, and DUST, respectively. The associations of BC, OM, and SO_4^{2-} remained significant in the other two models. We observed larger estimates in subgroups with older maternal age, living in urban areas, using unclean cooking energy, and with access to piped water. The associations varied among countries, and by different constituents.
Conclusions: The carbonaceous fractions and sulfate play a major important role among $PM_{2.5}$ constituents on infant mortality. Our findings have certain policy implications for implementing effective measures for targeted reduction in specific sources (fossil fuel combustion and biomass burning) of $PM_{2.5}$ constituents against the risk of infant mortality.

1. Introduction

Infant mortality, defined as infant death in the first 12 months of life, is a major public health issue worldwide. The United Nations International Children's Emergency Fund reported an infant mortality rate of 2.7% in low-income countries in 2018, compared with the 0.3% rate in high-income countries. The report also listed 10 countries with the highest infant mortality rate, with 8 countries from Sub-Saharan Africa (Hug et al. 2018). The WHO report indicated that the risk of infant death in the African Region (51/1000) is over six times that in the WHO

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European Region (8/1000) (Hug et al. 2019). Apart from social disadvantages such as poverty, regional conflicts, and weakness of health care systems, exposure to air pollution and other environmental issues may also play a part (Karimi and Shokrinezhad 2020). There is increasing evidence that suggests a link between exposure to fine particulate matter ($PM_{2.5}$) and infant mortality (Heft-Neal et al., 2018; Woodruff et al., 2008). However, most studies have been conducted in high-income regions such as Europe and North America (Hajat et al., 2007; Lipfert et al., 2000), with very few reports from low-income and middle-income countries (LMICs) (Goyal et al., 2019; Heft-Neal et al., 2018).

Most LMICs, especially those in Africa, have been experiencing rapid population growth compared to the past 30 years. This has led to an increase in air pollution levels due to large-scale construction, industrial production, increased energy use, vehicle emissions, and expansion of agricultural activities. A study from Africa revealed that in the period from 1990 to the present, the death toll from air pollution in Africa has risen by 36% with the continuous growth in the size of the urban population (Roy 2016), which also includes increased numbers of child deaths. To build a broader knowledge in Africa, some recent epidemiological studies have used local variations in $PM_{2.5}$ concentrations derived from different sources, such as satellite models, and they proposed that more similar studies will aid in causal interpretation of $PM_{2.5}$ impacts on health across broad developing-country geographies of Africa (Heft-Neal et al., 2018; Karimi et al., 2020; Xue et al., 2019). This evidence has enhanced the need for future studies on the adverse health effects of ambient air pollution in Africa. The harmful effect of $PM_{2.5}$ is due to its small size and contains variety of chemical components. These components may easily penetrate the alveoli of children and enter the bloodstream, which affects their immune system (Zhang et al. 2018). Understanding the role of exposure to ambient $PM_{2.5}$ constituents in infant mortality is important, especially for Africa.

The major $PM_{2.5}$ constituents include carbonaceous fractions, soluble ions, metals, and soil dust, which may be emitted from both primary and secondary sources (Liang et al., 2016; Philip et al., 2014; Yang et al., 2020). The $PM_{2.5}$ constituents vary greatly and depend on many factors, such as combustion sources, climate, season, and type of urban or industrial pollution. For Africa, the most common sources of these components are coal combustion and vehicle emissions due to the increase in urbanization and industrialization (Abera et al. 2020). In addition, this continent is the world's largest source of desert dust emissions and biomass burning and contributes approximately one-third of the Earth's biomass aerosol particles in the atmosphere (Bauer et al., 2019; Rushingabigwi et al., 2020). However, many obstacles exist ahead of carrying out environmental health studies in Africa, because African countries suffer from a lack of continuous ground-based air quality monitoring, and there are great challenges to accessing data on health indicators.

Epidemiological studies have examined the associations of $PM_{2.5}$ total mass with infant mortality, but with inconsistent results (Goyal et al., 2019; Jung et al., 2020; Karimi et al., 2020). Some studies revealed little evidence on early life exposure to the total mass of $PM_{2.5}$ and infant mortality (Goyal et al. 2019). A plausible reason may be that $PM_{2.5}$ is a complex mixture, and the toxicological effect of $PM_{2.5}$ varies by different constituents in different study locations. However, previous studies have only focused on the associations between $PM_{2.5}$ total mass and infant mortality in Africa (Heft-Neal et al., 2018; Xue et al., 2019). For example, Heft-Neal et al. used satellite-based predictions of $PM_{2.5}$ and found a 9% rise of infant mortality per 10 $\mu g/m^3$ increase in $PM_{2.5}$ exposure . This suggests a greater need to look at how different $PM_{2.5}$ constituents play their role in infant mortality in Africa and whether there were different estimates across countries.

To date, there has been no investigation into the health effects of $PM_{2.5}$ constituents and infant mortality in African countries. Therefore, we designed this study to examine the associations between exposure to various $PM_{2.5}$ constituents and infant mortality in 15 countries of Africa. We also aimed to compare associations by country and explore the potential effect modifiers from available risk factors.

2. Methods

2.1. Study population and health data

This is a cross-sectional study based on the Demographic and Health Surveys (DHS) dataset, which provides nationally representative and routine survey data for multiple countries in Africa. The DHS is a publicly available dataset that has been used in some previous studies (Goyal et al., 2019; Xue et al., 2019). In this analysis, we included 15 countries (Guinea, Cameroon, Mali, Nigeria, Chad, Benin, South Africa, Burundi, Uganda, Ethiopia, Tanzania, Zambia, Zimbabwe, Angola, and Malawi) with eligible data (Table S2 Supplementary Materials). Each woman of reproductive age (15–49) in the selected household within each cluster (approximately 20–30 households) was interviewed, and detailed information was obtained on each of her birth records over the previous years. This information contains whether the child has died, and if yes, at which years a child died, maternal age, education level of the mother, access to safe water, maternal smoking status, place of residence, sex of the child, whether the family has access to toilet facilities, household economic status, vaccination status of the children, types of energy used for cooking, whether a child uses a bed net to control malaria, and other covariates. After excluding observations recorded in DHS but with missing important variables, a total of 602,863 study participants were enrolled, of which 39,762 infants died during the study period. We considered DHS data between study periods from 2005 to 2015 to reconstruct a village-level birth history and their mother's records that comprise sociodemographic information of women from different study locations in each year. The dataset can be accessed online after receiving approval (https://www.dhsprogram.com/). For more information, see the text of the Supplementary Materials and Figure S1.

To assess the degree to which country-specific indicators may moderate our results, we retrieved data for world development indicators in each country. We considered the following indicators: the prevalence of anemia in children, annual health expenditure by the government, and the annual percentage of the Gross National Income poverty gap. These indicators have been used by previous studies on $PM_{2.5}$ and under-five child mortality in LMICs (Owili et al. 2017). In some countries, data were not recorded every year, and we used the nearest future values recorded as explained in previous studies (Owili et al. 2017). The detailed information can be accessed online at (https://databank.worldbank.org/home.aspx).

2.2. Exposure assessment

Total $PM_{2.5}$ mass was represented using the V4.GL.03 product of the Atmospheric Composition Analysis Group (ACAG) of Washington University in St. Louis (https://sites.wustl.edu/acag/datasets/surface-pm2-5/#V4.GL.03). This product estimates global surface $PM_{2.5}$ concentrations from 1998 to 2018 using a combination of satellite observations, chemical transport model simulations, and ground-based observations (Hammer et al., 2020; van Donkelaar et al., 2016). In brief, aerosol optical depth (AOD) retrievals from multiple NASA satellite products are combined based on their observed relative uncertainties. This combined AOD is related to near-surface $PM_{2.5}$ concentrations using the spatially and temporally varying geophysical relationship between the $PM_{2.5}$ and AOD simulated by the GEOS-Chem chemical transport model. These geophysical estimates are then calibrated to global ground-based measurements of $PM_{2.5}$ with a geographically weighted regression. The resulting annual mean $PM_{2.5}$ dataset had a spatial resolution of approximately 1*1 km and a cross-validated R^2 of 0.92 (Hammer et al. 2020).

Following the approach of (Philip et al. 2014) and (Van Donkelaar et al. 2019), we partitioned total $PM_{2.5}$ into organic matter (OM), black carbon (BC), nitrite (NO_3^-), sulfate (SO_4^{2-}), ammonium (NH_4^+), and soil dust (DUST) using the relative contribution of each component, as simulated by the GEOS-Chem model (v11-01; http://geos-chem.org). Full details of the simulation are given in Hammer et al. (2020), but in brief, over Africa, this simulation is run at a spatial resolution of 2° × 2.5° with the lowest model layer height of approximately 100 m. Global anthropogenic emissions are from the emissions database for global atmospheric research (EDGAR v4.3.1) inventory (Crippa et al. 2016), biomass burning is from the global fire emissions database (GFED4) inventory (Giglio et al. 2013), and meteorologically driven dust emissions follow the dust entrainment and deposition (DEAD) scheme (Fairlie et al. 2007). The lack of ground-based measurements available over Africa, unfortunately, inhibits a robust evaluation directly over Africa. This approach, however, has been found to provide meaningful results even in the absence of local calibration, as demonstrated by significant geophysical agreement (Hammer et al., 2020; Philip et al., 2014; Van Donkelaar et al., 2019), driven in part by the observational constraint provided by satellite retrievals. Uncertainty in emissions and meteorology may, however, lead to some increase in uncertainty over Africa.

We matched all mothers' and their children's information from all DHS datasets that fell within the study period from 2005 to 2015 with exposure data that were obtained from the satellite model. Clusters (each containing 20–30 households) were selected from a sampling frame independently in each stratum. The sampling frame is a complete list of enumeration areas created based on the recent population censuses that were conducted in the respective country. Thus, the clusters are evenly distributed across each country (Aliaga and Ren 2006). In addition, for each cluster of sampled households, geographical coordinates were taken at the centroid of the cluster using a global position system (GPS). For privacy purposes, the reported coordinates in the DHS were randomly displaced for approximately 2 km and 5 km for each cluster that was collected from urban and rural areas, respectively. For exposure assignment, we matched the concentration of $PM_{2.5}$ and its constituents based on the centroid coordinates of each cluster, and participants from selected households of the same cluster shared the same exposure level (Figure 1). We compared the concentrations of $PM_{2.5}$ from the cluster centroid and those averaged within a 10 km buffer around each cluster, and generally no difference was observed. Therefore, we used the average concentration of fine particulate matter for each cluster to match the participants who were interviewed. For detailed information on how exposure is calculated, we matched averaged concentrations of $PM_{2.5}$ and its constituents over the following 12 months of each child's birth record. For example, if the child was born in the fourth month of year *t,* we averaged the concentrations of the following 9 months (9/12) in year t and those of the first 3 months (3/12) in year t + 1 for both $PM_{2.5}$ and its constituents.

To account for the meteorological factor, temperature and relative humidity data were obtained from ECMWF Reanalysis v5 - Land (ERA5-LAND) from the European Centre for Medium-Range Weather Forecasts (ECMWF). This information can be obtained online through (https://www.ecmwf.int/en/forecasts/dataset/ecmwf-reanalysis-v5). This simulation is run at a spatial resolution of 9*9 km at the hourly scale. A similar procedure was used to match average levels of temperature and relative humidity to each participant within clusters.

2.3. Statistical analysis

We estimated the associations between exposure to $PM_{2.5}$ constituents and infant mortality using multivariable logistic regression models, and separate models were built for each constituent. In our all models, we adjusted for covariates including maternal age, education level of mother (no education, primary, secondary, and higher), mother smoking status (Yes, No), access to toilet facilities (Yes, No), household access to safe water (Yes, No), place of residence (Urban, Rural), types of energy used for cooking (clean fuel, unclean fuel), wealth index (poorest, poorer, middle, richer, richest), if a child had diarrhea before two weeks of the survey (Yes, No), child received a vaccination (Yes, No), birth order of the child (firstborn, not firstborn), the gender of the child (male, female), the country-level prevalence of anemia, child stunting record, government health expenditure per annually and poverty level as measured by GNI per annually, temperature and relative humidity. We considered these variables in our analysis based on previous research conducted to determine the key factors that influence infant mortality in most LMICs (Schell et al. 2007). We adapted a methodology similar to previous studies to fully evaluate the associations of $PM_{2.5}$ constituents (Du et al. 2020). We defined the following three models as follows: 1) the single-constituent model to test the contribution of each $PM_{2.5}$ constituent to infant mortality with adjustment of other covariates in our main model; 2) the constituent-$PM_{2.5}$ model by adding $PM_{2.5}$ to the single-constituent model; and 3) constituent-residual models, to validate the residual attributed by each $PM_{2.5}$-constituent relationship.

To test for possible effect modification, we conducted stratification analysis by considering the major covariates that may influence our results, such as mother age (>30 years old, ≤30 years old), infant gender (males, females), mother smoking (Yes, No), cooking energy sources (clean, unclean), place of residence (rural, urban), access to toilet facility (Yes, No), access to piped water (Yes, No), and childbirth order (firstborn, not firstborn). We also examined the associations of $PM_{2.5}$ constituents with infant mortality for each country based on the single-constituent model.

All statistical analyses were conducted using R software (Version 3.6.1). The estimated results are presented as odds ratios (ORs) and their 95% confidence intervals (CIs) associated with an interquartile range (IQR) increase in $PM_{2.5}$ and its constituents. The statistical tests were two-sided, and p-values < 0.05 were considered statistically significant.

3. Results

3.1. Descriptive statistics

The descriptive statistics of the study participants are presented in Table 1. In this study, a total of 39,762 (6.6%) infant deaths were identified among 602,863 birth records between 2005 and 2015 from 15 countries, as shown in Supplementary Materials Table S2. Generally, the infant records had a balanced gender. Approximately 58.7% of the mothers had an educational level of primary school or higher, and only 0.6% of the mothers were smokers. For household information, 71.7% of participants resided in rural areas, 57.5% had no access to safe water, and 92.4% used unclean fuel for cooking (Table 1). Descriptive additional covariates are listed in Table S1.

The average concentrations of ambient $PM_{2.5}$ and its constituents over the study period are presented in Table 2. The cumulative annual average concentration of ambient $PM_{2.5}$ total mass was 37.81 $\mu g/m^3$, which exceeds the Air Quality Guidelines recommended by the World Health Organization of 10 $\mu g/m^3$ annually (Krzyzanowski and Cohen 2008). There was a significant difference in $PM_{2.5}$ levels for different countries, as indicated in Supplementary Materials (Table S3), while DUST, BC, OM, and SO_4^{2-} consisted of larger proportions of $PM_{2.5}$, with means of 19.46, 8.72, 7.14, and 1.53 $\mu g/m^3$ respectively (Table 2). The correlations between $PM_{2.5}$ and each of the $PM_{2.5}$ constituents are listed in Table S5 of the Supplementary Materials. Generally, we observed moderate to high correlations between $PM_{2.5}$ and OM, BC, and soil dust (Spearman correlation coefficients from 0.65 to 0.81), while there were weak correlations between $PM_{2.5}$ and SO_4^{2-}, NO_3^- and NH_4^+ (Spearman correlation coefficients from 0.05 to 0.18).

3.2. Regression results

Table 3 provides the ORs and 95% confidence intervals (CIs) for the associations between $PM_{2.5}$ constituents and infant mortality. In general, we found positive and significant associations between $PM_{2.5}$ total mass and infant mortality, with an OR of 1.03 (95% CI: 1.01, 1.06) associated with an IQR increase in $PM_{2.5}$ concentrations. Exposure to

Table 1
Descriptive statistics of the study participants.

Variables	Values / Number of cases (%)
Mother age	31.45 ± 11.0
Place of residence	
Urban	174,413 (28.9)
Rural	428,450 (71.1)
Mother smoking status	
Yes	3,731 (0.6)
No	599,132 (99.4)
Household use of cooking fuels	
Unclean fuel	557,237 (92.4)
Clean fuel	45,626 (7.6)
Household access to safe water	
Yes	256,267 (42.5)
No	346,596 (57.5)
Household access to toilet facilities	
Yes	455,638 (75.6)
No	147,225 (24.4)
Maternal education	
No education	249,267 (41.3)
Primary	212,563 (35.3)
Secondary	123,238 (20.4)
Higher	17,795 (3.0)
Wealth quantile of household	
Poorest	140,414 (23.3)
Poorer	132,170 (21.9)
Middle	124,088 (20.6)
Richer	112,853 (18.7)
Richest	93,338 (15.5)
Infant gender	
Male	292,014 (48.4)
Female	310,849 (51.6)
Infant death	
Yes	39,762 (6.6)
No	563,101(93.4)

Notes: Wealth quantile of the household is a composite measure of a household's cumulative living standard and was calculated using easy-to-collect data on a household's ownership of selected assets, such as televisions and bicycles, materials used for housing construction, and types of water access and sanitation facilities.

Table 3
Odds Ratio (and its 95% confidence interval) of infant mortality associated with an IQR increase in $PM_{2.5}$.

Pollutants	Single-constituent model	Constituent-$PM_{2.5}$ model	Constituent-residual model
$PM_{2.5}$	1.03 (1.01, 1.06)*	–	–
OM	1.04 (1.02, 1.05)*	1.04 (1.02, 1.06)*	1.04 (1.02, 1.06)*
BC	1.04 (1.02, 1.06)*	1.03 (1.02, 1.04)*	1.03 (1.02, 1.05)*
SO_4^{2-}	1.02 (1.00, 1.03)*	1.02 (1.01, 1.03)*	1.02 (1.00, 1.03)*
NO_3^-	1.00 (0.99, 1.01)	1.00 (0.99, 1.01)	1.00 (0.99, 1.01)
NH_4^+	1.00 (0.99, 1.01)	1.00 (0.99, 1.00)	1.00 (0.99, 1.01)
DUST	1.04 (1.01, 1.06)*	1.03 (0.99, 1.06)	1.02 (0.98, 1.06)

Abbreviations as in Table 2.
Notes: All models were adjusted for maternal age, education, access to safe water, maternal smoking status, place of residence, sources of cooking fuel, sex of the child, whether family has access to toilet facilities, household economic status, vaccination status of the children, government expenditure on health services per year, anemia prevalence, whether a child uses bed net to control Malaria, ambient temperature, and relative humidity.
Statistical significant (p-values < 0.05) estimates are indicated in *.

some of the constituents also demonstrated a significant increase in the odds of infant mortality. In the single-constituent model, the ORs were 1.04 (95% CI: 1.02, 1.06), 1.04 (95% CI: 1.02, 1.05), 1.02 (95% CI: 1.00, 1.03), and 1.04 (1.01, 1.06) for BC, OM, SO_4^{2-}, and DUST, respectively. However, we observed no significant association for NH_4^+ (OR = 1.00, 95% CI: 0.99, 1.01) and NO_3^- (OR = 1.00, 95% CI: 0.99, 1.01) in the same model. The effect estimates of infant mortality with the $PM_{2.5}$ constituents were slightly changed in the constituent-$PM_{2.5}$ model and constituent-residual models, although the associations of DUST did not remain. Therefore, the overall results suggested the robustness of associations for OM, BC, and SO_4^{2-} in all models (Table 3).

According to the results of stratification analysis (Table 4), there were larger associations of $PM_{2.5}$ constituents with infant mortality in subgroups with higher maternal age (OR = 1.04, 95 %CI: 1.00, 1.08), those residing in urban areas (OR = 1.13, 95% CI: 1.07, 1.18), those using unclean cooking energy (OR = 1.55, 95% CI: 1.36, 1.77), and those with access to piped water (OR = 1.24, 95% CI: 1.19, 1.29). The estimates of the remaining subcategories were slightly affected. Additionally, to account for the associations of indoor air pollution, we performed a sensitivity analysis on the main model that excludes the covariate for unclean fuels (Table S6). The results show only a slight change in the OR of infant mortality, which suggests that the unobserved effect of indoor air pollution may not bias the estimated associations of long-term exposure to ambient $PM_{2.5}$ and its constituents with infant mortality (Supplementary Materials Table S6).

Finally, we estimated the association between $PM_{2.5}$ constituents and infant mortality for each specific country, as indicated in Table 5 and Table S3 in the Supplementary Materials. Generally, the estimates varied greatly by country. For an IQR increase in $PM_{2.5}$ concentrations, the largest increments in infant mortality were observed in Burundi (OR = 1.46, 95% CI: 1.38, 1.53) and Chad (OR = 1.39, 95% CI: 1.32, 1.45), while for Angola and Benin, there were negative associations (Fig. 2). The results also showed that the effects of BC and OM were significant across many countries, with the largest estimates observed in Cameroon for OM (OR = 1.42: 95% CI: 1.32, 1.53) and Tanzania for BC (OR = 1.26: 95% CI: 1.17, 1.36). In addition, DUST exposure showed positive significance in eight countries (such as Guinea, Cameroon, and Chad), and their ORs ranged between 1.01 and 1.35, while most countries were located in western Africa (Fig. 1 and Figure S2 in Supplementary Materials). However, NO_3^- and NH_4^+ were found to have weak associations across many countries, except for South Africa, which was highly impacted by NH_4^+ (OR = 3.71; 95% CI: 3.17, 4.34).

Table 2
Descriptive statistics of $PM_{2.5}$ and its constituents during the study period from 2005 to 2015.

Pollutants (μg/m^3)	Mean ± SD	Percentiles					IQR
		Min	25th	50th	75th	Max	
$PM_{2.5}$	37.81 ± 26.94	0.01	12.94	29.71	61.78	108.85	48.84
OM	7.14 ± 5.83	<0.01	3.13	5.25	8.79	34.56	5.66
BC	8.72 ± 6.53	<0.01	4.32	7.06	10.90	41.56	6.58
SO_4^{2-}	1.53 ± 1.53	<0.01	0.42	1.01	2.17	11.89	1.75
NO_3^-	0.01 ± 0.04	<0.01	<0.01	<0.01	0.01	1.28	0.01
NH_4^+	0.06 ± 0.35	<0.01	<0.01	<0.01	0.02	6.49	0.02
DUST	19.46 ± 22.42	<0.01	0.89	7.09	37.64	101.56	36.75

Abbreviations: IQR, interquartile range; SD, standard deviation; $PM_{2.5}$, particulate matter with an aerodynamic diameter less than or equal to 2.5 μm; OM, organic matter; BC, black carbon; SO_4^{2-}, sulfate; NO_3^-, nitrate; NH_4^+, ammonium; DUST, soil dust.

Table 4
Odds Ratio (and its 95% confidence interval) of infant mortality associated with an IQR increase in $PM_{2.5}$ and its constituent, stratified by potential modifiers.

Variables	Categories	N	Odds Ratio (95 %CI)						
			$PM_{2.5}$	OM	BC	SO_4^{2-}	NO_3^-	NH_4^+	DUST
Mother age	>Median	301,561	1.04 (1.00, 1.08)*	1.04 (1.03, 1.06)*	1.03 (1.02, 1.04)*	1.01 (0.99, 1.03)	1.00 (1.00, 1.01)*	1.00 (0.99, 1.01)*	1.02 (0.98, 1.05)
	<Median	301,302	0.95 (0.92, 0.99)	1.00 (1.00, 1.03)	1.00 (0.99, 1.03)	1.02 (1.01, 1.05)*	1.00 (1.00, 1.01)	1.00 (1.00, 1.00)	1.00 (0.97, 1.04)
Infant gender	Males	292,014	1.01 (0.98, 1.05)	1.02 (1.00, 1.03)*	1.01 (1.00, 1.03)	1.01 (1.00, 1.03)	0.99 (1.00, 1.01)	0.99 (1.00, 1.00)	0.99 (0.96, 1.02)
	Females	310,849	0.99 (0.96, 1.03)	1.02 (1.01, 1.04)*	1.02 (1.00, 1.03)*	1.03 (1.01, 1.04)*	1.00 (0.99, 1.00)	1.00 (0.99, 1.00)	0.99 (0.96, 1.03)
Mother smoking	Yes	3,731	0.84 (0.59, 1.19)	0.95 (0.78, 1.13)	0.91 (0.77, 1.09)	1.05 (0.91, 1.19)	1.00 (1.00, 1.02)	1.00 (0.98, 1.00)	0.99 (0.70, 1.40)
	No	599,132	0.99 (0.96, 1.02)	1.03 (1.02, 1.04)*	1.02 (1.01, 1.04)*	1.02 (1.00, 1.03)*	0.98 (1.00, 1.00)	1.00 (1.00, 1.01)*	1.00 (0.98, 1.03)
Cooking energy	Clean	45,626	0.99 (0.96, 1.01)	1.02 (1.01, 1.03)*	1.01 (1.00, 1.02)*	1.02 (1.01, 1.03)*	1.00 (1.00, 1.00)	1.00 (0.99, 1.00)	1.01 (0.98, 1.03)
	Unclean	557,237	1.55 (1.36, 1.77)*	1.18 (1.11, 1.25)*	1.21 (1.13, 1.29)*	1.00 (0.95, 1.04)	1.00 (1.00, 1.02)	1.00 (0.98, 1.00)	1.53 (1.32, 1.77)*
Place of residence	Rural	428,450	0.95 (0.93, 0.98)	1.02 (1.00, 1.03)*	1.02 (1.01, 1.04)*	1.02 (1.01, 1.03)*	1.00 (0.99, 1.01)*	0.99 (1.00, 1.01)	0.97 (0.95, 0.99)
	Urban	174,413	1.13 (1.07, 1.18)*	1.05 (1.02, 1.06)*	1.00 (0.98, 1.02)	1.02 (0.99, 1.04)	1.00 (1.00, 1.02)	1.00 (1.00, 1.00)	1.16 (1.10, 1.21)*
Access to toilet facility	Yes	455,638	0.99 (0.96, 1.02)	1.04 (1.02, 1.05)*	1.04 (1.03, 1.05)*	1.01 (1.00, 1.02)*	1.00 (1.00, 1.01)*	1.00 (0.99, 1.00)	0.96 (0.94, 0.99)
	No	147,225	0.98 (0.94, 1.03)	1.01 (0.99, 1.03)	0.98 (0.96, 1.00)	1.03 (1.01, 1.05)*	1.01 (1.00, 1.01)	1.00 (1.00, 1.00)	1.11 (1.06, 1.15)*
Access to piped water	Yes	256,267	1.24 (1.19, 1.29)*	1.04 (1.02, 1.06)*	1.03 (1.01, 1.05)*	1.04 (1.02, 1.06)*	0.99 (1.00, 1.01)	0.99 (0.95, 1.01)	1.07 (1.02, 1.10)*
	No	346,596	0.91 (0.88, 0.94)	1.03 (1.01, 1.04)*	1.01 (1.00, 1.04)*	1.01 (0.99, 1.04)	1.00 (1.00, 1.04)*	1.00 (1.00, 1.04)*	1.01 (0.98, 1.04)
Childbirth order	Firstborn	148,107	1.02 (0.97, 1.06)	1.03 (1.01, 1.05)*	1.03 (1.01, 1.05)*	1.01 (0.99, 1.03)	1.00 (0.98, 1.01)	1.00 (1.00, 1.00)	1.02 (0.97, 1.06)
	Not	454,756	0.98 (0.96, 1.01)	1.03 (1.02, 1.04)*	1.02 (1.01, 1.03)*	1.02 (1.01, 1.03)*	1.00 (0.99, 1.00)	1.00 (1.00, 1.00)	1.00 (0.97, 1.02)

Abbreviations as in Table 2.
Statistical significant (p-values < 0.05) estimates are indicated in *.

4. Discussion

To our knowledge, this was the first multicountry study to explore the association between $PM_{2.5}$ constituents and infant mortality in Africa. We found positive relationships between $PM_{2.5}$ total mass and infant mortality, and there were the most robust associations of BC, OM, and SO_4^{2-} among all constituents. We observed certain effect modifiers, such as higher maternal age, using unclean cooking energy, living in urban areas, and with access to piped water. The estimates also varied by different countries. Our results are of great importance in understanding the contribution of each component of $PM_{2.5}$ to infant mortality in Africa and may also provide insights for future toxicological or mechanistic studies.

The number of studies on the associations between $PM_{2.5}$ and infant mortality has increased in the past few years (Goyal et al., 2019; Heft-Neal et al., 2018; Jung et al., 2020; Wang et al., 2019). For example, a previous study by Heft-Neal and colleagues (Heft-Neal et al. 2018) reported that a 10 μg/m^3 increase in $PM_{2.5}$ was associated with a 9% (95% CI, 4–14%) increase in infant mortality in Africa, which was slightly larger than our results of $PM_{2.5}$ total mass. Another study conducted in Tokyo-Japan observed a positive association as well as a 10 μg/m^3 increase in $PM_{2.5}$, and their OR of infant mortality was 1.06 (95% CI: 1.01,1.12) (Yorifuji et al. 2016). Generally, these results are comparable to our findings with an OR of 1.03 (95% CI; 1.01, 1.06).

However, few epidemiological studies have evaluated the associations of $PM_{2.5}$ constituents with infant mortality, especially for Africa (Heft-Neal et al. 2020). Our study found that some $PM_{2.5}$ constituents, such as BC, OM, and SO_4^{2-}, were robustly and significantly associated with infant mortality, with ORs ranging from 1.01 to 1.06 per IQR increase in respective constituents. A similar study conducted in LMICs observed a positive association between exposure to carbonaceous $PM_{2.5}$ and infant mortality, particularly neonatal mortality (Goyal et al. 2019). Other previous studies with regard to $PM_{2.5}$ constituents and children's health outcomes have been conducted elsewhere. For instance, one previous study in China reported significant associations of SO_4^{2-}, NO_3^-, NH_4^+, and OM with an increased risk of childhood pneumonia (Shi et al., 2021). Another study in the USA revealed a more toxic effect of EC on birthweight (Fong et al. 2019). Epidemiologic studies have demonstrated an association of $PM_{2.5}$, OM, NO_3^- and SO_4^{2-} with an increased risk of respiratory admissions, for childhood pneumonia, acute bronchitis, and asthma (Ostro et al. 2009). In our analysis, NO_3^- and NH_4^+ were not significantly associated with infant mortality, which may be due to the relatively low concentrations and larger measurement errors of these constituents. In addition, the effect of soil dust constituents was relatively unstable in our study, but some previous studies have linked exposure to dust and early childhood mortality (Heft-Neal et al., 2020; Karimi et al., 2020). Further studies are needed to verify these results.

In our stratification analysis, there were larger $PM_{2.5}$ constituent-infant mortality associations in subgroups with higher maternal age, which is consistent with most of the previous study findings (Goyal et al., 2019; Han et al., 2018). In addition, we observed larger estimates in subgroups that resided in urban areas and had access to piped water, which could be attributed to the rapid urbanization and industrialization of urban cities, where pollutant emissions from motor vehicles and factories are more severe (Kalisa et al., 2019; Katoto et al., 2019). Furthermore, families that use unclean cooking fuel were found to have a larger risk, which might be explained by the jointing effect of indoor air pollution, as reported by previous studies (Norbäck et al. 2019). Indoor air pollution in African countries has been described as the greatest threat to human health, particularly for mothers and children (Rees et al. 2019). However, based on a recent report from GBD 2019, child deaths associated with indoor air pollution decreased, whereas the

Table 5
Odds Ratio (and its 95% confidence interval) of infant mortality associated with an IQR increase in $PM_{2.5}$ constituent by each specific country.

Country	Odds ratio (95 %CI)					
	OM	BC	SO_4^{2-}	NO_3^-	NH_4^+	DUST
Angola	0.98 (0.97, 1.05)	1.24 (1.15, 1.33)*	1.02 (0.98, 1.06)	1.00 (0.99, 1.01)	1.00 (1.00, 1.01)	0.98 (0.97, 0.99)
Burundi	0.94 (0.90, 0.98)	0.96 (0.91, 1.00)	1.00 (0.94, 1.05)	0.99 (0.98, 1.00)	1.12 (1.09, 1.15)*	1.03 (1.01, 1.04)
Cameroon	1.42 (1.32, 1.53)*	0.98 (0.91, 1.05)	1.01 (0.96, 1.08)	1.00 (0.99, 1.01)	1.00 (1.00, 1.00)	1.24 (1.14, 1.34)*
Chad	0.89 (0.83, 0.94)	0.98 (0.91, 1.04)	1.04 (0.99, 1.08)	0.99 (0.98, 1.00)	1.06 (1.03, 1.08)*	1.27 (1.21, 1.34)*
Ethiopia	0.79 (0.71, 0.89)	0.95 (0.87, 1.04)	1.01 (0.93, 1.10)	1.01 (0.99, 1.01)	1.17 (1.12, 1.21)*	1.28 (1.18, 1.39)*
Malawi	1.05 (1.03, 1.06)*	1.13 (1.09, 1.15)*	1.02 (0.97, 1.07)	1.00 (1.00, 1.01)	1.00 (1.00, 1.00)	1.00 (0.99, 1.01)
Mali	0.97 (0.94, 0.99)	1.05 (1.00, 1.08)*	1.05 (0.99, 1.10)	1.00 (1.00, 1.00)	1.00 (0.99, 1.01)	1.10 (1.06, 1.14)*
Nigeria	1.23 (1.02, 1.28)*	0.79 (0.51, 1.22)	1.01 (0.99, 1.03)	1.01 (1.00, 1.02)*	1.00 (0.99, 1.02)*	0.97 (0.94, 1.02)
Benin	1.14 (1.01, 1.22)*	0.84 (0.78, 0.90)	1.02 (0.96, 1.08)	1.00 (0.99, 1.01)	1.00 (0.98, 1.00)	1.06 (1.02, 1.10)*
Guinea	0.97 (0.95, 1.01)	0.98 (0.92, 1.03)	1.03 (0.97, 1.08)	0.99 (0.99, 1.02)	1.00 (0.97, 1.01)	1.35 (1.27, 1.42)*
Tanzania	1.24 (1.08, 1.32)*	1.26 (1.17, 1.36)*	1.05 (0.98, 1.11)	1.02 (1.01, 1.03)*	1.00 (0.99, 1.00)	1.02 (1.01, 1.03)
Uganda	0.95 (0.94, 0.98)	1.04 (0.98, 1.09)*	1.08 (1.04, 1.12)*	1.00 (1.00, 1.01)	1.00 (0.98, 0.99)	0.99 (0.98, 1.00)
Zambia	0.94 (0.91, 0.96)	1.04 (1.00, 1.08)*	1.07 (1.02, 1.12)*	1.00 (0.99, 1.01)	1.00 (1.00, 1.01)	1.02 (1.01, 1.03)*
Zimbabwe	1.13 (1.10, 1.17)*	1.21 (1.14, 1.27)*	0.92 (0.85, 0.98)	0.99 (1.00, 1.01)	1.00 (0.99, 1.00)	1.00 (0.99, 1.00)
South Africa	1.06 (1.00, 1.13)*	1.11 (1.05, 1.16)*	1.03 (0.95, 1.09)	1.00 (1.00, 1.01)	3.71 (3.17, 4.34)*	1.01 (1.00, 1.01)*

Abbreviations as in Table 2.
Notes: All models were adjusted for maternal age, education, access to safe water, maternal smoking status, place of residence, sources of cooking fuel, sex of the child, whether family has access to toilet facilities, household economic status, vaccination status of the children, government expenditure on health services per year, anemia prevalence, whether a child uses bed net to control Malaria, ambient temperature, and relative humidity.
Statistical significant (p-values < 0.05) estimates are indicated in *.

number of deaths due to outdoor air pollution was increased. This trend made our decision to focus more on the health effects of outdoor $PM_{2.5}$ on infant mortality, and a proxy of indoor air pollution, in our case the type of fuels, was included as a confounding factor (Rees 2016). Nevertheless, further analysis targeting indoor air pollution exposure should be carried out in future studies in Africa.

Furthermore, we conducted a country-specific analysis in our study setting. Although the effect estimates varied among countries, there were generally positive associations between $PM_{2.5}$ exposure and infant mortality. We observed different exposure–response relationships of $PM_{2.5}$ with infant mortality across countries. This could be due to the different originations of pollution from natural aerosols and anthropogenic activities among these regions, which have been pointed out by previous studies to be the main sources of air pollution in Sub-Saharan Africa (Abera et al., 2020; Andela and van der Werf, 2014). It was revealed that most African countries with mineral activities and those located close to the desert had higher levels of ambient air pollution followed by industrial and domestic emissions (Bauer et al. 2019), which might be the reasons that some countries included in our study, such as Chad, Mali, and Ethiopia, have similar trends (OR of DUST ranged between 1.10 and 1.28) and a larger effect of air pollution. Nevertheless, more evidence from source apportionment studies is required to validate these results for country-specific estimations. The results showed that BC and OM were highly significant across many countries, while the highest effects were observed in Cameroon and Tanzania, which may be attributed to more sources of fossil combustion and biomass burning that are mainly driven by agricultural activities in Central, Eastern, and Western Africa (Bauer et al. 2019). In addition, DUST constituents showed a more evident effect in countries located in Western and North Africa, such as Guinea, Cameroon, and Chad, which is consistent with previous studies that focused on the contribution of soil dust emitted from the Saharan Desert to infant mortality (Heft-Neal et al., 2020; Karimi et al., 2020). However, the associations of NO_3^- and NH_4^+ were generally weak across many countries except South Africa, with an OR of 3.71 for NH_4^+, probably because of the higher industrial level in South Africa than in other countries (Bauer et al. 2019). In addition, the low exposure range of NO_3^- and NH_4^+ from our satellite model may bring uncertainty and bias to health risk assessments.

The biological mechanisms underlying the associations between exposure to $PM_{2.5}$ constituents and infant mortality have not been fully explicated. Exposure to $PM_{2.5}$ was found to cause poor development of children's lung systems at an early stage when approximately 80% of alveoli are being formed after one year of birth (He et al. 2019). $PM_{2.5}$ itself might also act as a vector for other pathogens, which have been reported to affect the lung systems and contribute to the onset of pulmonary diseases in children (Capasso et al. 2015). Additionally, many $PM_{2.5}$ constituents, such as carbonaceous fractions, may lead to inflammation and oxidative stress that affects the gestation period and uterine growth during pregnancy (Srám et al. 2005). More mechanistic studies are needed to support our findings, particularly in LMICs with higher air pollution levels.

This study may have several strengths. First, to our knowledge, this is the first cross-sectional study examining the long-term association between $PM_{2.5}$ constituents and infant mortality in Africa, and thus, our results contributed to very limited evidence. Second, we used a well-established exposure model with relatively high spatial resolutions and little bias in predicting historical concentrations of $PM_{2.5}$ and its constituents. Third, we used the most up-to-date DHS dataset that covers a long period across multiple countries, enabling us to trace historical health data in developing regions such as Africa.

However, our results should be treated with caution because of the following limitations. First, exposure characteristics to enhance the association between $PM_{2.5}$ constituents and infant mortality may be subject to measurement error due to the lack of ground-based air quality monitoring data in most African countries, which would help better calibrate our estimates under local conditions. Furthermore, our models provided some lower prediction values (i.e., NO_3^- and NH_4^+) in some of the clusters, which may cause bias in the corresponding health risk estimation. Second, we were not able to gather information on the specific cause of infant death. Third, due to lack of data, we could not assess the associations for other $PM_{2.5}$ constituents (such as metal), and we could not account for the confounding effect of other gaseous air pollutants such as ozone and nitrogen dioxide. Finally, our estimates of $PM_{2.5}$ chemical components have more uncertainty than the $PM_{2.5}$ mass estimates.

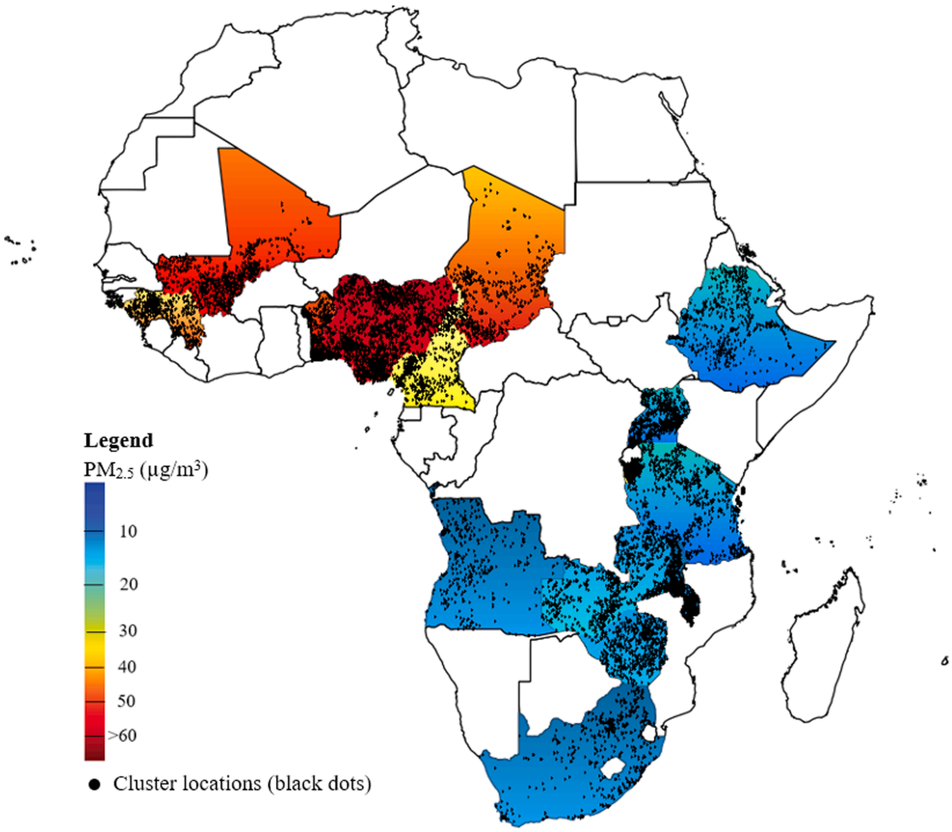

Fig. 1. Distribution of cluster locations (black dots) and average $PM_{2.5}$ concentrations across each country, 2005–2015.

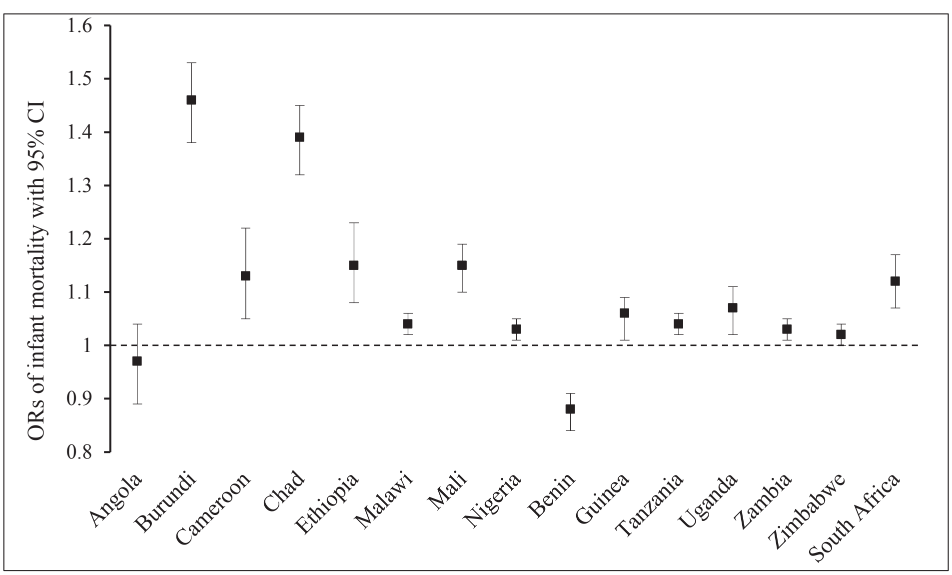

Fig. 2. Odds Ratio (and its 95% confidence interval) of infant mortality associated with an interquartile range increase in the total mass of $PM_{2.5}$ across selected countries.

5. Conclusions

In summary, this is the first study to assess the health effects of $PM_{2.5}$ constituents on infant mortality in Africa. Our results revealed that $PM_{2.5}$ total mass and some of its constituents were significantly associated with an increased risk of infant mortality. The constituents related to emissions of fossil fuel combustion and biomass burning, such as carbonaceous fractions and sulfate, are particularly relevant for the health effects on infants. In addition, more insights into $PM_{2.5}$ sources such as soil dust need further investigation, especially for regions close to deserts. Our findings have certain policy implications for implementing effective measures for targeted reduction in specific sources of $PM_{2.5}$ constituents against the risk of infant mortality.

CRediT authorship contribution statement

Jovine Bachwenkizi: Data curation, Formal analysis, Writting - original draft. **Cong Liu:** Data curation, Formal analysis, Writting - original draft. **Xia Meng:** Supervision, Writting - review & editing. **Lina Zhang:** Visualization, Formal analysis. **Weidong Wang:** Visualization, Data curation. **Aaron Donkelaar:** Data curation, Writing - review & editing. **Randall V. Martin:** Data curation, Writing - review & editing. **Melanie S. Hammer:** Data curation, Writing - review & editing. **Renjie Chen:** Supervision, Writting - review & editing. **Haidong Kan:** Supervision, Funding acquisition, Conceptualization, Writting - review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2021.106739.

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