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Title: DOES THE HOSPITAL ADMISSION OF PATIENTS WITH RESPIRATORY DISEASE INCREASE IN İZMİR IN THE DAYS IN WHICH PM10 LEVELS HIGH?

Short Title: THE RELATIONSHIP HOSPITAL ADMISSION AND AIR POLLUTION

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Abstract

Objective: Air pollution is caused by, especially from industrial facilities around the world, exhaust emissions from motor vehicles, fuel consumption for heating in residences . Exposure to outdoor air pollution has been associated with acute and chronic health problems in a wide range from irritant to death. It was aimed to determine whether air pollution increases the frequency of admission to the hospital and whether there is a difference between the disease subgroups, age and gender in two years period in İzmir province where air pollution is increasing.

Methods: Collection of health data for the project made by The Ministry of Health, in cooperation with the İzmir Provincial Health Directory Information Processing Department, information obtained on the age groups, sex, admission time, and diagnosis of illness (ICD10 code) on the residents of İzmir in 2016-2017.

Results: The daily numbers of patients who applied with respiratory system complaints and the air pollution were found to be related. Rather, both the air pollution and the admission increase in January-March period. In male patients, the risk of hospitalization increases is 1.14%. . In males, it was seen that there was the highest increase rate with the diagnosis of chronic rhinitis with an increase of 6.22% whereas in female patients was found to be 0.97%. , it was seen that there was a 2.62% increase in bronchiectasis, 2.53% in asthma and 2.49% in dyspnea .

Conclusion: There was a significant increase in respiratory diseases during the days when the air pollution was high , this was seen as the URTI and acute bronchitis in the young group and chronic respiratory diseases in the elderly group in hospital admissions. The reduction of air pollutants and inhalation of clean air through is the most important effect in providing healthier and longer life.

Keywords: respiratory disease, air pollution, morbidity

INTRODUCTION

Exhaust emissions of motor vehicles, heating fuel consumption of residences and especially industrial facilities waste and extracts cause air pollution. Worldwide, a fivefold increase in air pollutant emissions is expected by 2030 [1].

Air pollution is a significant risk factor for health. A global survey of diseases has shown that air pollution is one of the top ten risk factors for health worldwide [2]. Approximately 7 million people in the world and 400,000 people in the European Union (EU) are exposed to premature death due to air pollution [3].

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The effects of air pollutants on health can either be acute or chronic. Acute effects cause an increase in hospital admissions and treatment needs within the hours/days following the exposure, whereas chronic effects occur in the form of exaggeration of chronic diseases and premature deaths.

Exposure to outdoor air pollution has been associated with acute and chronic health problems in a wide range from irritancy to death [4].

Gas particles and PM10 exposure are associated with the incidence of upper airway symptoms such as rhinorrhea, nasal obstruction, cough, laryngospasm, and vocal cord dysfunction and may cause lower respiratory symptoms, especially coughing, shortness of breath and wheezing in children[5].

This exposure also causes an increase in cough and wheezing in adults with chronic pulmonary disease as well as healthy adults[6].

In this study, we aimed to determine the effect of high PM10 level over the frequency of admission to the hospital and examine if there is a difference between the disease subgroups, age, and gender in two years period in İzmir province where air pollution is increased.

MATERIAL METHOD

The collection of health data for the project was performed with the accompany of the Ministry of Health, İzmir Provincial Health Directory Information Processing Department. The obtained information included age groups, gender, admission time, and diagnosis of illness (ICD10 code) on the residents of İzmir in 2016-2017.

The reliability of the data was determined by making a comparison of respiratory diseases evaluated in the outpatient clinics. Risk analyses were performed using the case-crossover method and the conditional logistic regression technique with the obtained epidemiological data, air pollutant (PM10) level, meteorological conditions, age, sex, and location independent variables. Risk periods were determined by examining the temporal changes of the disease prevalence. A symmetric

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bidirectional case-crossover approach is used in this study. The level of PM10 at the time of hospital admission for each case was compared with the level of PM10 at a particular time point whereas there was no application. The cases were chosen from the respiratory tract disease applications during the study period and the control days were set as two weeks before and two weeks after each case day. The meteorological variables such as wind speed, wind direction, air temperature, air pressure, and relative humidity are kept constant in each analysis. The acute effect of air pollution can be seen immediately or even after a few days. In this study, the previous 4-day PM10 concentrations were also included in the analysis to determine the effect of PM10 (lag1, lag2, lag3, lag4) levels on hospital admission four days before the previous day.

STATISTICAL ANALYSIS

The odds ratio (odd radio, OR) values of the respiratory system diseases PM10, which give risk-level possibilities, were calculated using Stata 14.0 software.

The level of the relationship between air pollution level and hospital applications was calculated using OR at a 95% confidence interval. OR is evaluated with the predicted hospital applications against every 10 µg / m³ increase of the air pollutant's (PM10) concentration. The obtained risk ratios are multiplied by the number of patients applied, and the number and percentage of risk group patients are calculated. P <0.05 was considered significant.

All the procedures performed in this study were under the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study was conducted according to good clinical practice and the Declaration of Helsinki. The study was approved by the local ethics committee of Training and Research Hospital

RESULTS

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In this study, 3.072.029 were male (49,6%), and 3.119.299 were female (50,4%). A total of 6.191.328 patients have taken codes of respiratory system disease; ICD10 J00-J06, J10-J18, J30-J34, J40-J44, J45-J46, J47, R05 and R06 in Izmir province between 1.1.2016-31.12.2017.

2.408.525 (38.9%) of the patients included in the study were in the 0-14 age group, 1.238.808 (20%) were 15-34, 616.494 (10%) were 35-44, 1.155.939 (18.7%) were 45-64, and 771.562 (12.5%) were 65 years and older. It was seen that male applicants were only higher in the 0-14 age group, and the number of female applicants was higher in the 35-64 age group (Figure-1). No significant difference was found regarding gender in the 15-34 age group and age over 65 groups.

It was observed that more than half of the patients (53.6%) who applied to the health institutions in Izmir due to respiratory system disorders received the diagnosis of upper respiratory tract infection (URTI) between 2016-2017 (Table-1). As expected, asthma is more common in women (9.6% versus 5.2%) while COPD is more common in men (10,3% versus 4.2%). The rate of diagnosis of chronic rhinitis was also higher in females than males (11.8% versus 8.5%). Sex difference in other diagnoses was not significant (Table-1)

Compared to age groups, the number of URIs in the 0-64 age group and COPD in the 65 and older age group were found to be higher. It was found that half of URIs and acute bronchitis in the 0-14 age group, more than 1/3 of the pneumonia in the age group of 65 years and over, all of the COPD patients in the age group of 45 years and over, and 30% of the asthmatics in the 0-14 age group, 27% in the 45-64 age group, 40% of the bronchiectasis in the 45-64 age group, 1/3 of the cough in the 0-14 age group, and 2/3 of the dyspneic group in the age group of 45 and over (Table 2).

PM10 level averages were calculated as $38.57 \pm 29.52 \mu\text{g} / \text{m}^3$ for two years, and there was no significant difference between weekday and weekend PM10 averages. On the other hand, weekday

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patient admission average (10.809 ± 3.024) was significantly higher than weekend admission average (3.341 ± 1.115) ($p < 0.001$).

According to The World Health Organization clean air criteria for the European Union region, PM10 per day should not exceed $50 \mu\text{g} / \text{m}^3$. The number of days when air monitoring station data exceeded the PM10 averages of 20,30,40, 50,100 and $150 \mu\text{g} / \text{m}^3$ were respectively 597,393, 254, 155, 28, and 3 days in this period. It can be said that almost half of the year is above the PM10 average (Table 3).

When the daily numbers of patients who applied with respiratory system complaints high, the PM10 level was also high as seen in Figure 2. Instead, both the PM10 level and the admission rate increase in the January-March period (Figure 2).

In figure 3, daily mean PM10 concentrations in Izmir between 2016-2017 were seen. PM10 levels made a peak in January and in March (Figure 3). In the two-year period, the average concentration of PM10 in Izmir was calculated as $38.57 \pm 29.52 \mu\text{g}/\text{m}^3$ and the PM10 concentration was measured above this average 40% (266 days) of the year. Rather, both the PM10 level and the admission rate increase in January-March period. We calculated the risk rates by comparing 2 weeks before and 2 weeks after exposure with Stan statistical program. It was found that there were significant increases in disease rates after 1, 2, 3, 4 days of exposure to air pollution, which was expressed as lag1, lag2, lag3, lag4 with risk rates.

65,045 (1,05%) of the 6,191,328 patients who applied with respiratory system disorders during the 2-year period were related with increased air pollution (34,891 men (53,6%), 30,154 women (46,4%).

In terms of age groups, 18.378 (28.3%) were in the age group of 35-44, 15.937 (24.5%) were in the 45-64 age group, 13.213 (20.3%) were in the age group of 65 and over and 10.349 (15.9%) were in

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the 0-14 age group and the least number was 7.168 (11%) and belongs to 15-34 age group.

Regarding impact, 35-44 age group was found higher in males, and 45-64 age group was higher in females (Table-4).

In male patients, increase in the risk of hospital admission (for every 10 $\mu\text{g} / \text{m}^3$ increase in PM10) is 1.14% (between 0.45% and 5.55%), while the highest increase is 5,55 % and in the 35-44 age group (Table-5).

The rate of increase in this ratio which is calculated by the ratio of the number of patients according to the gender and diagnosis in Table 1 is shown in Table 6.

According to this, in males, it was seen that there was the highest increase rate with the diagnosis of chronic rhinitis with an increase of 6.22% .

The risk of the increase in hospital admissions in female patients was found to be 0.97% (between 0.40% and 1.89%) (for every 10 $\mu\text{g} / \text{m}^3$ increase in PM10), with a maximum increase of 1.89% in the age 65 and older group (Table-5). In females, it was seen that there was a 2.69% increase in bronchiectasis, 2.53% in asthma and 2.49% in dyspnea (Table-6).

DISCUSSION

Air pollutants (PM10, PM2.5, SO2, nitrous oxide, ozone, diesel particulates) have been shown to have adverse health effects even at low levels. PM pollutants have been shown to be more potent on mortality and morbidity when their diameters are smaller when classified according to their size. Also, they have severe effects on health with many different organic and inorganic pollutants that can be found in a particulate matter [7].

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In morbidity studies evaluating short-term health effects of air pollution, an examination of the effects of daily mean concentrations of pollutants on both hospital admission numbers and daily deaths often involves examining daily data containing at least two years of exposure in the context of meteorological data, which are confounding factors of air pollution effects. From the 1990s onwards, in such studies, the daily and 0-4 daily mean concentrations of pollutant concentrations were investigated using the time series analysis method to determine the effects on daily mortality or hospital applications. In a comprehensive US study, 115 million COPD, heart failure, cerebrovascular disease, and chest diseases were associated with daily PM_{2.5} concentrations of hospital admissions in 204 residential areas and with the increase in PM_{2.5} concentrations, hospital admissions for cardiac insufficiency were found to increase by 1.23% in increments of 10- $\mu\text{g} / \text{m}^3$ [8]. In Italy, the results of a study of hospital applications in 2013, in which emergency department referrals due to chest diseases increased by 0.75% and 1.23%, respectively, in 10 $\mu\text{g} / \text{m}^3$ increments of PM₁₀ and fine particulate matter concentrations in 25 cities [9]. In another study conducted with this method, Stieb et al. (2009) reported that cardiovascular and respiratory diseases were associated with gas and particulate matter concentrations for emergency department visits in 7 cities in Canada [10]. For PM₁₀ and PM_{2.5} increases, asthma showed that hospital applications increased 3-4 times a year. In Turkey, studies conducted in Erzincan between 2015 - 2016 and in Istanbul between 2013-2014, increase in PM₁₀ level of 10 $\mu\text{g} / \text{m}^3$ cause increase in respiratory disease by 2.57% and 1.17%, respectively [11,12].

In Erzincan, it was found that the frequency of referrals increased 2.88% for males and 2.33% for females, and 1.17% for males and 1.16% for females in Istanbul. In our study, two-year time series analysis in 2016-2017 found that the increase in PM₁₀ every 10 $\mu\text{g} / \text{m}^3$ increased the frequency of respiratory complaints by 1.05% in total, which was 1.14% for males and 0.97% for females.

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People with cardiac or pulmonary disease, such as asthma, COPD and heart disease, are at increased risk of premature death or emergency room visits when exposed to PM. The elderly are susceptible to PM exposure. This group is more vulnerable to risks such as admission to hospitals or emergency services and premature death from heart and lung disease [13]. In studies in Turkey, the risk of hospital admissions increased in age 65 and over and 15-34 in Erzincan, age group 0-14 have been found to be in Istanbul [11,12]. In our study, it was determined that the highest increase in hospital admission in men is in the 35-44 age group, the highest increase in women is in the group above 65 years and the highest increase in the total is in the group of 35-44 years.

Although we could not differentiate whether the application from an outpatient clinic or emergency department according to data of health ministry, this was the lack of the study, there is a significant correlation between the outpatient clinics and emergency department so it is possible to say that emergency applications have a significant increase within 10 days after the day of air pollution.

It is understood that the increase in hospital admissions during the two year period in which our study was carried out in january-march was due to the fact that fossil fuels were more used in İzmir due to the cold in these months and therefore PM10 concentrations in the air were measured higher(Figure 3).

As we know, exposure to air pollution can trigger new asthma events, exacerbate a pre-existing respiratory illness, and provoke lung cancer, chronic obstructive pulmonary disease development or progress. Air pollutants also affect the development of the lung negatively, creating an additional risk factor for the development of lung diseases in later life. In our study, an increase in the frequency of chronic rhinitis and bronchiectasis in males was also found.

Studies investigating the effects of air pollution on hospital admissions have found an increase in

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hospital admissions for asthma and chronic obstructive pulmonary disease (COPD) aged 65 years and over due to the increase in PM10 levels [14,15]. In a study conducted in Düzce in 2009, it was determined that the PM10 concentration above 100 µg / m³ was not associated with the rates of COPD and asthma and the rates of emergency service admission. In the same study, it was found that emergency admissions increased in COPD patients in winter in elderly (65 years and older) men, asthmatic patients in elderly (65 years and older) women in autumn [16]. In the study in Erzincan, the riskiest group was found to have acute bronchitis in both genders [11]. In our study, the riskiest group was found to have chronic rhinitis in men, bronchiectasis, and asthma in women. Coal fumes contribute to air pollution with NO_x, SO₂, PM, and ozone. Exposure to fine particulates (PM_{2,5}) at specific levels for a long time can lead to COPD. According to a recent systematic screening and meta-analysis, exposure to a concentration of total suspended solids greater than 200 µg / m³, 1.33 fold increase in COPD cases, and exposure to high levels of PM, causing an 11% increase in the incidence [17]. Asthma is an important respiratory disease and can be triggered by air pollution. PM is also known to exacerbate asthma symptoms and is also suspected of having a role in the development of asthma[18]. In the same way in our country, studies are supporting this data [11,12,19,20]. In our study, the increase in each 10 µg / m³ of PM10 level was found to increase hospital admission 2.23% in men over 65 and 2.19% in women in COPD, 2.56% in men over 65 and 2,53% in women in asthma, respectively.

Especially the diagnoses other than URTI (chronic rhinitis, asthma, COPD) increase with the increase in PM10 levels between 1-4th days. The acute effects of air pollution as well as the chronic effects negatively affect the health of the lungs.

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Studies showing a causal relationship between current levels of air pollution and morbidity/mortality have proved that the problem is vital for public health. Based on the results of the assessment of Austria, France, and Switzerland, mortality, chronic bronchitis incidence, hospital admissions, acute bronchitis among children, days of limited activity, asthma attacks are attributable to air pollution. The effect of smoking, environmental tobacco smoke and air pollution on chronic cough/sputum prevalence has been determined. Despite all methodological differences, studies of impact assessment demonstrate that public health benefits greatly from better air quality [21]. Our study is also an impact assessment study, and because of the lack of data, mortality has not been studied but the increase in the number of both acute and chronic respiratory disease cases by 1%, as expected in 2-year hospital admission, suggests that air pollution will cause an increase in hospital admissions in the future as well.

As a result; there was a significant increase in respiratory diseases during the days when the PM10 level which is an air pollutant was high in the two-year period in İzmir province, and this was seen as the URTI and acute bronchitis in the young group and chronic respiratory diseases in the elderly group in the hospital emergency and outpatient clinics. The number of days when air monitoring station data exceeded the PM10 averages of $50 \mu\text{g} / \text{m}^3$ were 155 in this period. Nearly one fifth of the year, PM10 can be said to be more than $50 \mu\text{g} / \text{m}^3$. This means that people living in İzmir have to breath dirty air once in 5 days. It is obvious that İzmir, which has taken migration rapidly in recent years, will become more polluted if the measures are not taken.

PM10 can be considered as a measure of air pollution and every $10 \mu\text{g} / \text{m}^3$ increase in İzmir leads to a 3% increase in the number of hospital admissions in the active working group.

The reduction of air pollutants and inhalation of clean air through is the most important effect in providing a healthier and longer life. Although it is recommended that patients with respiratory

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diseases do not go out on days when the air is dirty, especially in the winter months, the important thing is that the air is not polluted.

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Conflict of Interest: The authors declare no potential conflicts of interest

Ethical approval: All procedures performed in studies involving human participants were under the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study was conducted according to good clinical practice and the Declaration of Helsinki. The study was approved by the local ethics committee of Training and Research Hospital

Informed consent: Patient approval was not required. Information obtained from the registration data.

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Table- 1 Male and female numbers and ratios according to diagnosis in hospital applications in 2016-2017

OUTPATIENT CLINIC	Male (%)	Female(%)	Total(%)
URTI (J00-J11)	1672946(54,5)	1644680(52,7)	3.317.626(53,6)
PNEUMONIA (J15-J18)	25290(0,8)	23949(0,77)	49.239(0,8)
Acute Bronchitis (J20-J22)	403518(13,1)	383054(12,9)	786.572(12,7)
Chronic rhinitis (J30-J34)	259506(8, 5)	367893 (11,8)	627.399(10,1)
COPD (J41-J44)	316577(10,3)	131739(4,2)	448.316(7,2)
ASTHMA (J45,J46)	159250(5,2)	299112 (9,6)	458.362(7,4)
BRONCHIECTASIS	6338(0,2)	7144(0,2)	13.482(0,2)

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(J47)			
COUGH (R05)	124826(4,1)	141616(4,5)	266.442(4,3)
DISPNEA (R06)	103778(3,4)	120112(3,9)	223.890(3,6)
TOTAL	3072029	3119299	6.191.328

Table- 2 Diagnosis and rates according to age in hospital applications in 2016-2017

Diagnosis	0-14	15-34	35-44	45-64	65+	TOTAL
ÜRTİ	1646447(%49,6)	817156(%24,6)	317918(%9,6)	393791(%11,9)	142314(%4,3)	3.317.626
%	68,4	66,0	51,6	34,1	18,4	53,6
Pneumonia	6516(%13,2)	5299(%10,8)	4684(%9,5)	13750(%27,9)	18990(%38,6)	49239
%	0,3	0,4	0,8	1,2	2,5	0,8
A.Bronchitis	383072(%48,7)	98688(%12,5)	66205(%8,4)	143319(%18,2)	95288(%12,1)	786572
%	15,9	8,0	10,7	12,4	12,4	12,7
Chronic rhinitis	161820(%25,8)	167394(%26,7)	92901(%14,8)	149203(%23,8)	56081(%8,9)	627399
%	6,7	13,5	15,1	12,9	7,3	10,1
COPD	2322(%0,5)	8883(%2,0)	20809(%4,6)	172006 (38,4)	244296(%54,5)	448316
%	0,1	0,7	3,4	14,9	31,7	7,2
Asthma	111439(%24,3)	66827(%14,6)	61458(%13,4)	143330(31,3)	75308(%16,4)	458362
%	4,6	5,4	10,0	12,4	9,8	7,4
Bronchiectasıs	181(%1,3)	2035(%15,1)	2111(%15,7)	5342(%39,6)	3813(%28,3)	13482
%	0,0	0,2	0,3	0,5	0,5	0,2
Cough	86868(%32,6)	41540(%15,6)	27502(%10,3)	66060(%24,8)	44472(%16,7)	266442
%	3,6	3,4	4,5	5,7	5,8	4,3
Dyspnea	9860(%4,4)	30986(%13,8)	22906(%10,2)	69138(%30,9)	91000(%40,6)	223890
%	0,4	2,5	3,7	6,0	11,8	3,6
TOTAL	2408525(38,9)	1238808(%20,)	616494(%10)	1155939(18,7)	771562(%12,5)	6191328

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Table-3 Number of days when the air measuring station data exceeds the PM10 average of 20,30,40, 50,100 and 150 $\mu\text{g} / \text{m}^3$ between 1.1.2016-31.12.2017.

PM10 level	Number of days L
>20 $\mu\text{g}/\text{m}^3$	597 (% 85,4)
>30 $\mu\text{g}/\text{m}^3$	393 (% 56,2)
>40 $\mu\text{g}/\text{m}^3$	254 (% 36,3)
>50 $\mu\text{g}/\text{m}^3$	155 (% 22,1)
>100 $\mu\text{g}/\text{m}^3$	28 (% 4)
>150 $\mu\text{g}/\text{m}^3$	3 (% 0,4)

Table- 4 Number of patients associated with each 10 $\mu\text{g} / \text{m}^3$.increase in PM10 level according to gender and age groups

AGE group	Male	Female	TOTAL
0-14	6048	4301	10349
15-34	4020	3148	7168
35-44	14179	4199	18378
45-64	4723	11214	15937
65 and over	5921	7292	13213
TOTAL	34891	30154	65045

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Table- 5: Percentage increase in the number of hospital admissions associated with each 10 µg / m³.increase in PM10 level by sex and age groups

AGE	MALE	FEMALE	TOTAL
0-14	0,45	0,40	0,43
15-34	0,66	0,50	0,58
35-44	5,55	1,16	2,98
45-64	0,97	1,67	1,38
65 and over	1,54	1,89	1,71
TOTAL	1,14	0,97	1,05

Table-6 Distribution of the rate of hospital referral rates associated with a 10 µg / m³.increase at each PM10 level by diagnosis and sex.

Group at risk	Male	Female	TOTAL
URTI	0,45	0,44	0,45
PNEUMONIA	2,85	0,20	1,56
Acute Bronchitis	0,28	0,26	0,27
Chronic rhinitis	6,22	1,69	3,56
COPD	1,70	1,99	1,78
ASTHMA	1,53	2,53	2,18
BRONCHIECTASIS	2,62	2,69	2,66
COUGH	0,84	1,58	1,23
DYSPNEA	0,31	2,49	1,48
TOTAL	1,14	0,97	1,05

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Figure 1: Sex distribution according to age groups of outpatient polyclinics

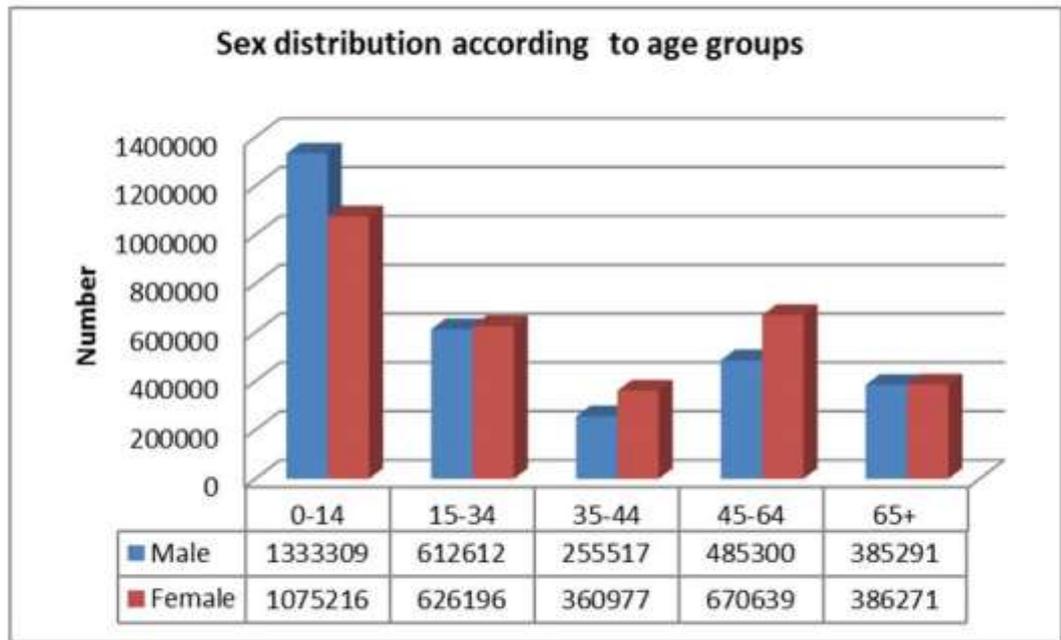


Figure 2: Temporal change of total number of applications per day in Izmir between 2016-2017

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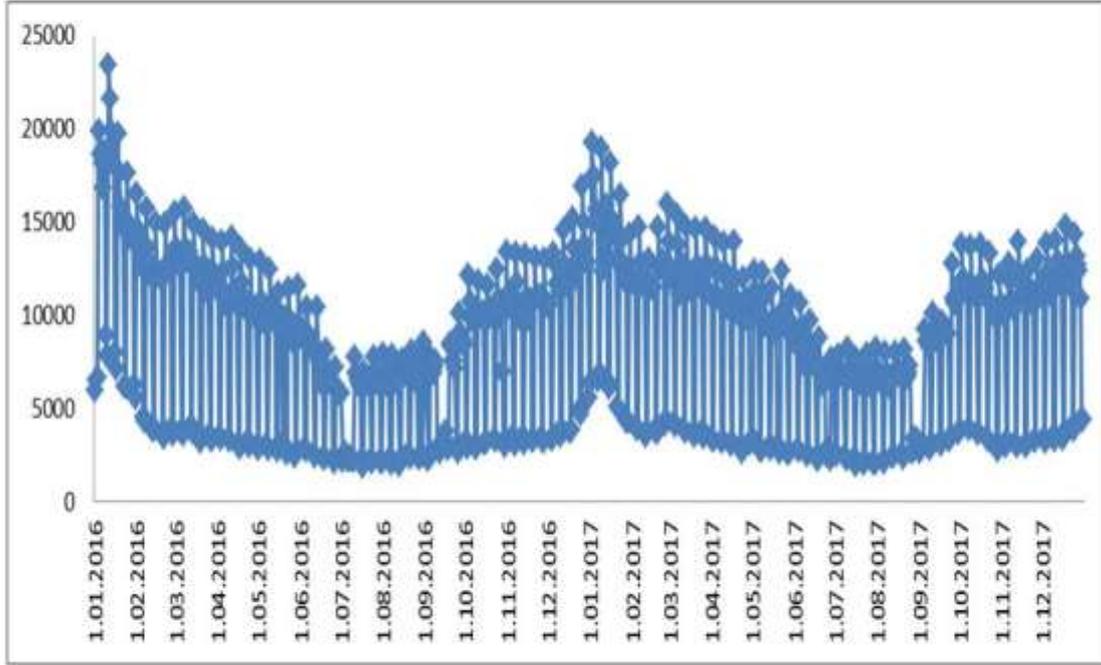
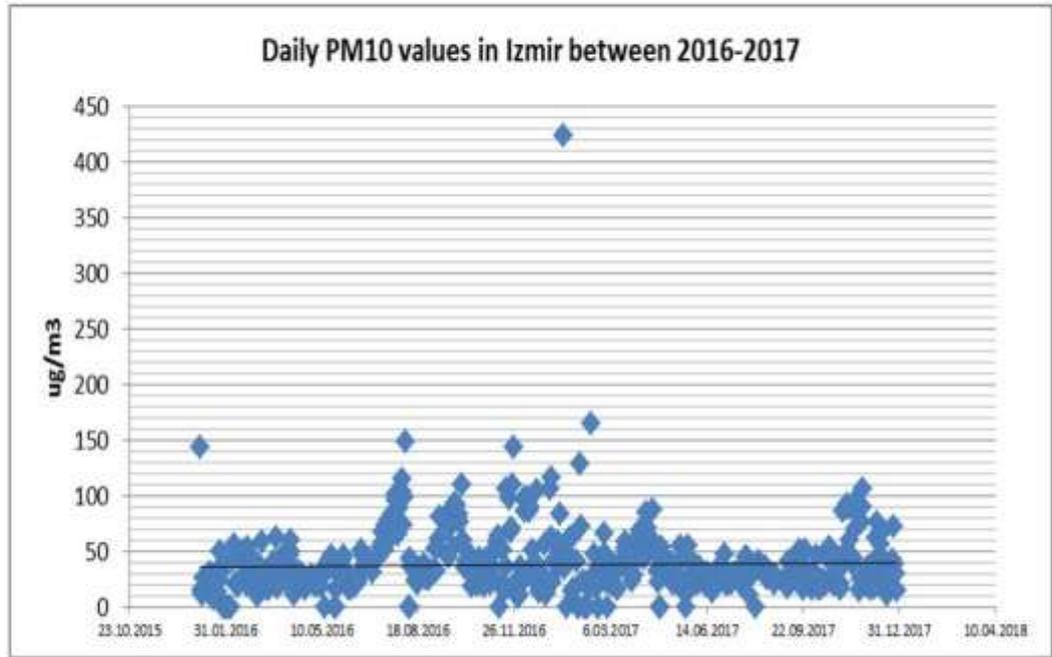


Figure-3 Daily PM10 values between 2016-2017 in Izmir(μ/m^3)

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