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Original Article

Effect of environment and season on acute decompensated heart failure: Data from low-to middle-income country

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ABSTRACT

Objectives: The environmental effect in heart failure (HF) patients is well established. However, the data is limited from low-to middle-income countries like India. This study determined the impact of environment on acute decompensated HF (ADHF) admissions and mortality in India.

Methods: Retrospectively, the data of all HF patients admitted between April 2017 and March 2019 was accessed through electronic hospital records. Simultaneously, the environmental-related data was collected from the central pollution control board.

Results: The study included 4561 patients of ADHF. The peak of monthly ADHF events (admission and mortality) was observed during the chilly month (January) while the lowest rates were observed in summer months (May–June). The most significant factor correlating inversely with the monthly ADHF admission ($r = -0.78$, $p = 0.003$) and mortality ($r = -0.65$, $p = 0.004$) was the maximum air temperature, and it was found to be the independent predictor for both ADHF mortality [$t = -2.78$, $\beta = -0.84$; 95%CI(-6.0 to −0.6), $p = 0.021$] and admission [$t = -4.83$, $\beta = -0.91$; 95%CI(-19.8 to −6.9), $p = 0.001$]. The above correlation was better seen in the elderly subset and male gender. Humidity and the air pollution attributes did not have a significant correlation with ADHF admission or mortality.

Conclusion: In conclusion, even in low-to middle-income country like India, a periodic effect of season was demonstrated for ADHF mortality and admission, with a peak in ADHF events noted during winter months especially in the regions having extremes of seasons. Air pollution could not affect the ADHF outcome for which further studies are needed.

1. Introduction

Several reports, mostly from developed countries, have evaluated the influence of season and air pollution on the heart failure (HF) admissions and mortality.[1–6] These studies had observed an increasing trend in HF admission and mortality during winter months and with increasing air pollution levels especially, particulate matter (PM) of size 2.5 μm. Longitudinal data correlating the influence of hospital mortality and readmissions in patients with HF are lacking from low- and middle-income countries such as India. A study by Chaturvedi et al had observed the prevalence of HF to be about 1% of the total population i.e. 8-10 million individuals and mortality of 0.1–0.16 million individuals per year.[7] The HF burden is likely underestimated as India contributes to 16% of the global population. The climate variations are immense throughout the country with Northern India being sub-tropically humid with a wide variation of temperature throughout the year ranging from the scorching heat during the hottest months (May and June) to the lowest of the temperature during winter months (December and January). Literature showed that the maximum toxic effect of air pollution was observed in Southeast Asia, as the majority (>90%) of the population in this region is exposed to the level of air pollutants well above the World Health Organisation

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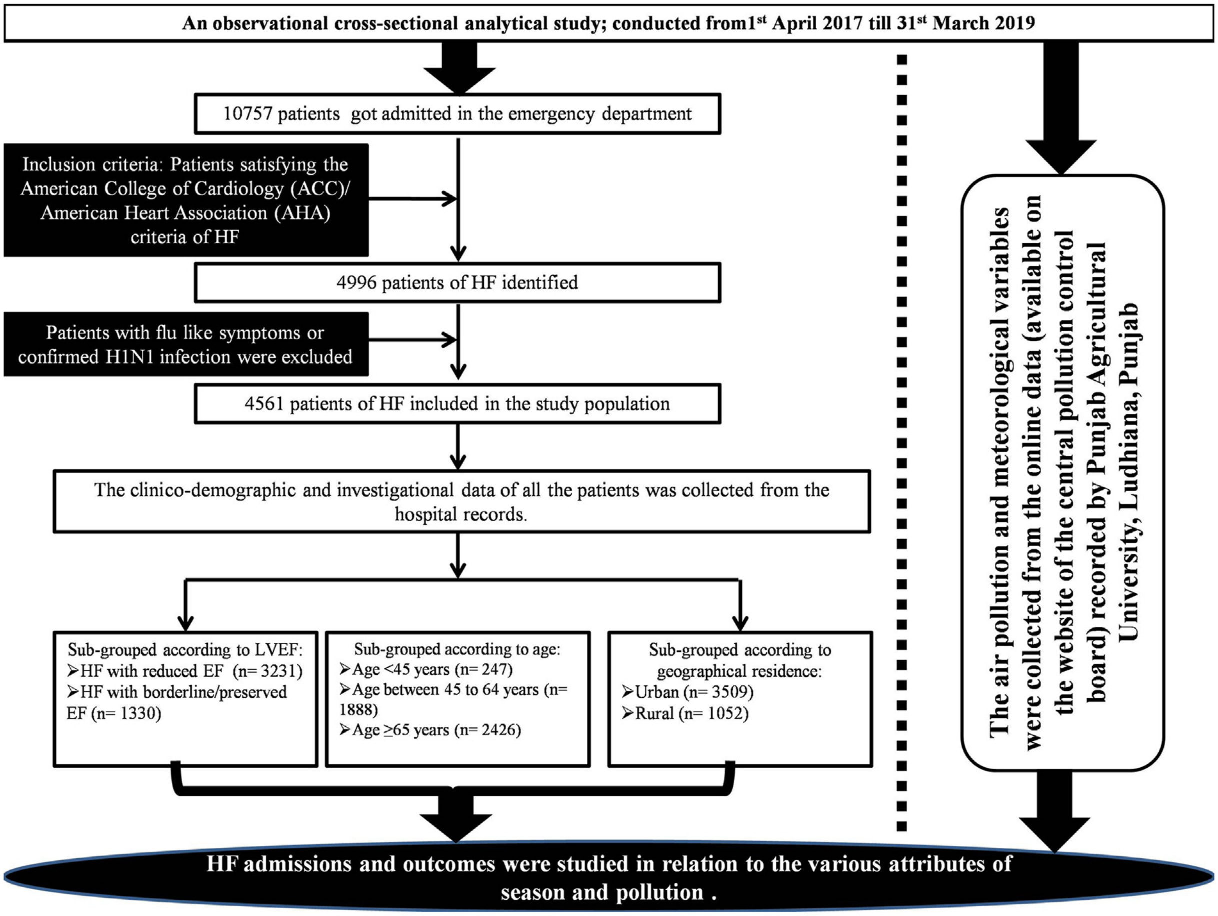

Fig. 1. The study design flow chart. HF: heart failure, LVEF: left ventricular ejection fraction.

(WHO) guidelines for air quality.[8] There is no data to date regarding the effect of season and air pollution on HF from low-to middle-income countries.

The objective of our study was to determine the effect of season and pollution on the acute decompensated HF (ADHF) admission and outcome in the northern region of India.

2. Methods

2.1. Study population

This is a retrospective, observational study conducted in a tertiary care centre, and hospital records were collected from April 2017 till March 2019. The study protocol was approved by the institute's committee on human research (dated 19-09-2019; No. BHUHS/2K18p-TH/3452) and the informed consent was taken. Further, they should also state that animal experiments conform to institutional standards. The ethical clearance was taken from the institutional ethics committee. All the patients satisfying the American College of Cardiology (ACC)/American Heart Association (AHA) criteria of heart failure were included in the study.[9] All the patients either presenting as first episode of ADHF or acute decompensation of chronic heart failure were included in the study. The patients presenting with suspected (influenza like illness) or confirmed H1N1 infection was excluded from the study as this was considered to be the major confounder for the ADHF admissions and outcomes. The patients were further categorised into two groups. The patients with left ventricular ejection fraction (LVEF) of ≤40% were categorised in group I and the ones with borderline (>40% to <50%) or normal (≥50%) LVEF were categorised in group II.[9]

The study was conducted in the Ludhiana district of northern India. It is spread over a total area of 3767 square kilometres. Ludhiana extends from the longitudes 75.25° East to 76.27° East and latitudes 30.33° North to 31.01° North.[10] Northern India has got predominately sub-tropical climate. The state has a wide variation in the season ranging from extremely hot season to cold season. Hot months occurs during mid-April to the end of June, while the winter season begins in the end of September with peaking around January.[10] Fig. 1 shows the flow chart of study protocol.

2.2. Data collection

The clinical, demographical, and investigational data of all the patients of ADHF were collected from the hospital records. The date of admission, duration of hospital stay, and discharge outcomes were also derived. The air pollution related and meteorological variables were collected from the online data (available on the website of central pollution control board) recorded by Punjab Agricultural University, Ludhiana, Punjab from the corresponding dates of admission of ADHF.

The variables included age (in years), gender, rural or urban stay, smoking, co-morbidities such as diabetes mellitus, hypertension and chronic kidney disease. According to the age, the study population was divided into 3 groups: age <45 years, between 45 and 64 years, and ≥65 years. Both the current and the former smoking

Table 1
Table showing the clinical, demographic, and investigational profile of the study group and comparison with both groups.

		Overall ADHF patients $n = 4561$	Group I (LVEF ≤40%) $n = 3231$	Group II (LVEF >40%) $n = 1330$
Age (in years)		65 (57–73)	65 (57–72)	66 (58–75)
Male Gender, n (%)		2754 (60%)	2102 (65%)	652 (49%)
Stay, n (%)	**Urban**	3509 (77%)	2486 (77%)	1023 (77%)
	Rural	1052 (23%)	745 (23%)	307 (23%)
Diabetes Mellitus, n (%)		1608 (35%)	1184 (37%)	424 (42%)
Hypertension, n (%)		2237 (49%)	1508 (47%)	729 (55%)
Smoking, n (%)		173 (4%)	129 (4%)	44 (3%)
Alcoholic, n (%)		214 (5%)	155 (5%)	59 (4%)
Anaemia*, n (%)		1146 (25%)	769 (24%)	377 (28%)
Severe anaemia, n (%)**		111 (2%)	66 (2%)	45 (3%)
Chronic kidney disease*, n (%)**		708 (16%)	532 (16%)	176 (13%)
CAD, n (%)	**ACS**	1791 (39%)	1412 (44%)	379 (28%)
	STEMI	572 (13%)	495 (15%)	77 (6%)
Valvular heart disease, n (%)		172 (4%)	104 (3%)	68 (5%)
Atrial fibrillation, n (%)		346 (8%)	210 (6%)	136 (10%)
Haemoglobin level (in g/L)		11.7 (10–13.2)	11.7 (10.1–13.3)	11.5 (9.9–12.9)
Platelet count (in x10^{3}cells/μL)		225 (165.5–288)	222 (165–287)	231.0
Blood glucose (in mg/dl)		144 (114–215)	149 (115–222)	133 (110–200)
Serum creatinine (in mg/dl)		1.2 (0.9–1.8)	1.27 (0.9–1.96)	1.1 (0.8–1.6)
Serum sodium (in milli Eq/L)		136 (132–139)	136 (132–139)	136 (132–139)
Serum Potassium (in milli Eq/L)		4.4 (3.9–4.9)	4.4 (3.9–4.9)	4.3 (3.9–4.9)
Serum Chloride (in milli Eq/L)		99 (94–102)	99 (94–102)	99.5 (94–102)
BNP (in pg/mL)		897 (598–1400)	992 (661–1620)	737 (524.5–961)
Raised Troponin I (in %)		1267 (28%)	991 (31%)	276 (21%)
LVEF (in %)		34 (27–45)	30 (25–34)	55 (48–60)
In-hospital mortality, n (%)		642 (14%)	495 (15%)	147 (11%)

ADHF: acute decompensated heart failure; CAD: coronary artery disease; GFR: glomerular filtration rate; ACS: acute coronary syndrome; STEMI: ST-segment elevation myocardial infarction; BNP: brain natriuretic peptide; LVEF: left ventricular ejection fraction.

were considered in the category of smoker. Diabetes mellitus and hypertension was labelled according to the guidelines.[11,12] if the patient was either on oral hypoglycaemic agents/insulin or having fasting blood glucose level ≥126 mg/dl or post-parendial blood glucose levels ≥200 mg/dl.[10] Hypertension was defined if either the patient was on antihypertensive drugs or having sustained systolic blood pressure (SBP) of ≥140 mm of Hg or diastolic blood pressure (DBP of ≥90 mm of Hg.[12] An estimated glomerular filtration rate (GFR) < 60 ml/min/1.73 m^2 persisting for >3 month duration was labelled as chronic kidney disease.[13] A haemoglobin level of <11 g/dl was used to define anaemia. Severe anaemia if haemoglobin level was <8 g/dl.[14] ST-segment elevation (STEMI) or acute coronary syndrome (ACS) was defined according to the American Heart Association (AHA) guidelines.[15] The air pollution variables were taken which included particulate matter- PM2.5 and PM10 (in μg/m^3), and gaseous pollutants such as nitrogen dioxide (NO_2) (in μg/m^3), ammonia (NH_3) (in μg/m^3), tropospheric ozone (O_3) (in μg/m^3), sulfur dioxide (SO_2) (in μg/m^3), and carbon monoxide (CO) (in μg/m^3). The peak and average values of each air pollution variable were noted according to the date of admission. Meteorological attributes were collected on a daily basis which included air temperature (in degree Celsius; minimum and maximum temperature were taken separately daily), and humidity (in %). The air temperature was taken daily as minimum, maximum daily values. Daily average value of humidity was taken. All the air pollution and meteorological variables were averaged on the monthly basis for the studying their impact on HF.

The outcomes in this study included monthly ADHF admission and all-cause mortality (in-hospital) which were calculated as the total number of admissions and deaths occurring during two consecutive years.

3. Statistical analysis

The statistical analysis was done with SPSS statistics 16.0 for windows (USA). The continuous variables were expressed as mean (±standard deviation) or median (interquartile range) for normally distributed or skewed data respectively. Categorical variables were expressed as a percentage (%). The total ADHF admission and mortality were calculated on monthly basis to correlate with the averaged attributes of environment and pollution using Kendall's tau-b correlation. The strength of correlation was assessed as strong, modest, and weak for ‘r’ values of >0.7, 0.3–0.7, and <0.3 respectively. The independent association of these attributes with study outcomes was analyzed using multiple linear regression analysis. The correlation of air pollution and meteorological attributes with ADHF admissions and mortality was done by gender and age. The difference in the correlation coefficients of the same variables within these sub-groups was done by transforming the correlation coefficient value (r values) into z scores which are known as Fisher's z transformation. The normality of the given data was checked with the Kolmogorov–Smirnov test. The difference between the two variables was considered significant if the two-sided p-value was <0.05.

4. Results

During the two years of study from April 2017 till March 2019, a total of 10,757 patients were admitted in the hospital. Of these, 4561 patients were diagnosed to have ADHF, 70.8% ($n = 3231$) were in group I and 29.2% ($n = 1330$) were in group II. The mean (± standard deviation) age of the study group was 64.6 years (±12.6) and predominately men (60%). The clinico–demographic profile and the laboratory parameters of the study group have been described in Table 1.

Fig. 2 depicts the monthly distribution of the total number of HF admissions over the year. The total HF admissions (Fig. 3A) were significantly higher during the winter while a considerably lesser number of admissions were observed during the summer. The monthly HF mortality (Fig. 3B) showed similar trend of higher mortality during winter months compared to the summer months. The January month contributed maximally to the total HF

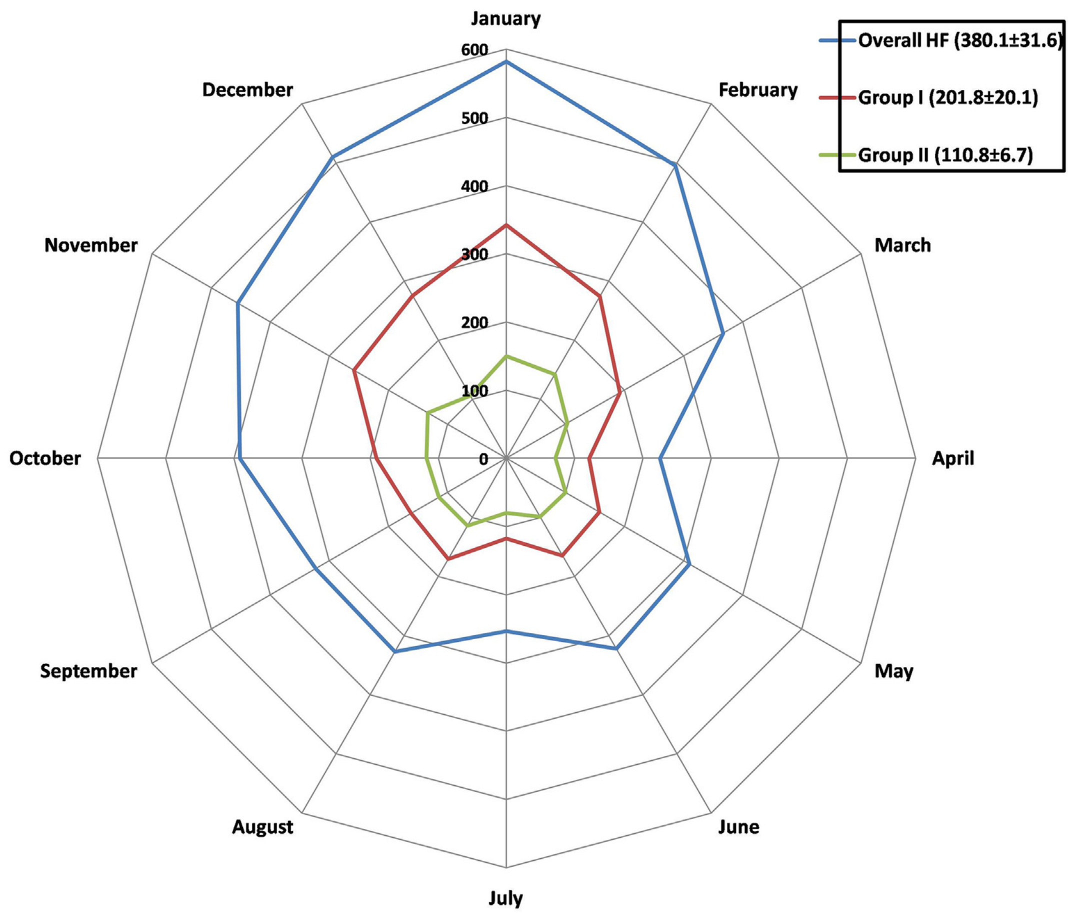

Fig. 2. Seasonal trend of monthly HF admissions. HF: heart failure, group I: heart failure with reduced ejection fraction, group II: heart failure with borderline/preserved ejection fraction. Parenthesis showing mean ± standard error of mean in each sub group.

admission (12.8% which is 4.5% above average) and monthly HF mortality (15% which is 6.7% above average) while least contribution to HF admission (4.9% which is 3.4% below average) and monthly HF mortality (5.9% which is 2.4% below average) was noted in the months of April and May. Overall, the monthly HF admission was 2.6 times higher in January month compared to the April month. Similarly, the monthly HF mortality was 2.5 times higher in January month compared to the April month.

The correlation of various attributes of environmental pollution, temperature, and humidity with the HF admission rate and duration of hospital stay has been described in supplementary table 1. The most significant attribute correlating maximally (inversely) with both monthly HF admissions ($r = -0.78$, $p = 0.003$) and monthly HF mortality ($r = -0.65$, $p = 0.004$) was average of the maximum air temperature. The correlation of the monthly HF admissions and maximum air temperature was significantly higher in the HFrEF compared to that of HFpEF ($r = -0.75$, $n = 3231$ vs $r = -0.65$, $n = 1330$; z score = −6.06, $p < 0.0001$). Supplementary figure 1 shows the comparative linear correlation for both study groups.

Air pollutants noted to have the maximal positive impact on hospital admission was mean ammonia and maximum NO_2. PM2.5 and PM10 did not have any significant effect on admission rates. Monthly HF mortality was also significantly correlating with mean NH_3 level. In multivariate linear regression analysis, the maximum air temperature was independently predicting monthly HF admission [$t = -4.83$, beta = −0.91; 95% CI (−19.8 to −6.9), p 0.001] while none of the other attributes demonstrated such distinct association. Similarly, the maximum temperature [beta = −0.86, $t = -3.82$; 95% CI (−3.4 to −0.9), $p = 0.004$] was independently predicting the monthly hospital mortality as well. According to our model, there was 13-point increase in estimated monthly HF admissions and 2-point increase in monthly HF mortality for each degree Celsius decrease in maximum air temperature (when all other attributes remain constant). Fig. 3 demonstrates the inverse correlation of monthly HF admissions with maximum air temperature. None of the air pollution attributes were found to be independent predictors of HF admissions or mortality.

The study population was divided into three groups as per the age (as mentioned above). Across all the age groups, the admission rate of total HF patients was moderately correlating (inversely) with maximum air temperature (Table 2). The correlation of monthly HF admissions with the maximum temperature was significantly higher in age group ≥ 65 years as compared to age group <45 years ($r = -0.74$, $n = 2426$ vs $r = -0.5$, $n = 247$; z score = −5.97, $p < 0.0001$).

The correlation (inverse) of HF admission and maximum temperature was significant for both males ($r = -0.8$, $p < 0.001$) and females ($r = -0.71$, $p = 0.002$); and the difference of correlation coefficient (favoring male gender) was statistically significant (z score = −6.98, $p < 0.0001$). The correlation of monthly HF mortality and maximum air temperature showed a similar trend by being significant for both the genders (males: $r = -0.68$, $p = 0.002$ and females: $r = -0.49$, $p = 0.03$), with the statistically significant difference of correlation coefficient (favoring male gender) (z score = −9.67, $p < 0.0001$). Pollution attributes correlating

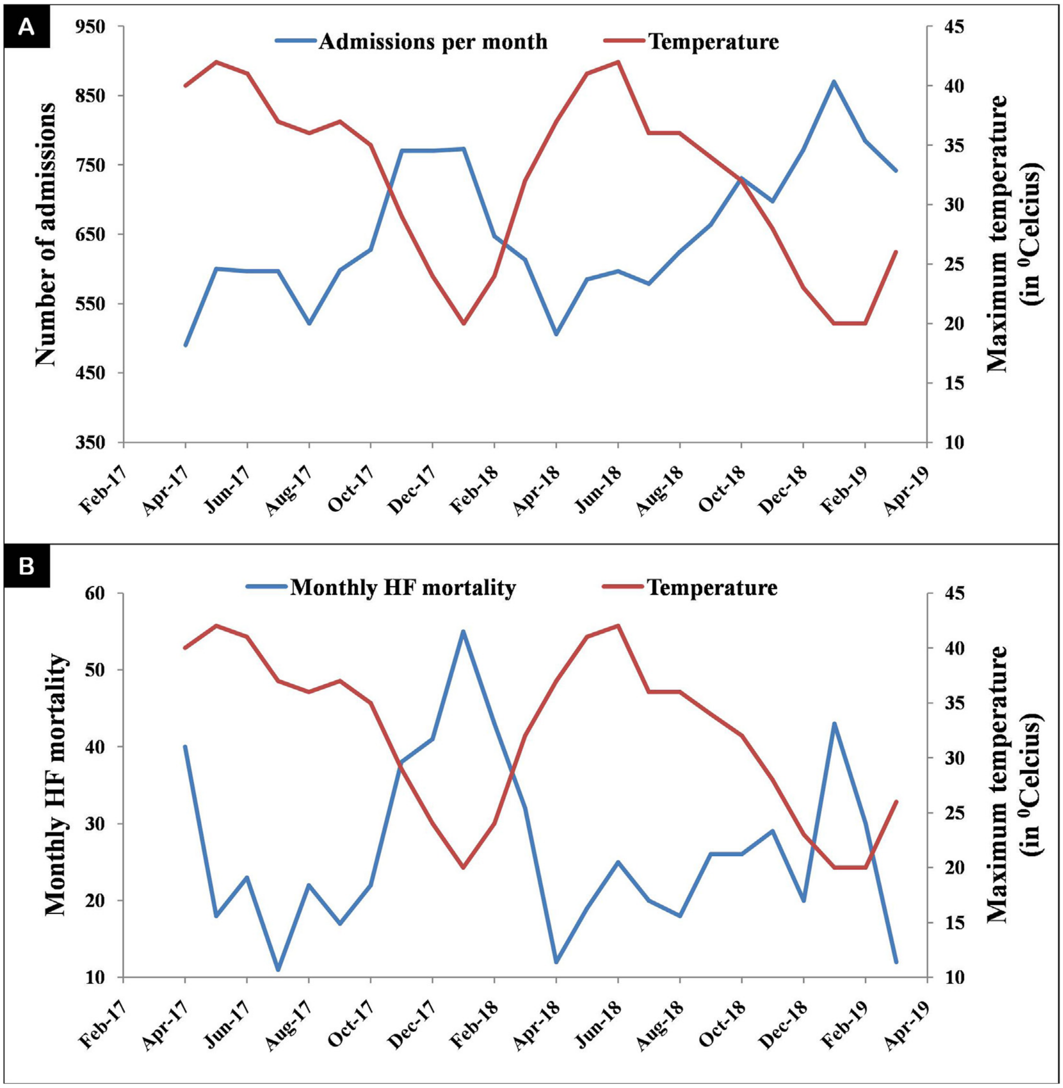

Fig. 3. Comparative cyclical trends of monthly HF admissions and maximum air temperature (panel A), and monthly HF mortality and maximum air temperature (panel B). HF: heart failure. *X* axis represents the time axis (in months). Primary *Y*-axis represents monthly HF admissions (panel A) and monthly HF mortality (panel B), and the secondary *Y*-axis represents the maximum air temperature (in ^{0}Celsius).

significantly with HF admissions were average NO $_2$ (r = 0.5, $p = 0.023$) and average NH_3 ($r = 0.6$, $p = 0.007$) level whereas none of the other pollution attributes were correlating significantly with the monthly HF mortality. Significant correlations of pollution attributes with HF admissions were noted with average NO_2 levels ($r = 0.5$, $p = 0.023$) and average NH_3 levels ($r = 0.6$, $p = 0.007$) whereas none of the other pollution attributes were correlating significantly with monthly HF mortality. Fig. 4 shows the seasonal distribution of monthly HF admission and mortality according to age, and gender.

The correlation (inverse) of monthly HF admission and maximum air temperature was significant for both urban ($r = -0.8$, $p < 0.001$) and rural ($r = -0.64$, $p = 0.005$) stay. The correlation of monthly HF mortality and maximum air temperature showed a similar trend for both the urban ($r = -0.43$, $p < 0.05$) and rural ($r = -0.57$, $p = 0.011$) stay. In urban patients, the monthly HF admission was correlating positively with air pollutants like average NH3 ($r = 0.57$, $p = 0.011$) and maximum NO2 ($r = 0.5$, $p = 0.023$) and HF mortality was not correlating with any of the air pollution attributes. In rural patients, the monthly HF admission was correlating positively with air pollutants like maximum PM2.5 ($r = 0.49$, $p = 0.027$), maximum PM10 ($r = 0.55$, $p = 0.013$), maximum NO2 ($r = 0.55$, $p = 0.013$), and maximum NH3 ($r = 0.52$, $p = 0.019$), and monthly HF mortality was correlating positively with air pollutants like maximum PM10 ($r = 0.52$, $p = 0.019$), maximum NO2 ($r = 0.65$, $p = 0.004$), and average NH3 ($r = 0.68$, $p = 0.002$).

5. Discussion

Heart failure contributes a significant burden of cardiovascular diseases related morbidity and mortality. These patients run a high risk of recurrent hospitalization due to their limited cardiac reserve and even subtle changes in the hemodynamic status of the patients might lead to HF decompensation. Low temperature during the winter season has been shown to cause vasoconstriction and thereby increasing the afterload leading to the decompensation of HF.[16]

The present study had identified a significant peaking of HF admission rates during winters. Previous studies have also

Table 2
The table showing correlation of HF admission and mortality with various significant environmental attributes in various age groups.

	Age ≥65 years $n = 2426$		Age 45–64 years $n = 1888$		Age <45 years $n = 247$	
	Total HF admissions	Monthly HF mortality	Total HF admissions	Monthly HF mortality	Total HF admissions	Monthly HF mortality
Maximum NO2	$r = 0.39$, $p = 0.08$	$r = 0.28$, $p = 0.215$	$r = 0.55$, $p = 0.014$*	$r = 0.24$, $p = 0.297$	$r = 0.35$, $p = 0.125$	$r = 0.38$, $p = 0.09$
Average NH3	$r = 0.46$, $p = 0.014$*	$r = 0.27$, $p = 0.215$	$r = 0.55$, $p = 0.014$*	$r = 0.24$, $p = 0.297$	$r = 0.76$, $p = 0.001$*	$r = 0.35$, $p = 0.125$
Maximum temperature	$r = -0.74$, $p < 0.001$*	$r = -0.57$, $p = 0.011$*	$r = 0.75$, $p = 0.001$*	$r = -0.51$, $p = 0.026$*	$r = -0.5$, $p = 0.027$*	$r = -0.4$, $p = 0.08$
Minimum temperature	$r = -0.67$, $p = 0.003$*	$r = -0.59$, $p = 0.009$*	$r = -0.64$, $p = 0.004$*	$r = -0.58$, $p = 0.01$*	$r = -0.39$, $p = 0.08$	$r = -0.35$, $p = 0.125$
Mean temperature	$r = -0.67$, $p = 0.003$*	$r = -0.56$, $p = 0.009$*	$r = -0.64$, $p = 0.004$*	$r = -0.52$, $p = 0.022$*	$r = -0.45$, $p = 0.045$*	$r = -0.41$, $p = 0.07$

HF: heart failure; NO2: nitrogen dioxide; NH3: ammonia.

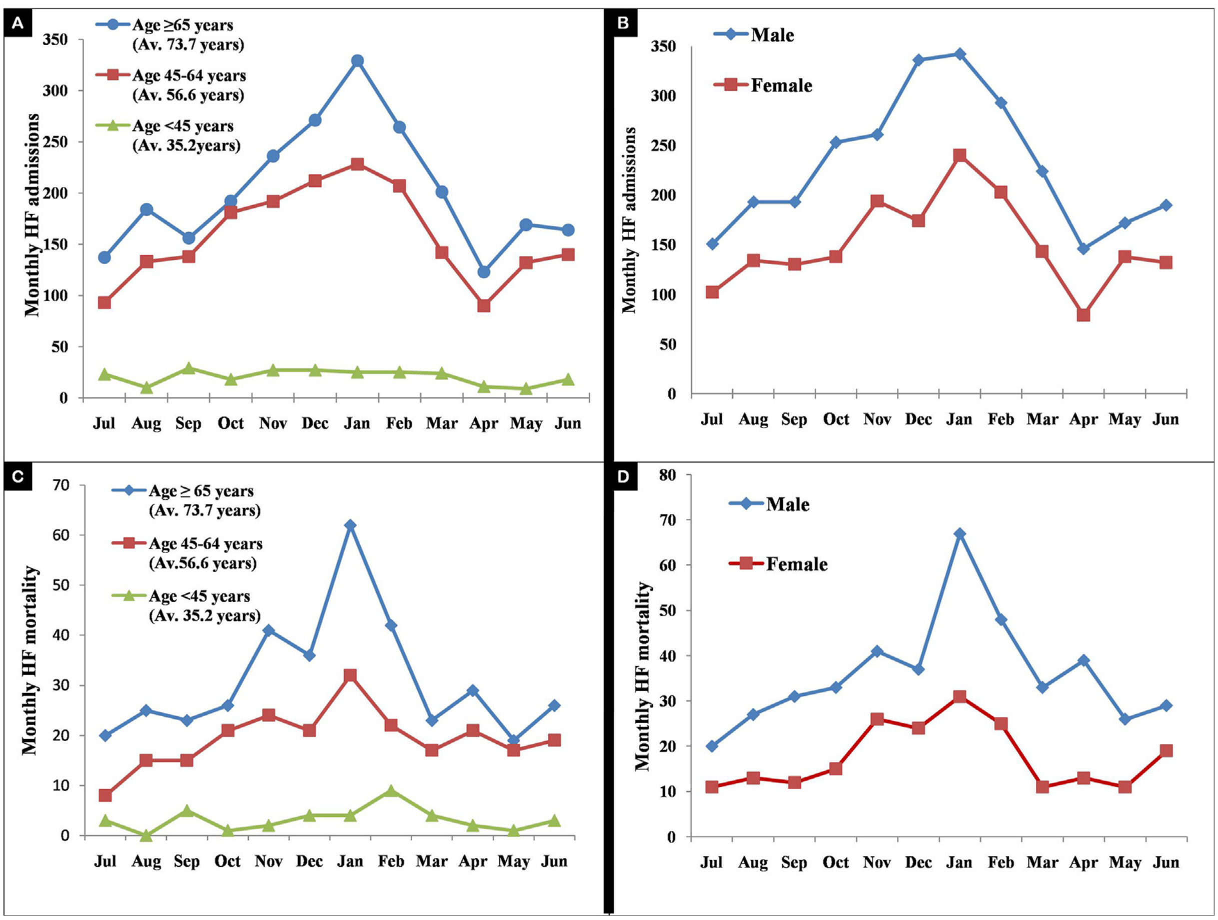

Fig. 4. Seasonal trends of monthly HF admissions according to age groups, gender and urban/rural stay (panel A & B) and monthly HF mortality according to age group and gender (panel C & D).

described a similar trend of increased HF admissions during the winter season.[1,17–19] Our study population had shown a peaking of HF admissions among across all range of EF i.e. both for group I and group II. The correlation was significantly more in HF with reduced EF patients i.e. group I. To the best of our knowledge, this observation has not been made in the literature earlier. Our study illustrated 13 points increase in monthly HF admissions with 1° Celsius decrease in the maximum temperature. A similar trend was witnessed by Escolar V et al where they had found with an increase in mean temperature of 1^0Celsius, the estimated hospitalization will decrease by 0.6.[17]

It is observed that mortality is increased in decompensated HF patients during the winter season. This has been attributed to the increased systemic adrenergic activity and decreased exercise capacity during the winter season.[20] All these factors increase the HF mortality by the escalation of plasma non-epinephrine levels.[21] Feldman DE et al had observed maximum monthly heart failure mortality in January month. Our study further strengthens the observation of the peaking of HF mortality from November till January.

The present study observed the consistent correlation of temperature with monthly HF admissions and mortality across all the age groups, but the correlation was significantly stronger in the elderly group (age ≥65 years). The literature cited similar seasonal variation HF and other cardiac diseases like hypertension and coronary events in the elderly.[1,22] The elderly have a reduced cold-induced-thermoregulation due to a decline in muscle mass and metabolic rate, and so they are more prone to have negative effects of low environmental temperature.[23] This striking vulnerability of the elderly to the winter exacerbations highlights the importance of creating a general awareness in the elderly to improve the overall outcome of this fatal disease.

The winter peaking of both HF admissions and mortality was observed in both male and female gender. But the seasonal effect was more in the males in comparison to the females. An opposite gender difference was reported by Stewart et al where they had observed the seasonal variation more marked in females as compared to males.[1]

The environmental pollution in the form of gases and PM is well known to have a worse effect on cardiovascular diseases in the form of increased HF hospitalization and its mortality, increased risk of myocardial infarction, hypertension, and stroke.[16,24–26] The data from low-to middle-income countries is lacking. After extensive literature search, three studies partially representative of developing countries were found.[27–29] The PM exposure is far higher in the developing countries than the cut-offs mentioned in the WHO 2006 guidelines.[27] Our results did not reveal any consistent correlation of environmental pollution with the HF admissions and outcome. This could partially be explained by the "leveling off" effect seen with the air pollutants where-in the exposure-response curve flattens at a high concentration of pollutants, therefore, the association becomes weaker at higher PM2.5 concentrations.[30] In our study, the average annual PM2.5 concentrations was 112 $\mu g/m^3$ which was far higher than the cut-offs mentioned in the world health organization (WHO) 2006 guidelines. So, the pollutant level was high throughout the year not producing any variation in HF admissions and its outcome. Other reason could be that the effect of temperature huge enough to overshadow the effect of air pollution on HF outcomes. To reach at that conclusion of air pollution impact on HF one need to have a very complex regression analysis.

5.1. Study limitations

There are a few limitations that were observed in this study. First, its retrospective study design carries inherent limitations. Secondly, people residing in the surrounding rural areas might have a lesser impact of the pollution which has not been taken into account in this study. Thirdly, this study was conducted in the northern region of India which may not be a true representative of all the regions of the country given the vast variation in seasons and environmental pollution. Fourth, the study is not powered enough to determine the effect of the air pollution on HF outcome. Therefore, another study is needed to understand its impact.

6. Conclusion

In conclusion, our study is unique in assessing the seasonal variation of HF admission and mortality from a low-to middle-income country like India; specifically in the northern region where extreme variation of seasons exists. A strong inverse correlation was noted between the temperature and the HF admission and mortality, and it continued to persist even among HF with reduced EF patients and HF with borderline/preserved EF patients. There was more than double the monthly HF admission in winter months compared to the summer months. The winter peaking of both HF admission and mortality was markedly seen in the elderly subset. Similarly, the male gender had shown a better correlation for the same parameters than the female gender. In our study, air pollution did not correlate well with any of the HF parameters due to various reasons as mentioned above.

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None.

Declaration of competing interest

The authors declare no conflict of interest.

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Nil.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ihj.2022.07.006.

What is already known?

- The western data shows that the seasonal variation has a huge impact on the heart failure admission and outcome.

What this study adds?

- This study adds to the literature that the seasonal effect on HF occurs even in a low-to middle socioeconomic status country like India.
- The environmental pollution has no effect on HF outcomes in low-to middle-income country like India due to "leveling off" effect.
- The seasonal effect is consistent for both HF with all range of ejection fraction.

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