Abstract

**Background:** Air pollution in the outdoor ambient environment ranks among the leading risk factors, contributing to both the global and regional burden of disease in South Asia (Lim et al., 2012; WHO, 2004). Several systematic reviews provide an elegant consolidation of the evidence on adverse health effects of ambient air pollution for estimation of the attributable burden of disease. In the most recent burden of disease assessment performed as part of the Global Burden of Disease (GBD) 2010 project (Lim et al., 2012), nearly 627,000 premature deaths and 17.8 million disability adjusted life-years (DALYs) were attributable annually in India to ambient air pollution (AAP), in the form of fine particulate matter.

Time-series studies of the effects of short-term exposure on morbidity and mortality from cardiovascular or respiratory diseases have provided some of the most consistent evidence of serious adverse health effects of air pollution for regulatory policies in North America (Samet, Dominici, Curriero, et al., 2000; Samet, Dominici, Zeger, et al., 2000; Samet, Zeger, et al., 2000), Europe (Katsouyanni et al., 1997) and Asia (HEI, 2010). A comprehensive review of literature of Asian studies in 13 countries conducted by the Health Effects Institute (HEI), USA in 2010, identified some 43 studies (published between 1987 and 2007) reporting health effects in relation to ambient air pollution in India (HEI, 2010). The studies report results primarily from cross-sectional assessments of respiratory morbidity, estimating relative prevalence of respiratory symptoms and lung function in relation to inter-zonal differences in air quality within cities.

More recently, results from a coordinated set of time-series studies examining the association of natural all-cause mortality with PM$_{10}$ exposures in the cities of Chennai, Delhi and Ludhiana have been published (Balakrishnan et al., 2011; R. Kumar et al., 2010; Rajarathnam et al., 2011). These studies estimated similar risks of mortality associated with PM$_{10}$ exposure (ranging from 0.15% to 0.4% increase in risk per 10-g/m$^3$ increase in concentration).
in PM$_{10}$ concentrations) as reported in the multicity studies conducted in China, South Korea, Japan, Europe, and North America. These initial studies in India (performed with data over a three year time period between 2002 and 2004) pointed out to the need for additional validation of the methods, using data over extended time periods as well as the need to develop model refinements to address unique features of exposure and health datasets available through relevant Governmental agencies in India.

Using an extended data over a 7 year period (between 2002-2008) the present thesis was conceptualized to both expand the initial results reported from Chennai as well as develop statistical methods to address limitations resulting from exposure misclassification and exposure missingness in semi-parametric models that examine such associations using time-series analyses. Such methods would afford the opportunity for application with other city data-sets in India, for the (much needed) expansion of the evidence base on short-term health effects of air pollution.

**Aims and Objective:** The study is aimed at developing semi-parametric methods (or models) to describe exposure-response relationships between daily average ambient PM$_{10}$ concentrations and short term health effects in Chennai city through time-series analyses.

The three primary objectives for this study were to

(i). Generate exposure-response functions for associations between daily average particulate matter (PM$_{10}$) concentration, daily all-natural cause mortality, daily mortality due to cardiovascular and respiratory causes and daily hospital admissions due to cardiovascular and respiratory illness through time-series analysis

(ii). Compare and validate alternative exposure reconstruction methods for use in time-series analyses for PM$_{10}$ and all-natural cause mortality and

(iii). Develop and validate auto-regressive Poisson regression models to specifically address missing covariate information in time-series analyses for PM$_{10}$ and all-natural cause mortality

**Methods:** Air quality and mortality data was collected for the period 2002-2008 from Tamil Nadu Pollution Control Board (CPCB) and Chennai city corporation respectively, while morbidity data was collected for the 3 year period between 2005-2007 from two government hospitals in Chennai (Madras Medical college and Kilpauk Medical College).
Meteorological data for the same period was collected from Regional Meteorological Center in Chennai. First, Poisson Regression Models for PM$_{10}$, All-natural cause mortality and Cardio-respiratory Morbidity using simple city level cumulative averages for PM$_{10}$ were developed to estimate short term effects of PM$_{10}$ on daily all-natural cause mortality, mortality due to cardiovascular and respiratory disease and daily hospital admission due to cardiovascular and respiratory disease. Next, models using alternative exposure series (including Single monitor models, Multiple monitors models and a Zonal model) were developed to refine the effect estimate of daily all-natural cause mortality due to PM$_{10}$ exposure. Finally an auto-regressive Poisson regression model was developed to address auto correlation in daily mortality in the presence of missing daily PM$_{10}$ exposures.

**Results:** The city average model estimated a 0.67% (95% CI 0.31-1.04%) increase or RR of 1.007 (95% CI 1.003-1.010) for daily all-natural cause mortality and a 0.94% (95% CI 0.41-1.46%) increase or RR of 1.009 (95% CI 1.004-1.015) for daily mortality due to cardiovascular and respiratory disease per 10$\mu g/m^3$ increase in PM$_{10}$ exposure (expressed as a 4-day cumulative average) respectively. The model for hospital admission due to cardiovascular and respiratory illness estimated an RR of 1.014 with 95% CI (1.003, 1.024) per 10$\mu g/m^3$ increase in PM$_{10}$ exposure (expressed as a 3-day cumulative average).

A simulation study comparing alternative exposure models identified the Zonal model as the best performing model among all models examined including the city average model. The zonal model estimated an RR of 1.0056 with 95% CI (1.004, 1.008) per 10$\mu g/m^3$ increase in PM$_{10}$ exposure.

A simulation study for validation of the auto regresssive Poisson regressive model with missing covariates revealed that the model performed well in case of low missingness in exposure and high correlation across measurements at different locations on a day. The autoregressive model estimated an RR for all-natural cause mortality of 1.0032 with 95% CI (1.001, 1.005) per 10$\mu g/m^3$ increase in daily average PM$_{10}$.

**Conclusion:** The excess risk estimates obtained across models in the study are very similar to the summary estimates obtained from the meta-analyses of all Asian studies (HEI, 2010). This risk estimate also falls in the range of estimates found in the European meta-analysis of 29 studies (Katsouyanni et al., 2001) and NMMAPS study in the USA (Samet, Dominici, Zeger, et al., 2000). Finally, similar to studies in Asia and North America, the associations with daily hospital admissions due to cardiovascular and respiratory illness

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Development of a representative exposure series occupied a central role in model development. Specifically, the issues of missing data and small footprints of monitors are likely to be encountered in many other Indian cities as well as in other developing countries. This study explored several approaches to improve outputs of models for estimating the exposure-response relationship between PM$_{10}$ and mortality or morbidity through time series analyses. These models utilized methods built on earlier datasets on Chennai (Balakrishnan et al., 2011) but were able to use data over an extended period of time to provide more refined and robust effects estimates for all-cause mortality. Finally, the development of an autoregressive Poisson model to address serial correlation in outcomes in the face of missing exposure data together with simulation studies to validate the model has significantly enhanced the ability to address model uncertainties. Until such time when infrastructural investments allow the design of more sophisticated monitoring mechanisms, the methods developed in this study may allow data currently being collected to be used for baseline assessments in situations where similar exposure issues prevail. So, it is hoped that this study methods will be useful for application in time series analysis in other Indian cities in the future and this study together with future studies will catalyze policy changes and contribute to the improvement of air quality and public health in India.