



The Outcome of an Emergency Respiratory Admission: Influence of Air Pollution and Humidity

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Abstract

Background: Both prevailing air pollution or humidity levels may influence the outcome of an acute hospital episode; we investigated whether higher pollutant or humidity levels on the day of a respiratory admission were associated with worse outcomes.

Methods: Between 2002 and 2016, we studied all emergency medical admissions (96,526 episodes in 50,731 patients) and investigated air pollutant levels (sulphur dioxide) and humidity levels on the day of admission. We employed a logistics multiple variable regression model, to identify the extent to which the prevailing pollutant or humidity levels influenced 30-day hospital mortality outcome, stratified by respiratory or non-respiratory type, having adjusted for other outcome predictors including Acute Illness Severity and Case Co-morbidity/Complexity.

Results: Respiratory admission were older-70.2 yr. (IQR: 55.0, 79.9) vs. 59.6 yr. (IQR: 39.1, 77.8], had a longer hospital length of stay – 7.0 days (IQR: 3.4, 14.7] vs. 5.1 days (IQR: 1.9, 11.8%) and a higher 30-day hospital episode mortality – 7.9% (95% CI: 7.7%, 8.2%) vs. 4.0% (95% CI: 3.8%, 4.2%). The pollutant level on the day of admission (SO₂ quintiles) predicted worsening outcomes from Q2 – OR 1.40 (95% CI: 1.21, 1.62) to Q5 – OR 2.57 (95% CI: 2.18, 3.03) with an overall Odd Ratio for SO₂ level of 1.27 (95% CI: 1.23, 1.32). There was significant interaction between pollutant and humidity levels and respiratory category. With saturated air (humidity>95%), the predicted 30-day hospital mortality for SO₂ quintiles Q3 and Q5 was 11.2% and 12.4% respectively but with dry air (humidity<70%) the predicted mortality rose to 14.2% and 16.7% respectively. At any given humidity and pollutant level, respiratory patients had worse outcomes.

Conclusion: Baseline air pollutant and humidity levels influenced 30-day hospital mortality outcomes. At any given levels, the outcome for respiratory patients was significantly worse.

Keywords: Air pollution; Humidity; Interactions; Mortality outcomes

Introduction

According to the World Health Organization (WHO) report in 2008, 1.3 million deaths were estimated to be related to ambient air pollution globally. By 2012, this figure had nearly tripled to 3.7 million [1]. Long-term ambient air pollution exposure has been associated with an increase in all-cause mortality [1]. It is an etiological and aggravating factor of many respiratory diseases such as chronic obstructive pulmonary disease (COPD) [2,3], asthma [4], and lung cancer [5,6]. Poor air quality also deleteriously impacts other organ systems and is associated with cardiovascular [7,8], gastrointestinal [9] and neurological diseases [10].

Concern raised regarding the public health implications of urban air pollution in a paper from our institution [11] in Dublin resulted in legislation in 1990 controlling the marketing, sale and distribution of bituminous coals. The average black smoke concentration fell by approximately 35.6 µg/m³ with an estimated reduction in respiratory deaths by 15.5% and cardiovascular deaths by 10.3% [12].

Both temperature and humidity are also important determinants of mortality. The humidity-mortality relationship is U-shaped and large in magnitude at the extremes [13]. In the epidemiological literature regarding the effects of humidity on health is difficult to interpret. This is due to the fact that the effects of humidity are often inferred from measurements that are directly linked to temperature (relative humidity) or synoptic climatological analyses [14].

In general, water vapour status is linked to mortality and morbidity through its role in affecting fluid homeostasis and thermoregulation due to impaired surface evaporation rates with high humidity levels and dehydration which could be worsened by dry weather conditions [14]. Low humidity levels have been associated with increases in COPD exacerbations [15] and bronchial hyper reactivity in asthmatic patients [16]. Low absolute humidity was found to be a critical determinant of human influenza mortality [17] and is thought to trigger a variety of other respiratory tract infections [18]. Humidity could also indirectly adversely impact respiratory disease via the spread of bacteria, fungi, and dust mites [13]. Over the last 10 years reports in the literature have also suggested that humidity may modify the effects of air pollution on respiratory disease.

Our hospital serves an inner city catchment area with high levels of social deprivation living in close proximity to severe motor traffic congestion [19]. Car ownership levels in the area have increased substantially in the last 5 years to levels proceeding the economic recession of 2008-2014. In this study therefore we examined data relating to 106,586 emergency medical admissions to St James' Hospital, Dublin over a 16-year period (2002-2017) to evaluate how ambient Sulphur Dioxide (SO₂) concentrations and humidity levels on the day of admission impact the 30-day mortality outcomes of acute respiratory and non-respiratory admissions.

Methods

Background

St James's Hospital, Dublin serves as a secondary care centre for emergency admissions in a catchment area with a population of 270,000 adults. All emergency medical admissions were admitted from the ED to an Acute Medical Admission Unit, the operation and

outcome of which have been described elsewhere [20,21]. As a city centre hospital St James’s admits person resident elsewhere but working in the capital in addition to visitors to Dublin who became acutely ill. The number of emergency medical admissions resident in the catchment area was 74.5%; this compares with a figure of 59% for emergency department presentations where the social influences on emergency department visitations on two London hospitals have been examined [22].

Data collection

An anonymous patient database was employed, collating core information of clinical episodes from the Patient Administration System (PAS), the national hospital in-patient enquiry (HIPE) scheme, the patient electronic record, the emergency room and laboratory systems. HIPE is a national database of coded discharge summaries from acute public hospitals in Ireland [23,24]. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) has been used for both diagnosis and procedure coding from 1990 to 2005 with ICD-10-CM used since then. Data included parameters such as the unique hospital number, admitting consultant, date of birth, gender, area of residence, principal and up to nine additional secondary diagnoses, principal and up to nine additional secondary procedures, and admission and discharge dates. Additional information cross-linked and automatically uploaded to the database includes physiological, haematological and biochemical parameters.

Our hospital catchment area contains many small areas characterised by a high deprivation status [19]. The Republic of Ireland census (Central Statistical Office) report small area population statistics (SAPS); the smallest reporting unit is the Electoral Division (ED). Of the total of 3409, 74 Electoral Divisions are in the hospital catchment area. The catchment area population, measured in 2006, was 210,443 persons, with a median population per ED of 2845 (IQR 2020, 3399). Deprivation metrics have been determined by the Small Areas Health Research Unit (SAHRU) of Trinity College Dublin using methodology similar to Townsend [25] and Carstairs [26] to derive a Deprivation Score based on four indicators, relating to unemployment, social class, type of housing tenure and car ownership [27]. The assignment of patients to small area population area used the ArcGIS Geographic Information System software implementation of the well-known Point-in-Polygon algorithm as outlined by Shimrat [28].

Acute illness severity score

Derangement of biochemical parameters may be utilised to predict clinical outcome. We derived an Acute Illness Score based on laboratory data – this is an age adjusted 30-day inhospital mortality risk estimator, representing an aggregate laboratory score based on the admission serum sodium (Na), serum potassium (K), serum urea, red cell distribution width (RDW), white blood cell count (WCC), serum albumin and troponin values at admission and applied as an Acute Illness Severity score [29,30]; the score predicts 30-day in-hospital mortality from the biochemical parameters recorded in the Emergency Department [31]. The Illness Severity score can be enhanced with data from the ICD9/10 discharge codes to compute Co-Morbidity (as per the Charlson Index [32]) and chronic disabling disease status [33]. This Risk Score is exponentially related to the 30-day episodes mortality outcome with a range of model adjusted mortality outcomes from 2.5% (2.3%– 2.6%) to 32.1% (30.4%–33.8%). We have demonstrated using a nomogram that this laboratory models

derives most of its predictive power from the values of albumin, urea and haemoglobin recorded at the time of admission [34].

Air quality

For the current study, data over the last decade (2002-2016) from three stations within our hospital catchment area (Winetavern and Coleraine Street or Rathmines stations) were assessed and hourly SO₂ were recorded, according to methods detailed elsewhere [35]. A single average value for each day was calculated for the analyses. We divided the daily levels into equally spaced quintiles – SO₂ quintile cut-points were 0.93, 1.54, 2.32 and 4.14 µg/m³ respectively.

Statistical Methods

Descriptive statistics were calculated for demographic data, including means/standard deviations (SD), medians/interquartile ranges (IQR), or percentages. We examined 30-day in-hospital mortality as the primary outcome. We performed comparisons between categorical variables and 30-day in hospital mortality using chi-square tests; multiple comparisons were adjusted for multiplicity using Scheffe’s comparison statistic. Logistic regression analysis was employed to examine significant outcome predictors ($p < 0.10$ by Wald test from the univariate analysis) of 30-day in hospital mortality to ensure that the model included all variables with predictive power. Adjusted Odds Ratios (OR) and 95% confidence intervals (CI) were calculated for those significant model predictors. A stepwise logistic regression analysis examined the association between 30-day mortality and the following predictor variables: Acute Illness Severity [30,36,37], Charlson Co-Morbidity Index [32], and Chronic Disabling Disease [33], sepsis status [38] and Deprivation index according to the Quintiles of the SAHRU deprivation number.

We used the margins command in Stata to estimate and interpret adjusted predictions for sub-groups, while controlling for other variables such as time, using computations of average marginal effects. Margins are statistics calculated from predictions of a previously fitted model at fixed values of some covariates and averaging or otherwise over the remaining covariates. In the multiple variable logistic model we adjusted univariate estimates of effect, using the previously described outcome predictor variables. The model parameters were stored; post-estimation intra-model and cross-model hypotheses could thereby be tested.

Statistical significance at $P < 0.05$ was assumed throughout. Stata v.15 (Stata Corporation, College Station, Texas) statistical software was used for analysis.

Results

Patient demographics

A total of 96,526 episodes in 50,731 unique patients were admitted as medical emergencies from the hospital catchment area over the 15-year study period (2002-2016). These episodes represented all emergency medical admissions, including patients admitted directly into the Intensive Care Unit or High Dependency Unit, respectively. The proportion of males was 48.6%. The median (IQR) length of stay (LOS) was 4.4 (1.8, 8.9) days. The median (IQR) age was 58.7 (38.0, 76.2) yrs, with the upper 10% boundary at 84.9 yrs. (Table 1).

The demographic characteristics (Table 1) are outlined for with comparison of the characteristics of respiratory and non-respiratory

cases, by principal admission diagnosis. The characteristics are tabulated by Acute Illness Severity [29,30], Chronic Disabling Score [33], Charlson Co-morbidity Index [32] and Sepsis status [38]. In terms of baseline characteristics, respiratory admissions were older 70.2 yr. (IQR: 55.0, 79.9) vs. 59.6 yr. (IQR: 39.1, 77.8), had a longer hospital length of stay – 7.0 days (IQR: 3.4, 14.7) vs. 5.1 days (IQR: 1.9, 11.8%) and a higher 30-day hospital episode mortality – 7.9% (95% CI: 7.7%, 8.2%) vs. 4.0% (95% CI: 3.8%, 4.2%). Respiratory admissions were clearly at higher risk as evidenced higher levels of Acute Illness Severity, Chronic Disabling Score, Charlson Co-morbidity Index and Sepsis grade.

	Other (N=58723)	Respiratory (N=37803)	p-value
Age (yr)			
Mean (SD)	58.03 (21.73)	66.17 (17.85)	<0.001
Median (Q1, Q3)	59.6 (39.1, 77.6)	70.2 (55.0, 79.9)	-
Length Stay (day)			
Mean (SD)	13.74 (35.33)	16.43 (36.18)	<0.001
Median (Q1, Q3)	5.1 (1.9, 11.8)	7.0 (3.4, 14.7)	-
Gender			
Male	28800 (49.2%)	18080 (47.9%)	<0.001
Female	29789 (50.8%)	19636 (52.1%)	-
30-day Hospital Mortality			
Alive	56246 (96.0%)	34723 (92.1%)	<0.001
Dead	2344 (4.0%)	2993 (7.9%)	-
Illness Severity Score			
1	2234 (4.2%)	313 (0.9%)	<0.001
2	4844 (9.2%)	1070 (3.0%)	-
3	7510 (14.2%)	2542 (7.2%)	-
4	9080 (17.2%)	4787 (13.6%)	-
5	9982 (18.9%)	7042 (19.9%)	-
6	19132 (36.2%)	19545 (55.4%)	-
Disabling Disease			
0	8098 (13.8%)	1727 (4.6%)	<0.001
1	15993 (27.3%)	7027 (18.6%)	-
2	17806 (30.4%)	10180 (27.0%)	-
3	11035 (18.8%)	10273 (27.2%)	-
4	5658 (9.7%)	8509 (22.6%)	-
Charlson Index			
0	32705 (55.9%)	9922 (26.4%)	<0.001
1	12501 (21.4%)	14104 (37.5%)	-

	13264 (22.7%)	13608 (36.2%)	-
Sepsis Group			
1	45421 (77.5%)	25520 (67.7%)	<0.001
2	10764 (18.4%)	10260 (27.2%)	
3	2405 (4.1%)	1936 (5.1%)	

Table 1: Characteristics of respiratory medical admission episodes.

Temperature and Humidity Variation with Season

The median and range (IQR) for Humidity levels were 84% (78%, 91%) with respective 10 and 90 cent values at 54% and 91%. The variation by season range from a maximum of 88% (83%, 91%) in winter to a minimum of 80% (74%, 87%) in summer. Humidity cut-points per quintile were at 77%, 82%, 86% and 91% values; high humidity was taken to be at Q3 or above (>= 83%). The median temperature was 11.1°C (7.2, 12.8) with respective 10 and 90 cent values at 4.4°C and 15.2°C. The variation by season range from a maximum of 17.3°C (15.2, 19.5) in summer to a minimum of 3.7°C (1.8, 5.7) in winter.

Logistic multiple variable predictor model of air pollutant level (SO₂) humidity and their interaction of 30-day mortality outcome

Both humidity and the air pollutant level on the day of admission predicted the 30-day hospital mortality; higher levels of pollutant or drier air predicted worse outcomes. The SO₂ level on the day of admission showed worsening outcomes with rising pollutant levels. The median increase in pollutant levels was from Q2-0.59 µg/m³ (IQR: 0.31, 0.76) to Q3-1.87 µg/m³ (IQR: 1.70, 2.08) and Q5 – 5.90 µg/m³ (IQR: 5.00, 8.25). The 30-day hospital mortality risk increased from Q2 (comparisons with base Q1 level) – OR 1.40 (95% CI : 1.21, 1.62) to Q5 – OR 2.57 (95% CI : 2.18, 3.03) with an overall Odd Ratio for SO₂ level of 1.27 (95% CI : 1.23, 1.32) (Table 2, Figure 1).

Humidity had a weaker trend to predict worse outcomes as the level of humidity fell; the interaction term between air pollution level, the level of humidity and being a respiratory patient was significant (Table 2). Mortality was higher with drier air overall. We used margins statistics to estimate and interpret adjusted predictions for sub-groups, while controlling for other variables, using computations of average marginal effects. We adjusted these predictors for other confirmed outcome factors including the Acute Illness Severity, Chronic Disabling Disease Score, Charlson Co-morbidity Index, and Sepsis status. All of these variables were powerful 30-day mortality outcome predictors-Acute Illness Severity OR 3.90 (95% CI: 3.58, 4.26), Charlson Co-morbidity Index-OR 1.52 (95% CI: 1.43, 1.61), Chronic Disabling Disease Score-OR 1.16 (95% CI: 1.11, 1.22), Sepsis Status-OR 2.18 (95% CI: 2.04, 2.33) and Deprivation Index based on area of residence-OR 1.08 (95% CI: 1.04, 1.13). A Respiratory Patient classification was also a powerful (worse) outcome predictor OR 1.88 (95% CI: 1.61, 2.20).

The risk of a death by the 30-day of a hospital episode increased essentially as a linear function of to the underlying SO₂ Quintile at the time of hospital admission (Figure 1). For example, when the air was saturated (humidity>95%) the predicted mortality overall at the third and fifth quintiles of SO₂ were 11.2% and 12.4% but with lower

humidity values between 50% and 70% would have risen to an estimated 14.2% and 16.7% respectively.

Predictor variable	Odds ratio	Std. Err.	z	P> z	[95% Interval]	Conf.
SO2 Quintile						
QII	1.4	0.1	4.6	0	1.21	1.62
QIII	1.73	0.13	7.2	0	1.49	2.01
QIV	2.39	0.19	11	0	2.05	2.79
QV	2.57	0.22	11.2	0	2.18	3.03
Humidity Group						
>=70%<85%	1.26	0.15	1.9	0.05	1	1.61
>=85%<95%	1.28	0.17	1.9	0.06	0.99	1.65
>=95%	1.39	0.26	1.7	0.08	0.96	2.02
Illness Severity	3.9	0.17	30.6	0	3.58	4.26
Charlson Index	1.52	0.05	13.8	0	1.43	1.61
Disabling Group	1.16	0.03	6.3	0	1.11	1.22
Sepsis	2.18	0.07	22.7	0	2.04	2.33
Deprivation	1.08	0.02	4	0	1.04	1.13
Average Temp	0.98	0.01	-4.2	0	0.97	0.99
Respiratory	1.88	0.15	7.8	0	1.61	2.2
SO2 # Humidity	0.95	0.01	-3.8	0	0.92	0.97

Table 2: Multivariable logistic regression model of mortality outcome.

Logistic multiple variable predictor model interaction of respiratory or non-respiratory status with air pollutant level (SO₂) and humidity interactions

There was significant interaction between Respiratory/Non-Respiratory status, air pollution level (SO₂) and humidity on day of admission and 30-day mortality outcomes. Although admission day level (SO₂) and lower humidity levels linearly increased the risk of adverse 30-day mortality outcomes, at any given level of pollutant (quintile of SO₂) of humidity category, the outcome for respiratory was worse compared with non-respiratory patients (Figure 2). For example, the predicted overall mortality at the highest quintile of SO₂ Q5 with humidity>95% for non-respiratory and respiratory was 12.5% (95% CI: 11.0%, 14.1%) and 14.9% (95% CI: 13.2%, 16.5%) respectively but with very dry air (humidity<70%) mortality for the same quintile was much higher predicted non-respiratory and respiratory 16.1% (95% CI: 14.3%, 18.0%) and 18.8% (95% CI: 16.9%, 20.7%) respectively (Table 2, Figure 2).

Discussion

These data demonstrate that the level of humidity interacted with the prevailing level of SO₂ air pollution to influence the outcome of an emergency medical admission. The predictive value was independent of Acute Illness Severity, Chronic Disabling Disease Score, Charlson Co-morbidity Index and Sepsis status. While mortality increased with

increasing SO₂ concentrations at all humidity levels; drier air predicted worse outcomes across the SO₂ concentration quintile range. The SO₂ cut-points were distribution determined with cut-points at 0.93, 1.54, 2.32 and 4.14 µg/m³ respectively; for humidity with a range of 50%-100%, we used mathematical cut-points of 50, 70, 85, and 95. But, as clearly demonstrated in Figure 1, increasing levels of SO₂ at time of admission were associated with worse outcomes but the underlying level of humidity worsened such outcomes (Figure 2).

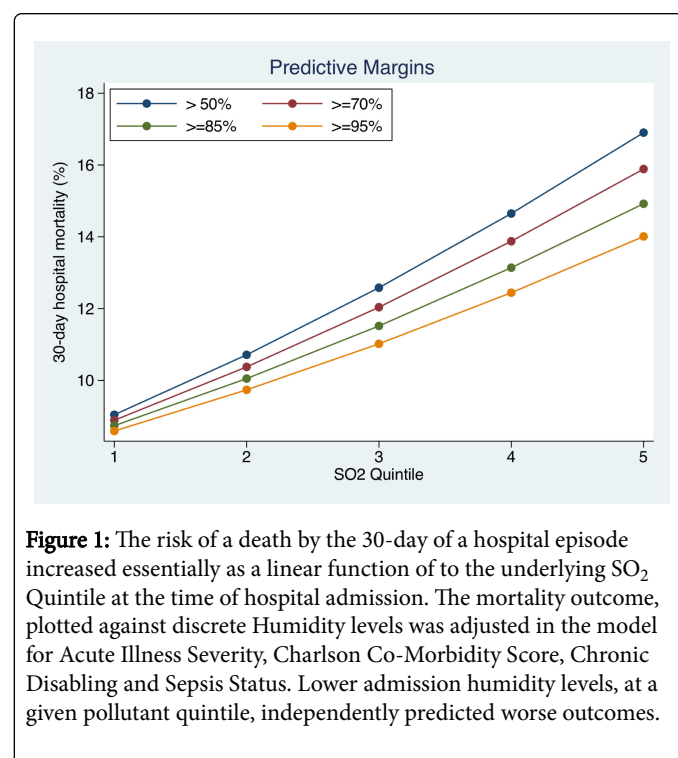


Figure 1: The risk of a death by the 30-day of a hospital episode increased essentially as a linear function of to the underlying SO₂ Quintile at the time of hospital admission. The mortality outcome, plotted against discrete Humidity levels was adjusted in the model for Acute Illness Severity, Charlson Co-Morbidity Score, Chronic Disabling and Sepsis Status. Lower admission humidity levels, at a given pollutant quintile, independently predicted worse outcomes.

For example, at the third and fifth quintile of SO₂, the predicted 30-day per patient mortality at a humidity level of >95% was predicted overall, irrespective of a respiratory or non-respiratory admission, at 11.2% and 12.4% but with lower humidity values between 50% and 70% would have risen to an estimated 14.2% and 16.7% respectively. For respiratory patients, these values would have been 12.8% and 14.2% for the former and 16.1% and 18.8% for the latter.

The results of this study are consistent with reports in the literature showing interactions between humidity and pollution driven morbidity and mortality. For example, studies have demonstrated an ameliorating effect of higher humidity on the impact of air pollution on chronic bronchitis and emergency COPD admissions [39]. Two large studies examining the effects of ambient particulate matter on mortality in 29 cities across Europe showed that the impact of pollution was higher in drier countries [40,41].

The impact of SO₂ concentration on mortality outcomes was disproportionately exerted on patients with a respiratory presentation. A respiratory patient classification was a powerful predictor of mortality across the SO₂ quintile range. These results are consistent with data from a large study examining mortality data from 38 large Chinese cities which showed that the impact of particulate air pollution on deaths from cardiorespiratory diseases was more than twice as high as the effects on other cause mortality [42].

SO₂ is a known respiratory irritant and bronchoconstrictor, but its effects seem limited to patients with asthma and bronchitis, although sensitivity to exposure varies widely [43]. Exposure to SO₂ gas has also been shown to modulate autonomic function. Work by Tunnicliffe and colleagues demonstrated changes in heart rate variability in humans associated with exposure to SO₂ (200 ppb for 1 h) [44]. This data is supportive evidence for systemic effects of SO₂ exposure resulting in downstream effects on other organ systems.

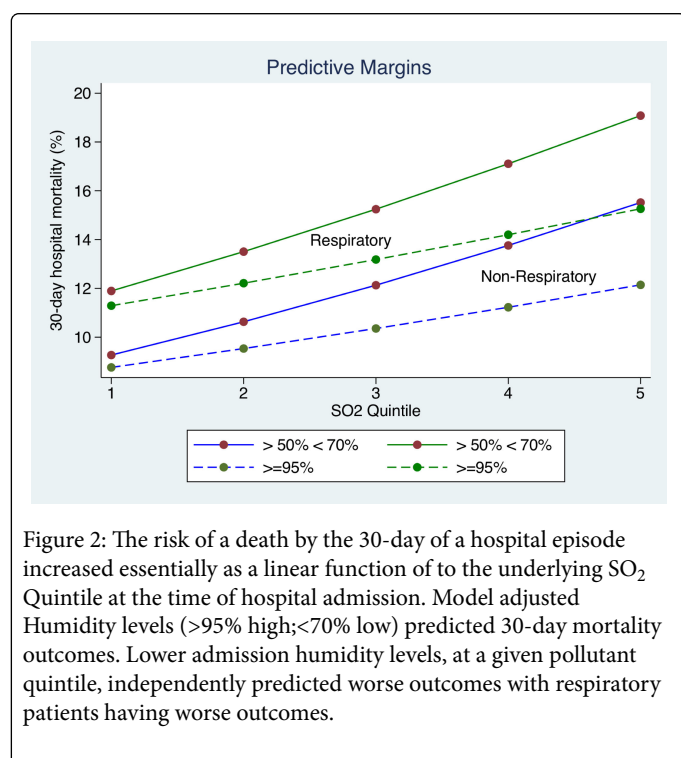


Figure 2: The risk of a death by the 30-day of a hospital episode increased essentially as a linear function of the underlying SO₂ Quintile at the time of hospital admission. Model adjusted Humidity levels (>95% high;<70% low) predicted 30-day mortality outcomes. Lower admission humidity levels, at a given pollutant quintile, independently predicted worse outcomes with respiratory patients having worse outcomes.

There is emerging evidence from the epidemiological literature of a protective effect conferred by higher humidity on the harmful effects of ambient air pollution on the airways. In fact, there are data that demonstrate the potential of ambient temperature and relative humidity to alter DNA methylation on genes related to coagulation, inflammation, cortisol, and metabolic pathways [45]. Within the lung, the relative humidity of inspired air must be approximately 95% for optimal alveolar and small airway function. Levels below 95% would result in excessive evaporation from mucosal surfaces and airway dehydration, and levels closer to 100% would risk droplets precipitation at lower temperatures [46]. Low environmental humidity values may therefore create problems in individuals with underlying airway disease or poor alveolar efficiency. More humid air may also help reduce the number of inorganic salt molecules in ambient aerosols when the level of solute deliquescence is surpassed [47].

As opposed to NO₂ and various particulate pollutants, SO₂ is a water soluble gas which could explain its susceptibility to the effects of ambient water vapour status as noted in this study. SO₂ reacts with the mucus layer of the upper airways while more soluble gases such as NO₂ are more likely to reach the alveoli [48]. SO₂ may alter the production and/or composition of mucus of the upper airway with potential resultant effects on the ciliary epithelium. It is also possible that gases such as SO₂ may affect airway sensory cells resulting in airway hyper reactivity and increased mucus secretion [48].

Our hospital catchment area is predominantly inner city, with over 50% of population classified as deprived [19]; 47 of the 74 Electoral Divisions (small local areas) categorised in the top quintile of the National Deprivation Index [49]. This deprived population of lower socioeconomic status (SES) may typically suffer from higher air pollution level exposure [50]. Lower SES has been also linked to different pulmonary diseases including COPD, asthma, COPD and pulmonary hypertension [51]. Presentations to our emergency services with a predominant respiratory disease component represent 19.5% of all emergency medical hospital episodes although they occur in only 9.6% of unique patients. This discrepancy in health care utilization is likely in part attributed to higher levels of motor traffic pollution. We previously described that in respect of respiratory admissions that SES influenced both the admission rate incidence and 30-day in-hospital mortality [52] and that air pollution on the day of admission influenced 30-day mortality outcomes [53].

This study was conducted in a single inner city centre and this may limit the generalizability of our results. Across the island of Ireland pollutant profiles might vary considerably from one area to another. Indeed legislation in place restricting the burning of soot producing fuel for home heating in Dublin City does not apply to rural areas. This may contribute to differences in particulate air pollution regionally. Variation in volatile organic compound concentrations in rural and urban may also be of significance in quantifying the humidity effect on health outcomes given that water vapour interacts with VOC's to form harmful organic aerosols.

Conclusion

The data demonstrated an interaction between humidity and prevailing levels of SO₂ air pollution in an inner city area with high levels of social deprivation and motor traffic congestion. The harmful effects of SO₂ pollution were higher among patients presenting with respiratory disease than other presentations. Higher humidity levels favorably influenced the outcome of these emergency medical admissions across the SO₂ ambient concentration range. The study was based on a large database of clinical data spanning a 16 year period. These results are supported by emerging epidemiological data linking humidity to reduction in pollution driven morbidity and mortality.

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