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Chronic pulmonary complications in Iraq-Kurdistan chemical weapons victims

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Abstract

Aims: The Iraqi government performed numerous chemical attacks against north-west of Iran and Iraq non-military civilians during 1980-88. The aim of this survey was to investigate the long term respiratory complications among chemical injury victims of Iraqi Kurdistan region.

Methods: This cross-sectional descriptive study was performed in year 2008 on Iraqi Kurdish chemical injury victims who were invited by public invitation and 479 eligible patients entered the study by census sampling method. Then, physical examination, spirometry and thoracic high-resolution computed tomography were carried out on patients. Blistering after chemical weapon exposure was used to identify the significant exposure to sulfur mustard and patients were divided into two groups of having blisters and without blisters. Results of the two groups were compared by SPSS 16 software using Kolmogorov-Smirnov test, independent T-test, Fisher's exact test, Chi square test and multivariate regression.

Results: Among 479 participants, 45.7% were male and 54.3% were female. The mean age was 43.1±13.7. Spirometry was abnormal in 15.2% of patients and air trapping was present on CT scan in 46.6% cases and there was no significant difference between patients with blisters (n=278) and without a history of blistering. However, Blistering after chemical weapon exposure associated with more respiratory symptoms and worse lung function especially among Halabja inhabitants.

Conclusion: Iraqi Kurdish chemical injury victims suffer from severe respiratory complications which may reflect the absence of essential preventive training for reduction of contact with chemicals and early treatment after incidents.

Keywords: Chemical Weapon, Long-term Pulmonary Complications, Iraqi Kurdistan, Sulfur Mustard, Halabja, Spirometry

Introduction

During the Iran-Iraq war (1980-1988 AD), a large number of non-military civilians of Iran and Iraq were at the exposure of chemical gases including sulfur mustard during the chemical bombing, which 100 thousands of military and non-military Iranian civilians are suffering from the clinical problems induced by this gas up to now. In this regard, pulmonary disorder is the most common problem [1]. Iraqi Army had attacked Sardasht with 7 bombs of 250 kg with sulfur mustard in June 28, 1987, which 4 bombs were exploded in the central part of the city. From 8025 chemical injuries of this city, 3 thousand people who were at exposure to low doses of sulfur mustard faced with pulmonary complications with low-intensity and were treated as outpatients. 1500 people who were at exposure to higher doses of sulfur mustard faced with pulmonary complications with moderate to severe intensity that required hospitalization. Iraq employed chemical weapons in northern Kurdistan, between Iran and Iraq' borders when confronting with its people, which about 299 Kurdish cities and villages were attacked during the Al-anfal operation. The sad event of Halabja happened in March 17, 1988 [2]. Most people died in the early minutes after exploding the bomb and those who were saved had injured while they were crossing the road [3].

Chemical agents used by Iraq are divided into two main categories according to chemical composition and their effects. Nerve gases such as Tabun, Sarin, VX gas and tear gas are the main agents that effect on the receptors of muscarinic, nicotine, and the central nerve system, and lead to the paralysis of respiratory muscles and the inhibition of the respiratory center in the medulla oblongata and cause the death of injury with the symptoms of respiratory failure [4]. Mustard agent is an agent with Alkylating agent with the Mutagen and carcinogens effects which causes the acute symptoms of blisters with exposure to steam or liquid and leads to the defects of respiratory system, eye and skin. Although the mortality caused by it is low, it has a high morbidity [2, 5]. Sulfur mustard can change the structure of nucleic acids, cell membranes, and proteins due to its Alkylating and electrophilic property. After a while of inhaling, the cholinergic property of sulfur mustard causes too much secretion of secrete glands of air Hungarian. The inflammation combined with the mucosal bleeding causes that the

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coughing of injury victims is associated with no blood or blood mucus. Thus, in the acute stage of exposure to sulfur mustard, suffocation and eventually death might occur due to lung failure. The late respiratory complications, despite the tissue injury, immune system and genetic changes caused in lung, can lead to the chronic bronchitis, pulmonary fibrosis, bronchiolitis obliterans, bronchiectasis, asthma and tracheal and main bronchus stenosis [6, 7].

Although many studies had been conducted on the injuries of late pulmonary on Iranian chemical injury victims [2, 8, 9, 10, 11, 12], no study has been done to determine the acute and long-term effects of chemical agents on non-military civilians of Iraqi Kurdistan so far. After two decades of exposure to these individuals with chemical agents, the present study could be the most extensive study on the inhabitants of Iraq chemical areas. In this study, the severity of the caused complications was compared with the available findings from the previous studies on the injury victims of Sardasht, Iran and the possible role of early treatment of patients in early stages of exposure to sulfur mustard in the chemical reduction of late complications was discussed [3, 13].

The aim of this study was to investigate the long term pulmonary complications among chemical injury victims of Iraqi Kurdistan region.

Methods

This cross-sectional study was conducted in late 2008. The subjects of this study were all non-military civilians in the northwest regions of Iraq who were affected by chemical gases during 1983 to 1988. These people were called through radio, television, press, and also an official invitation from the military and government officials. 487 cases of Iraqi-Kurdish chemical injuries were referred for the study that 8 patients were excluded from the statistical analysis due to various causes (one due to infection to rheumatoid arthritis, one due to scleroderma, one due to tuberculosis, one due to chronic bronchiectasis, and 4 patients due to the occupational disease). Thus, 479 patients were selected as the participants of this study by census sampling method. Subjects with physical inability, having jobs with environmental pollution, pulmonary involvement induced by collagen vascular disease, immune deficiency and heart disease, organ transplantation, radiotherapy, chronic thyroiditis, recurrent pulmonary infectious disease, and even the use of drugs such as Phenytoin-Bleomycin, methotrexate or carbamazepine and other known drugs caused to lung disease were excluded from the study.

The necessary information was collected in Sulaymaniyah, Iraq during one week. Physical examination, spirometry and thoracic high-resolution computed tomography were carried out on all injury victims after face to face interview and the completion of the questionnaire and the study of the available evidence indicating an inpatient history in the therapy centers. Then pulmonary lesions induced by chemical agents were investigated in them. All these patients participated in this study with awareness and observing all principles of ethic and medicine. Blistering after the chemical weapon exposure was considered to identify the significant exposure to sulfur mustard. The subjects were divided into two groups of injury victims with blisters (first group) and without blisters (Group B).

The data collection tool was respiratory standard questionnaire (OPCW2002). Two pulmonary specialists visited all Iraqi patients and other respiratory complaints such as cough, hoarseness, wheezing, asthma and other identified pulmonary symptoms were investigated in patients. Spirometry tests and Hyper Resonance pulmonary scan test (HRCT) were done for all patients by an experienced and professional specialist. Spirometry was interpreted according to GOLD criteria [14]. Their pulmonary scan was studied based on age, sex, history of chemical gases exposure, the presence of air retention, broncіectasis, and mosaicity of parenchyma and severity of chronic disease (the similar device had been used for all patients).

Statistical Analysis was done by SPSS 16 software using Kolmogorov-Smirnov test, Chi square test, Fisher's exact test and independent T-test. Multivariate regression method was used to determine the effects of exposure to the chemical agents, age, smoking, and the location of incident on respiratory dysfunction (FEV1). The obtained values were calculated based on the mean±standard deviation and $p<0.05$ was considered significant.

Results

219 patients (45.7%) of the injury victims were male and 54.3% were female and the mean age was 43.1±13.7 (from 21 to 88 years old). 58% of injury victims were in the group exposed to the blister-causing chemical agent (first group) and 42% were in the group exposed to the non-blister-causing chemical agent (second group). The mean age of first group was 32.3±14.4 and the second group was 21.7±12.72 according to the time of the incident (about 21 years ago), respectively. Absolute and relative frequency of

Iraqi Kurdistan chemical injury victims were given in Table 1based on demographic. 16.7% of injuries had a history of smoking (those who were smoking from previous years and also continuing and those who were smoking a year before and then quitting smoking) which there was no significant difference between the first and second groups in this regard. All injuries had the respiratory complaints (especially cough) which these complaints were more common in the first group. 84.8% of injuries had normal pulmonary functions and 15.2% of injuries had abnormal pulmonary functions. Among those who had abnormal pulmonary function tests, 67.1% had the severe or very severe pulmonary obstruction (Table 1).

Table 1- Absolute and relative frequency of Iraqi Kurdistan chemical injury victims based on demographic data (Numbers in parentheses are based on percentage).

Group→ Demographic↓		Group I (marked)	Group II (unmarked)	Total	Significant level
Age at the study time (Years)	<30	56 (20.1)	28 (13.9)	84 (17.5)	0.122
	30-39	64 (23)	59 (29.4)	123 (25.7)	
	40-49	73 (26.3)	61 (30.3)	134 (28.3)	
	>50	85 (30.6)	53 (26.4)	138 (28.5)	
Gender	Male	112 (40.3)	107 (53.2)	219 (45.7)	0.005
Smoking	Non-smoking	236 (84.9)	163 (81.8)	399 (83.3)	0.276
	Quit smoking a year before	22 (7.9)	15 (7.5)	37 (7.7)	
	Smoking up to now	20 (7.2)	23 (11.4)	43 (9)	
Inpatient history in therapy center after the incident	No	94 (33.8)	97 (48.3)	191 (39.9)	0.001
	Yes	184 (66.2)	104 (51.7)	288 (60.1)	
Respiratory complaints and symptoms	Asthma	268 (94.4)	179 (89.1)	447 (93.3)	0.001
	Cough	268 (94.4)	181 (90)	449 (93.7)	0.005
	Criptation	126 (45.3)	61 (30.3)	187 (39)	0.001
	Wheezing	90 (32.4)	30 (14.9)	120 (25.1)	0.0001
	Hoarseness	243 (87.1)	148 (73.6)	391 (81.6)	0.0001
	Hemoptysis	120 (43.2)	63 (31.3)	183 (38.2)	0.009
Normal pulmonary function tests		228 (82)	178 (88.6)	406 (84.8)	0.049
Abnormal pulmonary function tests	Poor	1 (2)	1 (4.3)	2 (2.7)	0.896
	Moderate	15 (30)	7 (30.4)	22 (30.1)	
	Severe	23 (46)	9 (39.1)	32 (43.8)	
	Very severe	11 (22)	6 (26.1)	17 (23.3)	

Table 2- Relationship between pulmonary disease and smoking status in Iraqi Kurdistan chemical injury victims (Numbers in parentheses are based on percentage).

Severity of pulmonary disease→ Smoking status↓	Normal	Poor to moderate	Moderate to severe	Total
Current smokers	36 (8.9)	1 (40.2)	6 (12.2)	43 (9)
Quit smoking a year before	30 (7.4)	2 (8.3)	5 (10.2)	37 (7.7)
Non-smokers	340 (83.7)	21 (87.5)	38 (77.6)	399 (83.3)

Table 3- Absolute and relative frequency of Iraq chemical injuries according to Region (Numbers in parentheses are based on percentage).

Group → Geographic region↓	Group I (marked)	Group II (unmarked)	Total	Significant level
Halabja	188 (67.9)	143 (71.1)	331 (69.2)	0.045
Dukan	10 (3.6)	9 (4.5)	19 (4)	
Chamchamal	6 (2.2)	12 (6)	18 (3.8)	
Shaqlawa	73 (26.4)	37 (18.4)	110 (23)	

FEV1 was 6.9±25.4 in the group exposed to blister-causing chemical agent, and 77.3±24.3 in the group exposed to non-blister-causing chemical agent and totally 71.2±15.5, which there was a statistically significant difference between the two groups ($p<0.0001$).

Table 2 shows the relationship between pulmonary disease and smoking status in Iraqi Kurdistan chemical injury victims.

Considering that the most chemical injury victims were related to Halabja and Shaqlawa regions (Table 3), the most abnormal pulmonary function with moderate and severe severity were related to Halabja and Shaqlawa regions, respectively (Table 4).

58% of injury victims had abnormal HRCT. The most common of pulmonary scanning in these patients was air trapping in the lung, but there was no significant difference between the first and second groups in the

overall pulmonary scan observations. However, tracheomalacia was observed only in pulmonary scan of four subjects from the first group (Table 5).

Table 4- The absolute and relative frequency of different severities of respiratory disease in terms of Iraqi Kurdistan exposed regions (Numbers in parentheses are based on percentage).

Severity of pulmonary disease→ Geographic region↓	Normal	Poor to moderate	Moderate to severe	Total	Significant level
Halabja	277 (68.4)	19 (79.2)	35 (71.4)	331 (69.2)	0.191
Shaqlawa	99 (24.4)	3 (12.5)	8 (16.3)	110 (23)	
Chamchamal	16 (4)	1 (4.2)	1 (2)	18 (3.8)	
Dukan	13 (3.2)	1 (4.2)	5 (10.2)	19(4)	

Table 5- Prevalence of HRCT abnormal findings in Iraqi Kurdistan injury victims (Numbers in parentheses are based on percentage).

Group→ Injury rate↓	Group I (marked)	Group II (unmarked)	Total	Significant level
Abnormal HRCT	162 (58.3)	116 (57.7)	278 (58)	0.902
Air retention	135 (48.6)	88 (43.8)	223 (46.6)	0.301
Mosaicity of parenchyma	21 (7.6)	22 (10.9)	43 (9)	0.200
Emphysema	72 (25.9)	64 (31.8)	136 (28.4)	0.155
† Tree in bud	3 (1.1)	2 (1)	5 (1)	*1.000
Tracheomalacia	4 (1.4)	0 (0)	4 (0.8)	*0.143
Bronchiectasis	23 (8.3)	11 (5.5)	34 (7.1)	0.239

Discussion

Iraq-Kurdish Injuries referred according to the chemical bombing locations which their precise details were still unclear [15]. They were at exposure to the various chemical compounds in different time, and the appropriate and quick remedial measures had not been done for them after the incident. Some of these people were suffering skin blisters after this chemical incident, so that all had complains of respiratory problems. The findings of this study were consistent with the conducted studies on the chemical victims induced by sulfur mustard especially Sardasht region [2].

In this study, blistering on injuries' skins was used as a criterion for differentiate types of blister-causing chemical agents or nerve agents that Iraqi army used in the Kurdish region. Although blisters on the injuries' skin could be an image of exposure to sulfur mustard, its absence could not reject the exposure to low doses of sulfur mustard. Dr. Ghanei et al. showed during a study on Iranian patients that those who were exposed to low doses of sulfur mustard and did not have severe clinical symptoms such as blisters had encountered with the pulmonary complications of bronchiolitis [11]. Since it is not normally expected that the following chronic pulmonary problems are exposure to nerve gases, the significant complaints and respiratory symptoms in patients without blisters can also show their exposure to low doses of sulfur mustard. Therefore in this study, classification of Iraqi chemical injuries into two mentioned groups might be generalized to the group of high-dose exposure to the blister-causing chemical agents and low-dose exposure of these agents or other chemical compounds.

In this study, the evidence of pulmonary dysfunction in Iraqi chemical injuries was not consistent with the obtained findings of Sardasht patients. In the present study, only 15.2% of injuries had abnormal pulmonary function. Among these patients, 67.1% had pulmonary complications with severe or very severe range. Meanwhile, in the conducted study on 34 thousands of Iranian injuries with sulfur mustard (13 to 20 years after exposure), 57.7% had the pulmonary dysfunction and 34%, 4.5% and 1% had weak, moderate and severe pulmonary complications, respectively [2]. These findings indicated that the pulmonary complications in Iraqi injuries who had survived after exposure to chemical agent and had suffered lung tissue damage had had a more progressive process than the Iranian injuries. Therefore, there was a strong possibility that first, medical care was not done in Kurdish regions in a short time after the incident including protective inhaler techniques (mask) and oral therapy [9, 16]. Second, the residents of these regions had not already received adequate training to encounter with chemical weapons. Third, the injury patients of these regions had used other inhaled factors such as tobacco more than Iranian injuries which led to exacerbation of pulmonary complications resulting from exposure to the chemical agent.

On the other hand, in the conducted studies in Iran, the role of genetic factors has likely been known in higher effects of chemical agents on the lung of Kurdish-regions' injuries [7]. Despite the obtained findings of the studies on the injuries of Sardasht, Iran, the present study showed that the injury victims of Iraq-Kurdish regions had suffered severe pulmonary complications [15]. The prospective cohort study on 407 Iranian injuries had shown that the pulmonary function of patients who had more severe loss in their respiratory function primary and before was impaired more quickly. Whereas this subject was not relevant to conditions such as the time of exposure to chemical agents, living region, location at the time of the incident (in the open or closed environment), interval between injury and performing the first pulmonary

function test, having underlying diseases and other respiratory disease and other non-chemical causes, and also abnormal pulmonary findings during physical examination [17]. Therefore, in the present study, the primary complication might accelerate the pulmonary complications in patients. On the other hand, the injury victims who had not had specific treatment and proper medical care had been suffering from severe respiratory complications.

More than half of Iraqi injuries had abnormal findings in their pulmonary scans including 46.6% of air trapping and 7.1% Bronchiectasis. These findings were consistent with the obtained results from the previous study on 77 of Iranian injuries with sulfur mustard, since 38% of air trapping and 8.8% of Bronchiectasis had been shown in these patients [8]. It was observed in another study on 50 Iranian chemical patients after 14 years of exposure to sulfur mustard that 98% of subjects had abnormal pulmonary scans, while the most common finding of them was air trapping (76% of patients) [10]. 22% of patients had used maximum five cigarettes per year before exposure to chemical agents that left it due to respiratory complaints after the chemical injury. In the pulmonary scans of these patients, Bronchiectasis, air trapping in exhalation and pulmonary parenchyma mosaic manifestations could confirm the diagnosis of obliterans bronchiolitis [10, 18]. It is noteworthy that by the test of carbon Monoxide gas transport in patients exposed to sulfur mustard, it is seen that the air Hungarian involves more than the pulmonary parenchyma [19]. In a study conducted on 603 Iranian injury victims exposed to sulfur mustard, emphysema with pulmonary complications of weak 4.3%, moderate 12.5%, and severe 7.9% had been reported in the pulmonary scans of these patients [11]. Whereas in the present study, 28% of Iraqi injuries had shown emphysema panel in their pulmonary scans which was not due to the known pulmonary complications exposed to sulfur mustard, but it seemed that it was due to smoking or exposure to available compounds in smoke [20].

One limitation of this study than other cohort studies was that subjects were those who were themselves willing to participate in this study. Unfortunately, there were also no detailed information about their type and concentration of chemicals and their records of hospitalization after the incident. So after 20 years of exposure to chemical gases, there was the possibility of bias among participants in reminding, and the participants of this study might not be those who were suffering from late pulmonary complications. The distance of injuries from the location of medical examinations could also lead to bias in the study. It means that those who did not suffer from pulmonary damage caused by chemical agents and had no respiratory complains or were suffering from weak pulmonary lesions had not participated in this study. Therefore, it is likely that there are a few native people in the regions contaminated with chemical gases that have no significant pulmonary symptoms, but will suffer from pulmonary complications in the future. On the other hand, the findings of this study had not been compared with the normal people of the same regions (control group).

Further studies are needed to determine the health of other parts of Iraq- Kurdistan injury victims' body based on clinical parameters and bio-molecule.

Conclusion

Iraqi chemical injury victims were suffering from severe pulmonary complications. Early diagnosis and primary and rapid control can reduce the progressive process of pulmonary complications caused by chemical agents in the exposed regions, moreover; it can increase the life continuation in injured victims.

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