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Effect of Asian dust on pulmonary function in adult asthma patients in western Japan: A panel study

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AD, Asian dust; CI, confidence interval; GINA, Global Initiative for Asthma; IQR, interquartile range; LIDAR, Light Detection and Ranging; NO_2, nitrogen dioxide; O_x, photochemical oxidants; PEF, peak expiratory flow; PM_{10}, particulate matter smaller than 10 μm; $PM_{2.5}$, particulate matter smaller than 2.5 μm; SD, standard deviation; SO_2, sulfur dioxide; SPM, suspended particle matter

ABSTRACT

Background: Asian dust (AD) has become a major health concern. The concentration of AD is typically expressed in particulate matter less than 10 μm (PM_{10}) and 2.5 μm ($PM_{2.5}$). However, PM_{10} and $PM_{2.5}$ consist of various substances besides AD. Light detection and ranging (LIDAR) systems can selectively measure the quantity of AD particles to distinguish non-spherical airborne particles from spherical airborne particles. The objective of this study was to investigate the relationship between pulmonary function in adult asthma patients and AD using LIDAR data.
Methods: Subjects were 231 adult asthma patients who had their morning peak expiratory flow (PEF) measured from March to May 2012. A linear mixed model was used to estimate the association of PEF with sand dust particles detected by LIDAR.
Results: Increases in the interquartile range of AD particles (0.018 km^{-1}) led to changes in PEF of −0.42 L/min (95% confidence interval [CI], −0.85 to 0.01). An increase of 11.8 $\mu g/m^3$ in suspended particulate matter and 6.9 $\mu g/m^3$ in $PM_{2.5}$ led to decreases of −0.17 L/min (−0.53 to 0.21) and 0.03 L/min (−0.35 to 0.42), respectively. A heavy AD day was defined as a day with a level of AD particles >0.032 km^{-1}, which was the average plus one standard deviation during the study period, and six heavy AD days were identified. Change in PEF after a heavy AD day was −0.97 L/min (−1.90 to −0.04).
Conclusions: Heavy exposure to AD particles was significantly associated with decreased pulmonary function in adult asthma patients.

Introduction

The large-scale and long-range transport of sand dust from East Asia deserts (so-called Asian dust [AD], yellow sand, or kosa in Japanese) is an important source of particulate matter in East Asia. Recently, AD started containing considerable amounts of pollutants such as anthropogenic metal components, chemicals, and

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microorganisms due to rapid industrial expansion and an increased number of cars on the road in East Asia.[1–6] Therefore, AD has become a serious health concern. Studies have shown that heavy exposure to AD increases mortality rates, emergency treatment, and hospitalization for cardiovascular and pulmonary diseases.[7–10] In addition, other studies have shown that heavy exposure to AD increases the risk of hospitalization, and exacerbates pulmonary function and respiratory symptoms in patients with asthma in Japan and South Korea.[11,12]

The majority of studies have investigated the effects of AD on health based on the levels of particulate matter <10 μm in diameter (PM_{10}) and $PM_{2.5}$. However, PM_{10} and $PM_{2.5}$ are a complex mixture of various solid and liquid particles. Therefore, PM_{10} and $PM_{2.5}$ are unable to clearly distinguish AD particles from other particulate matter. To overcome this problem, Japanese studies started using Light Detection and Ranging (LIDAR) data.[12–15] LIDAR systems can measure particulate matter by illuminating a target with two length laser beams and analyzing the reflected light.[16,17] They can also distinguish non-spherical airborne particles, which are sand dust particles, from spherical airborne particles, which consist of air pollution aerosols including organic aerosols, inorganic sulfates and nitrates.[16,17] LIDAR systems are simultaneously applied within <1 km above ground, and measurements have been made continuously in various locations in Japan, South Korea, China, Mongolia, and Thailand.[16,17] LIDAR systems are able to measure the amount of long-range transported AD particles from East Asia to Japan. Therefore, the levels of non-spherical particles based on LIDAR measurements are equivalent to the concentration of AD particles. LIDAR systems calculate the levels of spherical and non-spherical particles using the extinction coefficient, which is a measure of how strongly a substance absorbs light. The extinction coefficient is proportional to the reciprocal of visibility (e.g., a non-spherical particles level of 0.1 km^{-1} equals a visibility range of 10 km).[18] On the other hand, LIDAR measurements do not distinguish particles by size and lack defined criteria for heavy AD.

LIDAR permits investigation of possible differences in the effects of AD particles (non-spherical particles) and particulate matter on pulmonary function. In this study, we investigated the effects of exposure to AD on pulmonary function in adult patients with asthma using LIDAR data.

Methods

Study design

A panel study was conducted using monitoring of daily morning PEF in adult patients with asthma from March to May 2012. A total of 231 outpatients aged >18 years old with asthma were recruited into the study from December 2011 to January 2012. The patients were residents who lived within 25 km of Tottori University Hospital in Yonago City, which is located in western Japan. The patients lived in five different locations: Yonago City, Matsue City, Sakaiminato City, Yasugi City, and Saihaku Town. On the basis of Global Initiative for Asthma (GINA) criteria, asthma was defined as positive if a case met (1) and (2) or (3) of the following criteria: (1) a history of intermittent wheezing; (2) airway hyperresponsiveness to methacholine; and (3) reversible airflow limitation (12% and 200 mL variability in FEV_1).[19] Allergic rhinitis and/or chronic sinusitis were defined based on diagnosis by an otolaryngologist. Treatment for each patient was determined using GINA criteria.[19] The study was approved by the institutional ethics committee (Ethics Committee of Tottori University, Approval Number 1656) and all patients gave written informed consent.

Definition of the period of heavy exposure to AD and monitoring of air pollutants

Particulate matter is classified into several categories according to its size. PM_{10} is defined as any particle measuring less than l0 μm in diameter with a 50% cut-off and $PM_{2.5}$ as any particle measuring less than 2.5 μm diameter with the same cut-off as PM_{10}.[20] In Japan, suspended particulate matter (SPM) is defined under the National Air Quality Standard as any particle with a diameter of less than 10 μm with a 100% cut-off.[21] The theoretical 50% cut-off diameter for SPM is assumed to be approximately 7 μm.[21] The particle diameter of SPM measured in Japan is intermediate to those classified under $PM_{2.5}$ and PM_{10} parameters. Although the daily fluctuations of SPM are similar to those of $PM_{2.5}$,[22] the constituents of particulate matter could differ among countries. The Japanese Ministry of the Environment monitors the levels of SPM instead of PM_{10}. Concentrations of SPM, sulfur dioxide (SO_2), nitrogen dioxide (NO_2), and photochemical oxidants (O_x) are monitored at many locations in Japan by the Japanese Ministry of the Environment. Data for SPM, SO_2, NO_2, and O_x were taken from those collected in Yonago City. Data for $PM_{2.5}$, and data for non-spherical and spherical particles from LIDAR were obtained from the Matsue observatory. LIDAR systems measure aerosol levels at 15-min intervals by distinguishing between non-spherical particles and spherical particles.[16,17] Daily particle levels are determined based on the median value of 96 measurements collected over a 24-h period from midnight of one day to midnight of the next day. The daily levels were only calculated when the number of available measurements exceeded 50% of the total number of measurements. This study used values measured from 120 m to 150 m above ground, which is the minimum altitude required by LIDAR systems to measure non-spherical and spherical particles. A heavy AD day was defined as a level of non-spherical particles higher than 0.032 km^{-1}, which corresponded to the average value plus one standard deviation from March 1 to May 31.

Recording of daily morning PEF and ACT scores

From February to May 2012, all patients recorded their daily morning PEF using a peak flow meter (Mini-Wright, Harlow, England, American Thoracic Society scale). February was used as the practice period. PEF was measured three times in the morning and before the patients inhaled corticosteroids or β_2-agonists or took oral drugs. Each patient recorded the best value from three attempts. At the end of each month, the Japanese version of the Asthma Control Test (ACT-J) scores were recorded.[23]

Statistical analysis

Linear mixed models that accounted for correlations among repeated measurements within a subject were used to estimate the effect of heavy exposure to AD, AD and spherical particles detected by LIDAR, and other air pollutants (SPM, $PM_{2.5}$, SO_2, NO_2, and O_x) on daily PEF.[24,25] The daily (24-h) averages of air pollutants and meteorological variables such as daily temperature, humidity, and atmospheric pressure were used. The linear mixed models include a random intercept for subjects in the analysis, individual characteristics (age, gender, smoking, presence of allergic rhinitis, treatment step and pulmonary function), and meteorological variables such as daily temperature, humidity, and atmospheric pressure, gaseous air pollutions (SO_2, NO_2, and O_3), and other parameters of AD particles, spherical particles, SPM, and $PM_{2.5}$ deviated from the evaluation. Estimates are given as the absolute difference in PEF per interquartile range (IQR) change in exposure, with 95% confidence intervals (CIs). The effect of heavy exposure to AD and the postexposure effect on PEF from 0 (heavy AD day) to 5 days post-heavy exposure to AD were evaluated because the effect of dust exposure on PEF can persist for up 3 days.[11] To investigate differences among subgroups, patients were divided according to characteristics such as age, gender, allergic rhinitis and/or chronic sinusitis, %FEV1, treatment step, and ACT scores. R ver. 3.0.3 (R Foundation for Statistical Computing, Vienna, Austria) was used for statistical analysis to estimate the effects of exposure to particulate matter on daily PEF. All quoted P values are two-sided and the significance level was set to 0.05.

Results

Patient characteristics

All 231 registered patients had their PEF recorded daily for >95% of the study period from March to May. Their characteristics are shown in Table 1. A treatment step, maintenance treatment, and pulmonary function tests were performed, and ACT scores were obtained on February 2012. Pulmonary function tests were performed after inhalation of β_2-agonists.

Levels of AD particles and spherical particles

Daily levels of AD particles and spherical particles are shown in each period in Figure 1. As mentioned above, a heavy AD day was defined as a level of AD particles higher than 0.032 km^{-1}. Using this definition, six heavy AD days were identified: March 30, April 24, April 25, May 7, May 16, and May 17.

Table 1
Characteristics of patients.

Number, n	231
Age (years)	61.9 ± 16.1
Gender; male/female, n	93/138
Smoking status	
Never, n (%)	156 (67.5%)
Former, n (%)	62 (26.8%)
Pack year history	46.2 ± 31.3
Current, n (%)	13 (5.7%)
Pack year history	25.7 ± 16.7
ACT score	
Mean	22.4 ± 3.3
25, n (%)	88 (38.1%)
20–24, n (%)	100 (43.3%)
<20, n (%)	43 (18.6%)
Pulmonary function	
FVC (L)	3.01 ± 0.74
FEV_1 (L)	2.16 ± 0.66
$\%FEV_1$ (%)	98.0 ± 23.5
Allergic rhinitis and/or chronic sinusitis, n (%)	94 (40.7%)
Treatment step	
Step 1, n (%)	3 (1.3%)
Step 2, n (%)	31 (13.4%)
Step 3, n (%)	46 (19.9%)
Step 4, n (%)	141 (61.0%)
Step 5, n (%)	10 (4.3%)
ICS dose	
Low dose, n (%)	51 (22.1%)
Medium dose, n (%)	118 (51.1%)
High dose, n (%)	59 (27.8%)
LABA use, n (%)	171 (74.0%)
Leukotriene receptor antagonist use, n (%)	106 (45.9%)
Theophylline use, n (%)	23 (10.0%)
Oral corticosteroids use, n (%)	8 (3.5%)
Omalizumab use, n (%)	3 (1.3%)

Data are shown as the mean ± SD or the number (%).
ACT, asthma control test; FEV_1, forced expiratory volume in 1 s; $\%FEV_1$, percentage of predicted FEV_1; FVC, forced vital capacity; ICS, inhaled corticosteroids; LABA, Long-acting β_2-agonists.

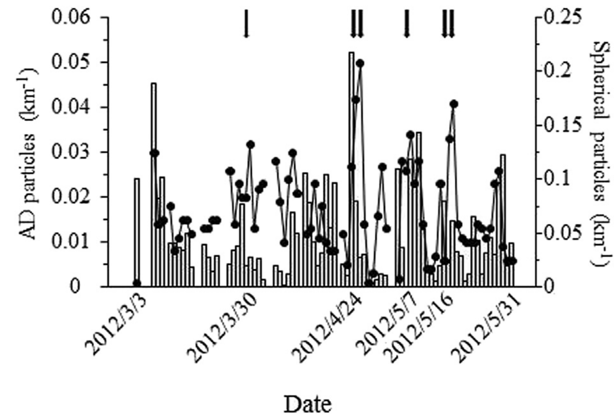

Fig. 1. Daily levels of Asian dust (AD) particles (line graph) and spherical particles (bar graph). A heavy AD day was defined as a level of AD particles higher than 0.032 km^{-1} by Light Detection and Ranging (LIDAR) data. Arrows indicate the heavy AD days.

PEF

The results of changes in PEF for an IQR increase in the levels of AD particles, spherical particles, SPM, and $PM_{2.5}$ after adjustment for individual characteristics and meteorological variables are shown in Table 2. There was no significant association of PEF with the levels of sand dust particles, air pollution aerosols, SPM, and $PM_{2.5}$. Associations between PEF and heavy exposure to AD after adjustment for air pollutants, individual characteristics, and meteorological variables are shown in Table 3. There was a significant negative association between heavy exposure to AD and PEF. To allow an evaluation of the effect of post-heavy exposure to AD on PEF, these changes are shown from 0 (heavy AD day; lag 0 days) to 2 days post-heavy exposure to AD (lag 0–1 days). The highest decrease of PEF occurred on day 0, but the significant association between heavy exposure to AD and decrease in PEF persisted until 1 day after heavy exposure to AD.

Table 4 presents the associations between daily PEF values after exposure to heavy AD and patient characteristics such as age, gender, allergic rhinitis and/or chronic sinusitis, $\%FEV_1$, treatment step, and ACT scores. In patients who were treated with step 4 (−1.42 L/min, 95% CI; −2.71 to −0.12, P = 0.032) and had an ACT score of 25 (−1.13 L/min, 95% CI; −2.21 to −0.04, P = 0.041), heavy exposure to AD was significantly associated with PEF.

Discussion

The criterion for a heavy AD day is unclear, and differs from country to country. To investigate an association between AD and

Table 2
Associations of PEF with exposure to AD particles, spherical particles, SPM, and $PM_{2.5}$, heavy AD in linear mixed-effects models after adjustment for individual characteristics and meteorological variables.

Exposure	IQR	Change in PEF (L/min)	95% CI	*P*-value
AD particles	0.018 km^{-1}	−0.42	−0.85 to 0.01	0.054
Spherical particles	0.061 km^{-1}	−0.31	−0.64 to 0.02	0.064
SPM	11.8 $\mu g/m^3$	−0.17	−0.53 to 0.21	0.397
$PM_{2.5}$	6.9 $\mu g/m^3$	0.03	−0.35 to 0.42	0.867

The linear mixed models included a random intercept for subjects in the analysis, individual characteristics, meteorological variables, gaseous air pollutions (nitrogen dioxide, ozone, and sulfur dioxide), and other parameters of AD particles, spherical particles, SPM, and $PM_{2.5}$ deviated from the evaluation.
AD, Asian dust; IQR, interquartile range; CI, confidence interval; PEF, peak expiratory flow; SPM, suspended particle matter; $PM_{2.5}$, particulate matter smaller than 2.5 μm in diameter.

Table 3
Association between PEF changes and exposure to heavy AD.

Lag time (days)	Change in PEF (L/min)	95% CI	*P*-value
Lag 0	−0.97	−1.90 to −0.04	0.01
Lag 0–1	−0.93	−1.72 to −0.15	0.02
Lag 0–2	−0.38	−1.06 to 0.30	0.27
Lag 0–3	−0.11	−0.74 to 0.53	0.74
Lag 0–4	0.06	−0.55 to 0.67	0.85
Lag 0–5	−0.17	−0.77 to 0.44	0.59

Calculated for an interquartile change in heavy AD exposure and adjusted for individual characteristics and meteorological variables.
Heavy AD day was defined as a level of AD particles higher than 0.032 km^{-1} by Light Detection and Ranging (LIDAR) data.
AD, Asian dust; PEF, peak expiratory flow; CI, confidence interval.

Table 4
Associations between daily PEF values after exposure to heavy AD and patient characteristics.

	Change in PEF (L/min)	95% CI	*P*-value
Age ≥ 65 (n = 121)	−0.77	−1.95 to 0.40	0.198
Age < 65 (n = 110)	−1.19	−2.65 to 0.27	0.111
Men (n = 93)	−1.07	−2.20 to 0.07	0.065
Women (n = 138)	−0.83	−2.40 to 0.75	0.304
Patients with AR and/or CS (n = 88)	−1.02	−2.16 to 0.13	0.081
Patients without AR and/or CS (n = 143)	−0.89	−2.47 to 0.70	0.272
$\%FEV_1$ ≥80% (n = 181)	−0.12	−1.22 to 0.98	0.834
$\%FEV_1$ <80% (n = 50)	−1.14	−3.51 to 1.23	0.346
Treatment step			
Step 1 (n = 3)	−2.30	−13.08 to 8.48	0.676
Step 2 (n = 31)	−0.75	−2.68 to 1.17	0.442
Step 3 (n = 46)	0.02	−1.61 to 1.65	0.981
Step 4 (n = 141)	−1.42	−2.71 to −0.12	0.032
Step 5 (n = 10)	0.47	−4.36 to 5.29	0.850
ACT score			
25 (n = 103)	−1.13	−2.21 to −0.04	0.041
20–24 (n = 92)	−0.09	−1.56 to 1.39	0.910
<20 (n = 36)	−1.70	−5.18 to 1.77	0.337

Estimates and 95% confidence intervals for changes in PEF (L/min) after adjustment for meteorological variables are presented.
ACT, Asthma Control Test; AD, Asian dust; AR, allergic rhinitis; CI, confidence interval; CS, chronic sinusitis; $\%FEV_1$, percentage of predicted forced expiratory volume in 1 s; PEF, peak expiratory flow.

health, a heavy AD day is defined based on the levels of PM_{10} and $PM_{2.5}$. There is a substantial body of evidence showing that exposure to particulate matter including desert sand dust is associated with respiratory mortality and hospitalization for respiratory diseases.[26–28] Many studies have also shown that short-term increases in levels of particulate matter are associated with a decrease of pulmonary function in healthy subjects[29–31] and in patients with asthma.[32–34] Many LIDAR observatories can quantitate the diffusion of sand dust particles originating from East Asian deserts by measuring the degree of scattered reflected polarization laser light at <1 km above ground.[16,17] Our key finding was that heavy exposure to AD had a significant negative association with PEF in adult patients with asthma, whereas PEF was not associated with daily levels of AD particles, SPM, and $PM_{2.5}$.

We found a downward trend in pulmonary function with increasing levels of AD particles, but the association was not statistically significant. In contrast, heavy exposure to AD clearly decreased pulmonary function. There are two possible reasons for this discrepancy. One is that a minimum amount of AD particles is needed to aggravate pulmonary function in adult asthma. The other is that the majority of patients in this study may have well-controlled asthma, because treatment may be excessive for the percentage of predicted FEV_1. Low level of sand dust particles may be unable to affect pulmonary function.

The Japan Meteorological Agency defines a heavy AD day based on a criterion of visibility <10 km due to dust arising from the deserts of East Asia, and also uses meteorological satellites. However, this definition is unclear because particulate matter excludes AD particles, and gaseous air pollutants are also able to decrease visibility. On the other hand, a heavy AD day using LIDAR measurements has not been clearly defined. Other studies have defined heavy AD day as a daily (24-h) average of AD particles (non-spherical particles) or 0.066 km^{-1} (moderate AD day) and 0.105 km^{-1} (heavy AD day)[13] or >0.1 km^{-1} using LIDAR data.[12] Additionally, these studies found that heavy exposure to AD is associated with an increased risk of hospitalizations in children with asthma and emergency ambulance dispatches due to illnesses such as cardiovascular stress. During this study period, there was no day, in which the daily average of AD particles exceeded 0.066 km^{-1}. Therefore, a heavy AD day was determined by the average plus one standard deviation in the levels of sand dust particles from March to May 2012. In this study, when a heavy AD day was defined as >0.032 km^{-1}, AD aggravated pulmonary function in asthma patients. During this study period, heavy AD days were April 23 and April 24 based on the Japan Meteorological Agency criterion. Based on the definition of the Japan Meteorological Agency definition, there was a significant change in PEF after heavy exposure to AD (−2.31 L/min; 95% CI; −4.16 to −0.46, P = 0.014).

We did not find a significant association of PEF with the daily levels of SPM, $PM_{2.5}$, AD particles, and spherical particles. Numerous studies reported the association of particulate matter exposure with pulmonary function in children with asthma. Although a few studies are unable to find significant relationship between particulate matter exposure and pulmonary function,[35–37] based on a systematic review and meta-analysis, there is a clear association.[37] In adult patients with asthma, McCreanor *et al.* found an association of short-term exposure to particulate matter with pulmonary function,[33] but Penttinen *et al.* failed to find an association between the two.[38] However, no definite conclusions can be drawn from the few studies performed on adult patients with asthma. It is possible that the effects of particulate matter on pulmonary function may be different between adults and children. Kumar *et al.* suggested that ambient particulate matter is likely to be more important than traffic-derived particulate matter in causing injury to the airway through production of pro-inflammatory cytokines.[39] The differences in association between particulate matter and pulmonary function among studies may be due to differences in the composition of the particulate matter.

Upon phagocytosis of a sharp substance such as silica, asbestos, and urate crystals, the phagolysosomal membrane of cells is damaged and the contents leak out into the cytoplasm.[40,41] The leakage of hydrolases initiates host cell injury. The quantity of sharp particulate matter may increase during a heavy AD days compared to non-heavy AD days due to an increase of AD particles. AD particles may cause greater airway injury compared to non-AD particles. Therefore, it may be important to examine differences in the shape of particulate matter, in addition to the composition.

To determine the type of patients who are more susceptible to heavy exposure to AD, subgroup analyses were conducted. In patients who were treated with step 4, and had an ACT score of 25, pulmonary function attenuated by exposure to heavy AD. Patients who needed heavy treatment to control asthma were more likely to have their pulmonary function attenuated by heavy AD. The number of patients with step 1 and 5 treatments was not enough to estimate the association between pulmonary function and heavy AD. Contrary to expectation, compared to patients with well control asthma (ACT scores, 20–24) or poor control asthma (ACT scores, <20), patients with total control asthma (ACT scores, 25) were more likely to have their pulmonary function attenuated by heavy AD. A possible explanation for this result may be that patients with well control or poor control asthma were affected by conditions other than heavy AD. For patients with total control asthma, exposure to heavy AD may have been a critical factor for deterioration of asthma.

The main physiological function of the nose is to condition inhaled air so that it reaches the lower airway in a state that does not threaten homeostasis.[42] The nasal passages have a great capacity to warm, humidify, and filtrate air.[43] Therefore, concomitant rhinitis among patients with asthma is a risk factor of deterioration of asthma.[44] However, contrary to expectations, in both patients with and without allergic rhinitis and/or chronic sinusitis, heavy exposure to AD was not significantly associated with PEF. In this study, 46% of the patients were being treated with a leukotriene receptor antagonist. Leukotriene receptor antagonists may reduce the effect of AD on pulmonary function. This may be one a reason as to why there was no association between heavy exposure to AD and PEF in patients with allergic rhinitis and/or chronic sinusitis.

Particulate matter is a complex mixture of solid and liquid particles, and can be classified into AD particles (non-spherical particles) and spherical particles using LIDAR.[16,17] As far as we are aware, this is the first study of the association of pulmonary function in adult asthma patients with AD particles and spherical particles. However, we did not find a significant association of pulmonary function with AD particles and spherical particles.

There are several limitations in the study. First, we did not assess the amount of pollen, which may affect pulmonary function in rhinitis patients. Second, we were unable to estimate the amount of exposure to particulate matter including SPM, $PM_{2.5}$, AD particles, and spherical particles in each individual. Third, we were unable to investigate the effects of the particulate matter on airway inflammation.

In conclusion, we found no association between pulmonary function in adult asthma patients and AD particles, spherical particles, SPM, or $PM_{2.5}$. However, heavy exposure to AD had a significant negative association with pulmonary function. Decreased pulmonary function persisted until 1 day after heavy exposure to AD.

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Conflict of interest

The authors have no conflict of interest to declare.

Authors' contributions

MW, JK, HS, and ES designed the study. MW, JK, MM, HY, YU, HT, YF, TI, HT, TK, AY, and TI contributed to data collection. MW and HN performed the statistical analysis and interpretation of the results. MW and HN wrote the manuscript. All authors read and approved the final manuscript.

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