Original Article

TANAFFOS

Effects of Chlorine Gas Exposure and Associated Factors on Spirometric Parameters in Detergent Industry Workers: a Four-Year Cross-Sectional Study

Farhad Malek [1], Amir Shomali [1], Majid Mirmohammadkhani [2,3], Kamyar Mansori [4], Daryoush Pahlevan [5]

[1] Department of Internal Medicine, Kosar Hospital, Semnan University of Medical Sciences, Semnan, Iran, [2] Social Determinants of Health Research Center, Semnan University of Medical Sciences, Semnan, Iran, [3] Department of Epidemiology and Biostatistics, Semnan University of Medical Sciences, Semnan, Iran., [4] Department of Biostatistics and Epidemiology, School of Medicine , Zanjan University of Medical Sciences, Zanjan, Iran, [5] Department of Community Medicine, School of Medicine , Social Determinants of Health Research Center, Semnan University of Medical Sciences, Semnan, Iran.

Correspondence to: Pahlevan D
Address: Department of Community Medicine, School of Medicine , Social Determinants of Health Research Center, Semnan University of Medical Sciences, Semnan, Iran
Email address: pahlevandaryoush@gmail.com

Background: This study aimed to determine the effects of chlorine gas exposure and the associated factors on spirometric parameters among detergent industry workers in Semnan, Iran.

Materials and Methods: This four-year cross-sectional study was concocted on 100 workers of two detergent factories in Semnan, Iran. Two questionnaires were used for data collection. The first questionnaire included demographic and occupational information, and the second questionnaire included spirometric parameters, such as forced vital capacity (FVC), forced expiratory volume in one second (FEV1), FEV1/FVC ratio, peak expiratory flow (PEF), and PEF 25-75%. The spirometric parameters were measured over four consecutive years by a trained technician. Next, to determine the effects of chlorine gas exposure and its associated factors on spirometric parameters, a generalized estimating equation (GEE) model was used. The correlation structure of GEE was considered to be autoregressive 1 (AR-1). Analyses were performed in STATA version 14.

Results: All spirometric parameters showed a decreasing trend during 2012-2015. The GEE model showed a significant association between chlorine gas exposure and all spirometric parameters; the beta-coefficients for the effect of exposure (year) on FVC, FEV1, FEV1/FVC ratio, PEF, and PEF 25-75% were -4.51, -6.46, -4.27, -6.09, and -10.29, respectively. Also, this model demonstrated a significant association between smoking and FEV1, PEF, and PEF 25-75%; the beta-coefficients for the effect of smoking on these parameters were -5.64, -8.88, and -5.75, respectively. Additionally, the GGE model showed a significant association between the body mass index (BMI) and FVC and FEV1 ($P < 0.05$); the beta-coefficients for the effect of BMI on these two parameters were - 0.59 and -0.48, respectively.

Conclusion: The spirometric parameters showed a decreasing trend over time among detergent industry workers; this decline was more remarkable among individuals with a history of smoking. Therefore, it seems necessary to implement screening programs and periodic active examinations for these workers.

Key words: Chlorine gas; Spirometric parameters; Detergent industry; Worker; Longitudinal study; Iran

INTRODUCTION

Occupational diseases, as defined by the World Health Organization (WHO), are diseases that are primarily contracted as a result of exposure to risk factors associated with work activities. Although these diseases have a lower incidence as compared to other debilitating disorders, studies show that a significant proportion of people are affected by these diseases, especially in industrial areas. The International Labor Organization (ILO) reported that about 2.78 million workers die annually due to work-related disorders worldwide, which is more than twice the rate of road accident and war mortalities (1-3).

Among work-related disorders, respiratory diseases are the most common occupational diseases with an increasing trend, accounting for 17% of all deaths from occupational diseases (1, 4). Among workers of various industries, workers exposed to gases and chemical vapors, particularly chlorine, are at a greater risk of respiratory diseases (4-6). Toxicology of chlorine is almost entirely related to the effects of this substance on the respiratory system. Symptoms of chlorine poisoning are similar in humans and animals and range from simple respiratory irritations, spasms, bronchoconstriction, and bronchial or alveolar injuries to acute and chronic respiratory diseases (7, 8).

Although there is a high chance of recovery after termination of chlorine exposure and timely diagnosis and treatment, severe and prolonged exposure may lead to permanent and irreversible damages to pulmonary function (7, 9). In humans, chlorine concentrations ≤10 ppm can enter the lower respiratory tract by breaking the defense system of the upper respiratory tract (10, 11). Various studies have reported complications, such as shortness of breath, irregular breathing, irregular heartbeats, obstructive ventilatory impairment, reactive upper airway dysfunction syndrome (RADS), and decreased lung residual volume after exposure to chlorine (12-14).

Considering the abovementioned complications, screening tests are necessary for assessing the lung health of workers, especially those exposed to chlorine. Today, there are various screening tests for work-related pulmonary disorders. Among these tests, spirometry, due to high accuracy, easy access, and low cost, is the most appropriate test to measure the pulmonary function of workers in different industries (10, 15). Conventional spirometry devices measure more than 20 different respiratory variables, the most valuable of which are forced vital capacity (FVC), forced expiratiory volume in one second (FEV1), and FVC/ FEV1 ratio (16). Spirometry, if performed regularly among workers exposed to respiratory pollutants, can show pulmonary dysfunctions before the onset of clinical symptoms and abnormal findings on chest imaging (17).

Given the importance of workers' health in a country's industrial progress and production, besides limited studies on the effects of chlorine exposure on Iranian workers' pulmonary function, this longitudinal study aimed to investigate the effects of chlorine exposure and the associated factors on spirometric parameters among industrial workers in Semnan, Iran.

MATERIALS AND METHODS
Study design and sample

In this four-year cross-sectional study, all workers of two factories in an industrial town were examined from July 2012 to July 2015. For the selection of factories, first, all factories with chlorine as the main material in the production process were determined (six factories), and then, two factories were randomly selected; both factories manufactured washing materials. The inclusion criteria were as follows: working in one of the factories during the study; having at least four years of work experience; having an acceptable respiratory function at the time of entering the study (2012); and being involved in the production process.

On the other hand, the exclusion criteria were as follows: contraindications to spirometry (cardiac arrest and chest pain in the past six weeks, active bloody sputum, uncontrolled hypertension, and flu in the past three days);

having a respiratory disease (asthma, rhinitis, bronchitis, and emphysema), a chest injury or surgery; working in other factories with exposure to other harmful materials; and addiction to any type of opium. Of 137 workers of the factories, 37 were excluded from the study, and a total of 100 subjects were finally examined.

Data collection

The pulmonary function was evaluated using a calibrated spirometer (Spirolab II, Via Del Maggiolino, 125, 00153, Rome, Italy). The spirometric parameters included the FVC, FEV1, peak expiratory flow (PEF), PEF occurring in the middle 50% of the patient's exhaled volume PEF (PEF 25-75%), and FEV1/FVC ratio. Spirometry was performed by an instructed technician under the supervision of a specialist in the first and last hours of shiftwork in the factories, based on the America Thoracic Society (ATS) criteria.

The spirometer was calibrated twice every day by the technician, according to the manufacturer's instructions. Based on the subject's height, age, and gender, the mean percentage of the predicted value for each spirometric index was calculated and reported. Before spirometry, essential instructions related to the test method and maneuvers were thoroughly given to the workers, and they were asked not to smoke or eat a heavy meal at least one hour before the test.

For spirometry, the subjects were asked to stand for five minutes, and then, special clips were placed on their noses in a comfortable standing position. For each subject, three acceptable maneuvers were performed, and if a difference was observed in the FVC values (>5%), the test was repeated up to eight times to obtain the best volume, based on the predicted percentage for pulmonary function. In this study, the predicted percentage for pulmonary function was the measured capacity by spirometry, divided by the anticipated capacity (according to gender, age, height, and race) in spirometry and multiplied by 100. Besides, chlorine gas in the workstation was measured using gas sampling pumps and gas chromatography and then compared with the threshold limit value (TLV).

Two questionnaires were used for data collection. The first questionnaire consisted of demographic and occupational information, including age, gender, body mass index (BMI), work history in the factory, smoking, medical history, and type of used mask, and the second one consisted of spirometric parameters, including FVC, FEV1, FEV1/FVC, PEF, and PEF 25-75%.

Statistical analysis

For descriptive analyses, the frequency (%) of the participants' demographic and occupational characteristics was reported. For analytical tests, a generalized estimating equation (GEE) model was employed to investigate changes in spirometric indices over time (four years). The dependent variables were spirometric parameters, and the dependent variable was exposure to chlorine gas among workers. The analyses were adjusted for age, BMI, medical history, smoking, and work experience in the factory. The correlation structure of GEE model was considered to be autoregressive 1 (AR-1). All analyses were performed in STATA version 14.

Ethical considerations

Before data collection, the study objectives were explained to the workers, and then, informed consent was obtained from each participant. Also, this study was performed according to the principles of the Declaration of Helsinki and approved by the Deputy of Research and Ethics Committee of Semnan University of Medical Sciences, Semnan, Iran.

RESULTS

This study was conducted on 100 workers of two factories in an industrial town in Semnan Province. Ninety-seven out of 100 participants were male in this study. The chlorine concentration was 3.8 and 3.4 ppm in the two factories, respectively, and the difference was not statistically significant (P>0.426). The mean (±SD) age of the participants was 34.8±7.44 years, ranging from 25 to 65 years. The age of the majority of participants ranged from 25 to 35 years. The mean (±SD) work experience of workers was 7.62±4.40 years, ranging from 1 to 25 years. Table 1

presents other demographic and occupational characteristics of the participants. Also, 88 (88%) subjects reported no history of smoking (Table 1).

Table 1. Demographic and Occupational Characteristics of Participants

Variable		Number (%)
Sex	Female	3 (3)
	Male	97 (97)
Age (Year)	25-35	58 (58)
	35-45	32 (32)
	45-55	8 (8)
	55-65	2 (2)
Body Mass Index (Kg/M2)	>=25	47 (47)
	<25	53 (53)
Smoking	Yes	12 (12)
	No	88 (88)
Job History	Yes	37 (37)
	No	63 (63)
Medical History	Yes	17 (17)
	No	83 (83)
Exposed to Chlorine Gas	Yes	80 (80)
	No	20 (20)

Table 2 presents the mean (SD) and minimum and maximum values of spirometric parameters according to

year (2012-2015). The mean FVC was 96.75 (95% UI: 93.94-99.55) and 83.37 (95% UI: 82.34-84.39) in 2012 and 2015, respectively. Also, the mean FEV1 was 95.19 (95% UI: 92.33-98.04) and 76.27 (95% UI: 75.41-77.12) in 2012 and 2015, respectively. The corresponding FEV1/FVC ratios were 81.99 (95% UI: 80.72-83.27) and 69.52 (95% UI: 68.75-70.28), respectively. Besides, the mean PEF and PEF 25-75% were 97.30 (95% UI: 93.13-100.0) and 85.46 (95% UI: 81.14-89.79) in 2012, respectively. The corresponding values were 78.74 (95% UI: 77.22-80.25) and 56.12 (95% UI: 54.62-57.61) in 2015, respectively.

Table 3 shows the results of the GEE model, used to determine the influential factors in the mean changes of spirometric parameters during 2012-2015. As can be seen, the beta-coefficient for the effect of year on FVC, FEV1, FEV1/FVC, PEF, and PEF 25-75% was -4.51, -6.46, -4.27, -6.09, and -10.29, respectively; in other words, with each year increase in exposure to chlorine gas, the values of FVC, FEV1, FEV1/FVC ratio, PEF, and PEF 25-75% decreased by 4.51, 6.46, 4.27, 6.09, and 10.29 units, respectively; these changes were statistically significant. Other related information is presented in Table 3.

Table 2. Mean (S.D) , Minimum and Maximum of Spirometric Parameters by Year

Parameters	Year	Number	Mean	S.D*	Minimum	Maximum
FVC	2012	100	95.75	14.13	45	137
	2013	100	93.20	9.09	70	111
	2014	100	85.86	6.22	70	98
	2015	100	83.37	5.17	71	96
FEV1	2012	100	95.19	14.37	38	136
	2013	100	88.25	7.30	71	102
	2014	100	80.51	4.38	68	89
	2015	100	76.27	4.31	60	84
FEV1/ FVC	2012	100	81.99	6.42	60.80	103
	2013	100	77.80	4.85	68	97
	2014	100	72.19	4.83	63	87
	2015	100	69.52	3.84	63	80
PEF	2012	100	97.30	19.92	28	168
	2013	100	87.56	10.99	60	110
	2014	100	82.37	9.49	60	105
	2015	100	78.74	7.62	60	96
PEF (25-75 %)	2012	100	85.46	21.57	26	132
	2013	100	79.75	9.14	52	96
	2014	100	62.75	9.43	46	85
	2015	100	56.12	7.51	43	72

Table 3. Determination of the Effective Factors on Mean Changes of Spirometric Parameters by 2012 -2015 (Generalized Estimating Equations)

| Variable	FVC		FEV1		FEV1/ FVC		PEF		PEF (25-75 %)	
	β-Coefficient	*P	β-Coefficient	P	β-Coefficient	P	β-Coefficient	P	β-Coefficient	P
Exposure (Year)	-4.51 (-5.28- -3.73)**	<0.001	-6.36 (-7.18- -5.55)	<0.001	-4.27 (-4.72- -3.82)	<0.001	-6.09 (-7.36- -4.81)	<0.001	-10.29 (-11.63- -8.95)	<0.001
Age	0.01 (-0.18- 0.21)	0.859	0.03 (-0.14- 0.22)	0.685	-0.03 (-0.11- 0.04)	0.378	-0.23 (-0.51- 0.05)	0.110	0.04 (-0.21- 0.29)	0.748
BMI	-0.59 (-0.98- -0.20)	0.003	-0.48 (-0.86- -0.11)	0.011	0.02 (-0.13- 0.18)	0.787	-0.25 (-0.69- 0.18)	0.249	-0.07 (-0.55- 0.39)	0.753
Work History	0.10 (-0.29- 0.50)	0.603	0.21 (-0.15- 0.59)	0.254	-0.005 (-0.14- 0.13)	0.942	0.43 (-0.01- 0.89)	0.059	0.01 (-0.36- 0.40)	0.931
Smoking	-4.17 (-9.48- 1.12)	0.123	-5.64 (-9.70- -1.57)	0.007	-1.49 (-3.63- 0.64)	0.171	-8.88 (-14.58- -3.19)	0.002	-5.75 (-11.06- -0.43)	0.034
Medical History	-.46 (-4.08- 3.15)	0.802	-0.006 (-2.90- 2.89)	0.996	1.12 (-0.36- 2.62)	0.138	3.63 (-0.65- 7.92)	0.096	1.04 (-2.46 - 4.55)	0.560
Use of Masks	-1.94 (-5.15- 1.26)	0.236	-1.88 (-4.53- 0.77)	0.165	-0.35 (-0.79- 1.50)	0.544	-1.05 (-4.56- 2.45)	0.557	-0.50 (-4.08- 3.07)	0.783

* P : P-Value

**:%95 Confidence Interval

Moreover, the results of the GEE model, after adjusting for potential confounding variables, demonstrated an inverse relationship between smoking and FEV1, PEF, and PEF 25-75% (P<0.05). The beta-coefficient for the effect of smoking on these parameters was -5.64, -8.88, and -5.75, respectively; in other words, the values of FEV1, PEF, and PEF 25-75% in smoking workers were 5.64, 8.88, and 5.75 units lower than non-smokers, respectively. Besides, the GGE model showed an inverse relationship between BMI and FVC and FEV1 (P<0.05). The beta-coefficient for the effect of BMI on these parameters was - 0.59 and -0.48, respectively, that is, with every one unit increase in BMI, the values of FVC and FEV1 decreased by -0.59 and -0.48 units, respectively (Table 3).

Finally, the GEE model showed that the beta-coefficients for the effect of mask use on FVC, FEV1, FEV1/FVC ratio, PEF, and PEF 25-75% were -1.94, -1.88, -0.35, -1.05, and -0.50, respectively. In other words, the FVC, FEV1, FEV1/FVC ratio, PEF, and PEF 25-75% were 1.94, 1.88, 0.35, 1.05, and 0.50 units lower in people who did not use a mask compared to those who used a mask, respectively; however, the differences were not statistically significant (P>0.05). Other variables did not show a significant relationship with these parameters (Table 3).

Figure 1 shows the trend of spirometric parameters during 2012-2015. As can be seen, all spirometric parameters, including FVC, FEV1, FEV1/FVC ratio, PEF, and PEF 25-75%, decreased over time.
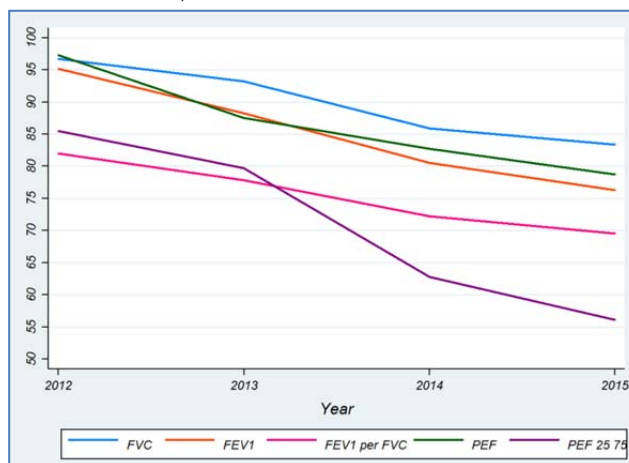
Figure 1. The Trend of Spirometric Parameters by Type of Parameter

DISCUSSION

The risk of chlorine gas inhalation is particularly important in industrial workers, because the adverse effects of exposure to this gas are severe and can lead to acute pneumonia, pulmonary edema, and transient bronchospasm if inhaled. This study aimed to determine

the effects of chlorine exposure and the associated factors on spirometric parameters among industrial workers in Semnan, Iran during 2012-2015. The results indicated that all spirometric parameters had a decreasing trend during 2012-2015. The GEE model showed a significant association between exposure to chlorine gas and all spirometric parameters. Based on the results, FVC, FEV1, FEV1/FVC ratio, PEF, and PEF 25-75% decreased by 4.51, 6.46, 4.27, 6.09, and 10.29 units, respectively.

Various studies have investigated the risk of chlorine inhalation in industrial workers. In these studies, spirometry has been one of the most common tools to evaluate pulmonary function. The results of these studies are consistent with the findings of our study. In this regard, a study by Neghab et al. demonstrated that the mean FVC, FVC/FEV1 ratio, and PEF were significantly lower in the exposed group as compared to the unexposed group (18). Also, in a longitudinal study by Gautrin et al., investigating changes in spirometric parameters and the associated factors in workers exposed to chlorine gas, the findings showed that the FVC, FEV1, FEV1/FVC ratio, PEF, and PEF 25-75% were significantly reduced over time (19).

In another study from South Carolina, USA, evaluating the pulmonary function before and after a large chlorine gas release, researchers observed a significant reduction in the mean FEV1 and FEV1/FVC ratio over time following exposure to chlorine gas (20). Also, Medina-Ramón et al. showed that the incidence of lung lesions in female cleaning workers increased due to exposure to liquid chlorinated bleach (21). Moreover, Drobnic et al. studied the effects of low concentrations of chlorine on swimmers during exercise and reported the symptoms of asthma and airway hyperresponsiveness to a smaller degree (22). Even in other industries, such as poultry, the rates of respiratory disorders and eye irritations were significantly higher in workers due to exposure to chloramine, and the pulmonary function parameters significantly reduced during shift work (23).

It can be concluded that long-term exposure to chlorine gas, even at low concentrations, can cause a decrease in spirometric parameters and lead to chronic lung diseases over time. The obtained results highlight the importance of implementing engineering control measures to reduce the concentrations of chlorine gas in different industries. Besides, by performing screening and active periodic examinations before confirming the effects of chlorine gas, individuals susceptible to chlorine gas complications must be identified, and appropriate intervention measures must be taken.

In this study, a significant association was found between smoking and spirometric parameters, including FEV1, PEF, and PEF 25-75%; in other words, FEV1, PEF, and PEF 25-75% in smoking workers were 5.64, 8.88, and 5.75 units lower than non-smokers, respectively. Similarly, Das and Blanc reported that in smokers or people with a chronic lung disease, functional lung injuries occurred more rapidly when exposed to chlorine (24). Similarly, Clark et al. showed that a history of smoking was associated with a greater reduction in FEV1 and FVC following exposure to chlorine (20). It seems that smoking and exposure to chlorine have a multiplicative interaction in pulmonary function and significantly increase or aggravate pulmonary lesions caused by chlorine gas (20). Since smoking, even in small amounts, can cause different respiratory disorders in these workers, design and implementation of smoking cessation programs, especially in workers exposed to chlorine gas, seem essential.

Moreover, the present results showed an inverse relationship between BMI and FVC and FEV1 (P<0.05); in other words, with every one unit increase in BMI, the values of FVC and FEV1 decreased by -0.59 and -0.48 units, respectively. These results are consistent with the findings of various previous studies. A study by Banerjee et al., determining the correlation between BMI and pulmonary function parameters in non-asthmatic individuals, showed an inverse relationship between BMI and spirometric parameters, including FEV1 (r=-0.531, P=0.009), FEF 25-75% (r=-0.653, P=0.001), and FEV1/FVC ratio (r=-0.603, P=0.002)] (25). Similarity, in another study by Bhatti et al., an inverse relationship was observed between BMI and

spirometric parameters (26). Therefore, regular screening programs, with lifestyle modification and weight control, are recommended for overweight and obese workers.

Finally, the results of the present study indicated that the FVC, FEV1, FEV1/FVC ratio, PEF, and PEF 25-75% were 1.94, 1.88, 0.35, 1.05, and 0.50 units lower in people who did not use masks as compared to those who did, respectively; however, the differences were not statistically significant (P>0.05), which might be due to the small sample size. Nonetheless, the use of mask as a protective device should be considered in high-risk occupations. It is also recommended to conduct further studies on a larger sample size to determine the effects of mask on these parameters more accurately.

This study has several strengths and limitations. To the best of our knowledge, this is the first longitudinal study from Iran, investigating the effect of chlorine gas exposure on the pulmonary function of detergent industry workers over four consecutive years. On the other hand, this study has several limitations that should be considered when interpreting the results. First, since spirometry was performed annually, it was not possible to study acute and transient changes due to chlorine gas exposure. Second, workers might have been exposed to chlorine gas and other chemicals affecting the spirometric parameters (e.g., outside the workplace), and it was not possible to control these environmental and occupational parameters; this issue was not considered in the results of this study. Therefore, design and implementation of occupational cohort studies with a larger sample size are recommended.

In conclusion, the results of the present study showed that all spirometric parameters (FVC, FEV1, FVC/FEV1 ratio, PEF, and PEF 25-75%) decreased dramatically over a four-year period among detergent industry workers; this decline was more significant in workers with a history of smoking. Therefore, it seems necessary to implement engineering control measures to reduce the concentration of chlorine gas. Also, screening and periodic active examinations are essential before confirming the effects of chlorine gas on different industrial workers, especially detergent industry workers.

Conflict of Interest

The authors declare no conflicts of interest.

REFERENCES

1. World Gastroenterology Organisation. World Gastroenterology Organisation Global Guideline: Helicobacter pylori in developing countries. *J Clin Gastroenterol* 2011;45(5):383-8.

2. Buchan J, Couper ID, Tangcharoensathien V, Thepannya K, Jaskiewicz W, Perfilieva G, et al. Early implementation of WHO recommendations for the retention of health workers in remote and rural areas. *Bull World Health Organ* 2013;91(11):834-40.

3. Hakimi A, Valavi E, Madhushimazrae S, Latifi M, Dashtbozorge B. The effect of continuous care model on parents' knowledge and controlling symptoms and recurrence in children with nephrotic syndrome. *Journal of Clinical Nursing and Midwifery* 2016;5(2):29-39.

4. Kim EA, Kang SK. Historical review of the List of Occupational Diseases recommended by the International Labour organization (ILO). *Ann Occup Environ Med* 2013;25(1):14.

5. Tsimakuridze M, Saakadze V, Tsereteli M. The characteristic state of health of ammonia nitrate producing workers. *Georgian Med News* 2005;(122):80-3.

6. Rahman MH, Bråtveit M, Moen BE. Exposure to ammonia and acute respiratory effects in a urea fertilizer factory. *Int J Occup Environ Health* 2007;13(2):153-9.

7. Medina-Ramón M, Zock JP, Kogevinas M, Sunyer J, Torralba Y, Borrell A, et al. Asthma, chronic bronchitis, and exposure to

irritant agents in occupational domestic cleaning: a nested case-control study. *Occup Environ Med* 2005;62(9):598-606.

8. Lopez V, Chamoux A, Tempier M, Thiel H, Ughetto S, Trousselard M, et al. The long-term effects of occupational exposure to vinyl chloride monomer on microcirculation: a cross-sectional study 15 years after retirement. *BMJ Open* 2013;3(6):e002785.

9. Pokrajac D, Kamber AH, Karasalihovic Z. Children with Steroid-Resistant Nephrotic Syndrome: A Single -Center Experience. *Mater Sociomed* 2018;30(2):84-8.

10. Kyrieleis HA, Löwik MM, Pronk I, Cruysberg HR, Kremer JA, Oyen WJ, et al. Long-term outcome of biopsy-proven, frequently relapsing minimal-change nephrotic syndrome in children. *Clin J Am Soc Nephrol* 2009;4(10):1593-600.

11. Vetrano KM. Molecular chlorine: health and environmental effects. *Rev Environ Contam Toxicol* 2001;170:75-140.

12. Brooks SM, Weiss MA, Bernstein IL. Reactive airways dysfunction syndrome (RADS). Persistent asthma syndrome after high level irritant exposures. *Chest* 1985;88(3):376-84.

13. Malo JL, L'archevêque J, Castellanos L, Lavoie K, Ghezzo H, Maghni K. Long-term outcomes of acute irritant-induced asthma. *Am J Respir Crit Care Med* 2009;179(10):923-8.

14. Shakeri MS, Dick FD, Ayres JG. Which agents cause reactive airways dysfunction syndrome (RADS)? A systematic review. *Occup Med (Lond)* 2008;58(3):205-11.

15. Kawasaki Y, Suzuki J, Nozawa R, Suzuki S, Suzuki H. Prediction of relapse by plasma lipoprotein(a) concentration in children with steroid-sensitive nephrotic syndrome. *Nephron* 2002;92(4):807-11.

16. Fakhouri F, Bocquet N, Taupin P, Presne C, Gagnadoux MF, Landais P, et al. Steroid-sensitive nephrotic syndrome: from childhood to adulthood. *Am J Kidney Dis* 2003;41(3):550-7.

17. Ali A, Ali D, Mehran H, Ali Z. Idiopathic nephrotic syndrome in Iranian children. *Indian Pediatr* 2008;45(1):52-3.

18. Neghab M, Amiri F, Soleimani E, Hosseini SY. The Effect of Exposure to Low Levels of Chlorine Gas on the Pulmonary Function and Symptoms in a Chloralkali Unit. *J Res Health Sci* 2016;16(1):41-5.

19. Gautrin D, Leroyer C, L'Archevêque J, Dufour JG, Girard D, Malo JL. Cross-sectional assessment of workers with repeated exposure to chlorine over a three year period. *Eur Respir J* 1995;8(12):2046-54.

20. Clark KA, Karmaus WJ, Mohr LC, Cai B, Balte P, Gibson JJ, et al. Lung Function before and after a Large Chlorine Gas Release in Graniteville, South Carolina. *Ann Am Thorac Soc* 2016;13(3):356-63.

21. Medina-Ramón M, Zock JP, Kogevinas M, Sunyer J, Basagaña X, Schwartz J, Burge PS, Moore V, Antó JM. Short-term respiratory effects of cleaning exposures in female domestic cleaners. *Eur Respir J* 2006;27(6):1196-203..

22. Drobnic F, Freixa A, Casan P, Sanchis J, Guardino X. Assessment of chlorine exposure in swimmers during training. *Med Sci Sports Exerc* 1996;28(2):271-4.

23. Lipsitch M, Cohen T, Cooper B, Robins JM, Ma S, James L, et al. Transmission dynamics and control of severe acute respiratory syndrome. *Science* 2003;300(5627):1966-70.

24. Das R, Blanc PD. Chlorine gas exposure and the lung: a review. *Toxicol Ind Health* 1993;9(3):439-55.

25. Banerjee J, Roy A, Singhamahapatra A, Dey PK, Ghosal A, Das A. Association of Body Mass Index (BMI) with Lung Function Parameters in Non-asthmatics Identified by Spirometric Protocols. *J Clin Diagn Res* 2014;8(2):12-4.

26. Bhatti U, Laghari ZA, Syed BM. Effect of Body Mass Index on respiratory parameters: A cross-sectional analytical Study. *Pak J Med Sci* 2019 Nov-Dec;35(6):1724-9.