

Role of Air Pollution in Inflammatory Bowel Disease Flares: A Retrospective Study

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ABSTRACT

Background:

To evaluate relation between air pollution and rate of flare and hospital admission among inflammatory bowel disease (IBD) patients.

Materials and Methods:

In this retrospective study, during a 10 months period, the number and average duration of hospitalization of patients admitted in GI ward due to IBD flare were recorded in an industrial capital city. Concomitantly the level of 4 major air pollutants including SO₂, CO, NO₂ and O₃ measured and the correlation between severity of IBD flare and air pollution determined by Pearson correlation coefficient.

Results:

Average number of admission was 7 patients per month (1-12). This figure for Crohn's disease (CD) was 2.9 and 3.7 for ulcerative colitis (UC). The average duration of hospitalization for UC and CD were 2.8 days (1-13) and 2.9 days (1-22) respectively. After comparison of average concentration of 4 major air pollutants with rate of IBD flare, there was a relation, although non-meaningful, between CO concentration and number and duration of admissions due to UC flare ($p=0.135$ & 0.08 , correlation coefficient 0.196 & 0.251 respectively). DATA analysis did not reveal any significant relation between SO₂ and NO₂ and the rate of admission due to IBD flare ($p>0.05$) and Interestingly there were a reverse meaningful correlation between concentration of O₃ and number and duration of admissions due to Crohn's disease flare ($p=0.016$ and 0.006 , Correlation Coefficient -0.338 & -0.413 respectively).

Conclusion:

It seems that CO as one of the major air pollutants can aggravates course of ulcerative colitis and on the other hand O₃ could have a potential protective effect on Crohn's disease. This issue should further be clarified in future studies.

Keywords: Inflammatory bowel disease; Crohn's disease; Ulcerative colitis; Environment; risk factors; Flare; Air pollution

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INTRODUCTION

Inflammatory bowel disease (IBD) defines as chronic and relapsing inflammation of the GI tract with 2 major types of ulcerative colitis (UC) and Crohn's disease (CD)(1). The clinical course of these diseases include attacks of aggravation and flare up interspersed between periods of silence and remission in 80% of cases(2). After the first attack of flare up, 40 to 65% of patients will experience an intermittent and periodic course while 5 to 10% would be



Fig. 1: The rate of admission due to IBD flare

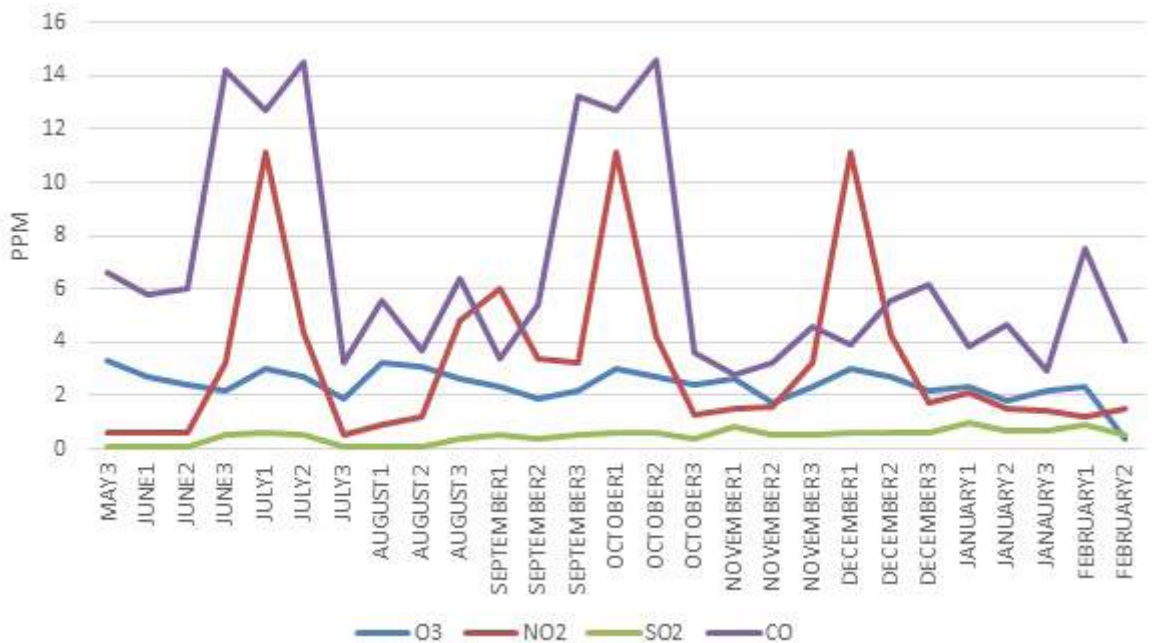


Fig. 2: Average concentration of air pollutants during study period (PPM: part per million, CO concentration divided by 10).

challenging a constant course(3,4).

Now a days it has been cleared the IBD results from continuous antigenic stimulation of GI tract microbiota including bacteria, viruses and funguses (5-9) and environmental factors, most known of them as

cigarette smoking, have a major role in aggravation or modulating of these antigenic stimulation (10-13). The significant increase of IBD prevalence in developing countries in the second half of 20th century highlighted the potential role of these environmental factors in

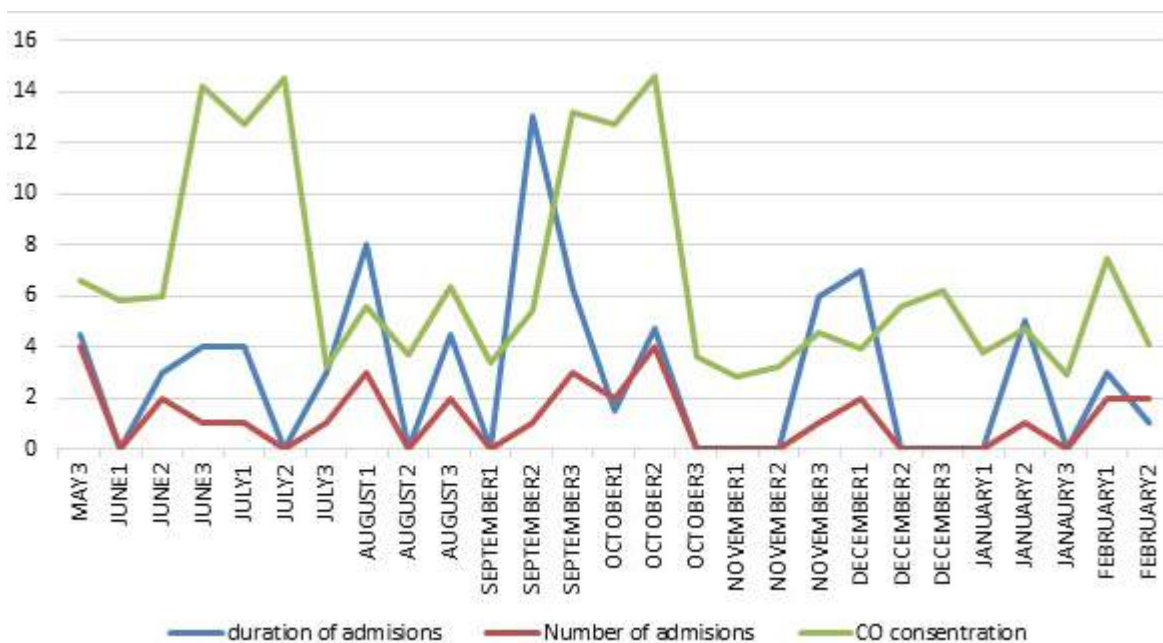


Fig. 3: Relation between CO concentration and average rate and duration of admission due to UC flare (CO concentration: PPM, rate: number of patients, duration: days).

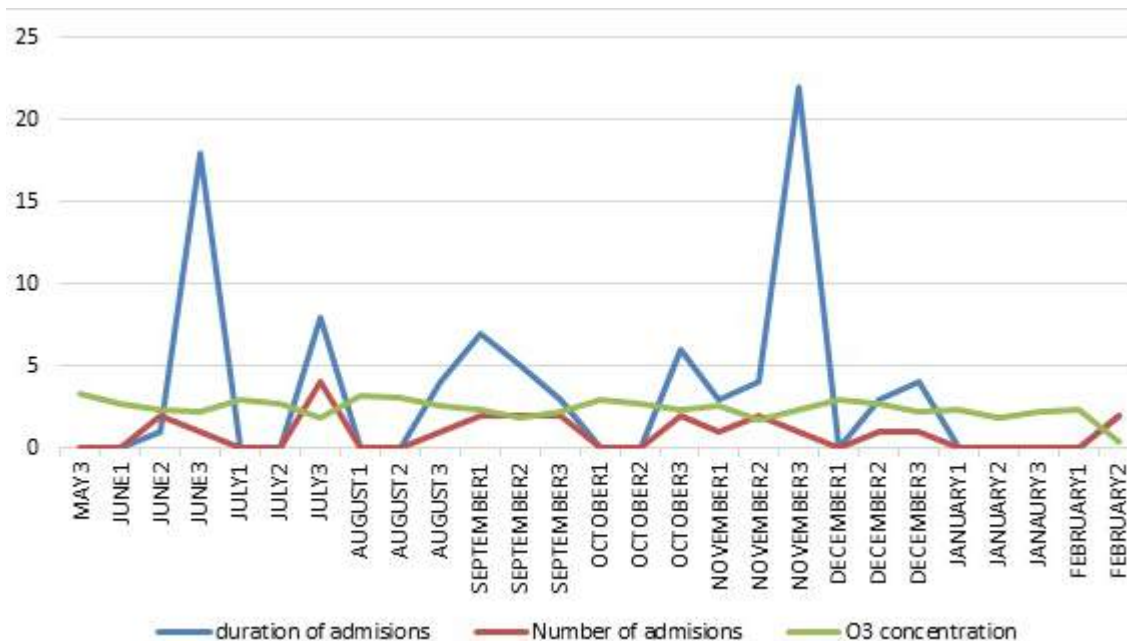


Fig. 4: Relation between O3 concentration and average number and duration of admission due to Crohn's flare (O3 concentration: PPM, duration: day).

pathogenesis of these disorders(12,14,15). One of the problematic and threatening environmental factors in recent years and in urban and industrial societies was air pollution especially the pollutants related to mega cities traffic and burning of fossil-fuel which include

levitate particles and nitrogen oxides(14-16). In fact the risk factors of industrialization were not fully evaluated and there was controversy about influence of air pollution and its different effects on people healthiness(16). In the previous studies, the level of

air pollution has been significantly related to the rate of hospitalization of adults suffering from IBD(17).

The aim of this study was to evaluate the relation between air pollution and hospitalization due to IBD flare up in GI ward of Ahvaz Imam Hospital as a referral center in Khuzestan province.

MATERIALS AND METHODS

In this retrospective cross sectional survey, by evaluating the records of Ahvaz aerology stations and air pollution committee of Ahvaz Jundishapur University, the DATA about 4 major air pollutants including CO, SO₂, O₃ and NO₂ and their average concentration during a ten months period since May 2012 to February 2013 gathered and by refer to archive of Imam Hospital as a referral center, all of the admission files due to IBD flare up during the same period investigated. Inclusion criteria included any admission in GI ward due to IBD flare and exclusion criteria was temporary admission of IBD patients for receiving Anti TNF (Infliximab). used Pearson Correlation Coefficient and analyzed by SPSS 19 software, any relation between increasing air pollution and IBD flare including rate of hospital admission and duration of hospital stay, evaluated.

RESULT

In a 10 months period from May 2012 to February 2013, overall there were 66 cases of admission due to IBD flare (37 cases of UC (56%) and 29 CD patients (44%), average 7 cases per month). The highest rate of admission recorded on September (10 cases of IBD flare) and February (12 cases) while the least rate of flare recorded on January (1 case of IBD flare) (Figure 1). Average duration of admission was 2.8 days with maximum hospital stay about 22 days in November.

In the same period, the concentration of 4 major air pollutants including CO, NO₂, SO₂ and O₃ measured in multiple meteorology stations around Ahvaz City as the capital of Khuzestan province and then the median concentration of each pollutant calculated. For CO, the least concentration recorded in early November (28 PPM) while the highest level was seen on mid-July and mid-October (average 146 PPM). The least concentration of NO₂ recorded in May and late July (0.5 PPM) and its highest level measured in early July, October and December (11.1 PPM). The lowest and highest concentration of SO₂ recorded in August (0.1 PPM) and January (1 PPM) respectively while minimum and maximum concentration of O₃ recorded in mid-February (0.4

PPM) and May (3.3 PPM) (Figure 2).

When the rate and duration of IBD flare compared with concentration of these air pollutants, there was a relation, although non-meaningful, between CO concentration and number and duration of admissions due to UC flare ($p=0.135$ & 0.08 , correlation coefficient 0.196 & 0.251 respectively) (Figure 3). DATA analysis did not reveal any significant relation between 2 other major pollutants including SO₂ and NO₂ and the rate of admission due to IBD flare ($p>0.05$). Interestingly there were a reverse meaningful correlation between concentration of O₃ and number and duration of admissions due to Crohn's disease flare ($p=0.016$ and 0.006 , Correlation Coefficient -0.338 & -0.413 respectively) (Figure 4).

DISCUSSION

Inflammatory bowel disease as a multifactorial category of chronic and relapsing disorders is a major health concern among industrial communities(18-20). Increases among incidence of IBD in the past few decades, suggests that environmental factors could contribute to disease pathogenesis and in this regard air pollution and its components could be a potential contributor of intestinal disease(14,16). Oral route accounts for much of the exposure to air pollutants and human studies have shown that larger particles are quickly cleared from the lungs and transported to the intestinal tract by mucociliary clearance(21). In this way, a large fraction of inhaled pollutants will be ingested and rapidly enter the intestine(22). Exposure of the bowel to air pollutants occurs via mucociliary clearance of particulate matter from the lungs as well as ingestion via food and water sources. Gaseous pollutants may also induce systemic effects. Plausible mechanisms mediating the effects of air pollutants on the bowel could include direct effects on epithelial cells, systemic inflammation and immune activation, and modulation of the intestinal microbiota(14). In medical literature, there are some studies that evaluated the relation between air pollution and IBD with inconsistent results(14,16, 17). Another Canadian study calculated the daily concentrations for ozone (O₃), NO₂, SO₂, CO, and particles<10 (PM10) or <2.5 (PM2.5) μm and by case crossover study design estimated the odds ratio associated with an increase in the interquartile range of the air pollutants. In animal models, colonic motility was tested, and visceral abdominal pain was measured using a behavioral response to oil of mustard and neostigmine. Findings of this study showed an increased risk of non-specific

abdominal pain among individuals aged 15 to 24 years. The risk of air pollution among 15–24 year olds in Montreal was significantly positive (same day CO: OR = 1.11, 95% CI = 1.05–1.17; NO₂: OR = 1.09, 95% CI = 1.01–1.16; SO₂: OR = 1.17, 95% CI = 1.10–1.25; PM_{2.5}: OR = 1.09, 95% CI = 1.04–1.15). Abdominal pain was increased by an acute gavage of pollution extract but not to chronic exposure to pollutants. Colonic transit was delayed following chronic but not acute exposure with the pollutants. this study concluded that short-term exposure to air pollution may trigger non-specific abdominal pain in young individuals(23).

In our study the relation between concentration of SO₂ and NO₂ and IBD flare was negligible but there was a positive relation (although statistically non-significant) between CO concentration and rate and severity of UC flare ($p=0.135$ & 0.08 respectively). These results were in concordance with Kaplan study that examined this association epidemiologically by using a nested case–control study design based on over 900 cases of IBD and close to 5000 controls in a United Kingdom primary care database. While there are a number of potential confounders, this study suggests that exposure to air pollution may be an important environmental factor for IBD especially among children and young adults living in areas with higher levels of SO₂ and/or NO₂ who were more likely to develop ulcerative colitis or Crohn's disease(16). This may be explained by the fact that children and young adults tend to be more active and spend more time outdoors leading to greater exposure to air pollutants(24). Accordingly another study showed an association between hospitalizations related to IBD and total pollutant density using county-based emission and hospitalization records in Wisconsin, USA. In this study, Data from the Wisconsin Hospital Association (WHA) for the year 2002 was used to identify the number of IBD-related hospitalizations for each of the 72 counties in Wisconsin. Average annual emissions density for each of the six criteria pollutants were obtained for each county from the Environmental Protection Agency. The findings of this study revealed the total criteria pollutant emissions density to be correlated significantly with adult IBD hospitalizations (Pearson's correlation coefficient (ρ) 0.28, $p=0.02$). On Poisson regression, a 1-log increase in the density of total criteria pollutant emission was associated with a 40% increase in the rate of IBD hospitalizations (incidence rate ratio 1.40, 95% CI 1.31-1.50) This was similar for both ulcerative colitis (UC) (IRR

1.48, 95% CI 1.27-1.73) and Crohn's disease (CD) hospitalizations (IRR 1.39, 95% CI 1.26-1.52)(17).

Interestingly while it has been shown that O₃ can induce inflammation in airways by affecting the innate immune signaling, impairment of antibacterial host defense and disruption of epithelial barrier(25,26), our finding revealed a reverse relation between Ozone concentration and Crohn's disease activity which necessitate further evaluation of this potential relation and clarifying if there is any complex relation same as sigarrete smoking(27). In previous studies it has been shown that treatment with Ozone can significantly reduce the severity of Necrotizing enterocolitis and acute necrotizing pancreatitis by modulating antioxidative defense and anti-inflammatory protection in experimental animal model(28,29) and also O₃ shows a preventative effect in the ileum by decreasing tissue damage and increasing antioxidant enzyme activity in an experimental model of Mtx-induced intestinal injury(30).

At present, the association between air pollution exposure and intestinal disease has not been clearly defined and although these correlations should be interpreted with caution as they are subject to a number of biases(14). This is particularly important in the case of mixed air pollution and also we should keep in mind the complex effect of sigarrete smoking on the course of IBD(10-13,25). Additionally, exposure assessment is calculated based on regional estimates of air pollutant levels rather than actual person-by-person monitoring. Furthermore, most of these studies are retrospective that cannot account for unmeasured confounders, such as diet, time spent outdoors, activity, and occupation(14). Another limitation is the focus on exposure to air pollution immediately before or during the outcome while long-term exposures are more likely to contribute to chronic illnesses such as IBD(14). While these limitations necessitate a cautious interpretation of findings, they should serve to emphasize the need for further evaluation about the effects of pollutants on the course of IBD.

Although the relation between air pollution and IBD is complex and inconclusive it seems that CO as one of the major air pollutants can aggravates course of ulcerative colitis and on the other hand O₃ could have a potential protective effect on Crohn's disease. This issue should further be clarified in future studies. In industrial cities, supervision on air polluting factories and preventing release of unusual amounts of these pollutants especially CO can potentially decrease the rate and severity of IBD flare.

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