

Anxiety, Depression, and Posttraumatic Stress in Iranian Survivors of Chemical Warfare

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THE 1980-1988 IRAN-IRAQ WAR inflicted enormous human costs, as each side sustained hundreds of thousands of casualties. According to Iranian government estimates, Iran sustained approximately 387 chemical attacks (via rocket, air, or artillery) during the 8-year war,¹ which resulted in high rates of medical morbidity and psychological distress among an estimated 60 000 Iranian survivors.² FIGURE 1 illustrates a map of chemical attack targets in the Iran-Iraq War.

Studies in war-afflicted civilians have reported high rates of war-related mental health problems. In a meta-analysis of 20 studies involving refugee populations living in high-income Western countries, Fazel et al³ found that at least 9% of adult refugees were diagnosed with posttraumatic stress disorder (PTSD), and approximately 5% met criteria for major depression and generalized anxiety disorder. Prevalence estimates are much higher in civilians still living in war-afflicted countries. For example, as part of a national mental health survey in Afghanistan, Cardozo et al⁴ found very high prevalence rates for symptoms of anxiety (72%), depression (68%), and PTSD (42%). Similarly, among community samples involving survivors of war, conflict, or mass violence, de Jong et al⁶ reported prevalence rates of PTSD

Context In the 1980-1988 Iran-Iraq War, extensive use of chemical weapons resulted in high rates of morbidity and mortality. While much is known about the physical consequences of chemical warfare, there is a paucity of information about the long-term effects of chemical attacks on mental health.

Objective To assess the long-term psychological impact of chemical warfare on a civilian population.

Design, Setting, and Participants Cross-sectional randomized survey conducted in July 2004 of 153 civilians in 3 towns exposed to warfare in northwestern Iran: Oshnaviyeh (low-intensity conventional warfare), Rabat (high-intensity conventional warfare), and Sardasht (both high-intensity conventional warfare and chemical weapons).

Main Outcome Measures Full or partial posttraumatic stress disorder (PTSD) diagnosis, anxiety symptoms, and depressive symptoms were assessed using Farsi versions of the Clinician-Administered PTSD Scale, Hamilton Scale for Anxiety, and Beck Depression Inventory, respectively.

Results Overall participation rate was 93%. Respondents had a mean age of 45 years and were all of Kurdish ethnicity. Among individuals exposed to both high-intensity warfare and chemical weapons, prevalence rates for lifetime PTSD, current PTSD, major anxiety symptoms, and severe depressive symptoms were 59%, 33%, 65%, and 41%, respectively. Among the low-intensity warfare group, the corresponding rates were 8%, 2%, 18%, and 6%, respectively, while intermediate rates were found among those exposed to high-intensity warfare but not to chemical weapons (31%, 8%, 26%, and 12%, respectively). Compared with individuals exposed to low-intensity warfare, those exposed to both high-intensity warfare and chemical weapons were at higher risk for lifetime PTSD (odds ratio [OR], 18.6; 95% confidence interval [CI], 5.8-59.4), current PTSD (OR, 27.4; 95% CI, 3.4-218.2), increased anxiety symptoms (OR, 14.6; 95% CI, 6.0-35.6), and increased depressive symptoms (OR, 7.2; 95% CI, 3.3-15.9). Exposure to high-intensity warfare but not to chemical weapons was also significantly associated with lifetime PTSD (OR, 5.4; 95% CI, 1.7-17.6), compared with those in the low-intensity warfare group. Further, compared with individuals exposed to high-intensity warfare alone, those exposed to both high-intensity warfare and chemical weapons were at higher risk for lifetime PTSD (OR, 3.4; 95% CI, 1.5-7.4), current PTSD (OR, 6.2; 95% CI, 2.0-20.1), increased anxiety symptoms (OR, 5.6; 95% CI, 2.5-12.6), and increased depressive symptoms (OR, 3.7; 95% CI, 1.8-7.2).

Conclusion Exposure to chemical warfare is an extreme traumatic event that has long-lasting adverse consequences on mental health.

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symptoms of 37% in Algeria, 28% in Cambodia, 18% in Gaza, and 16% in Ethiopia.

Few studies have examined the mental health consequences of exposure to chemical weapons. One study con-

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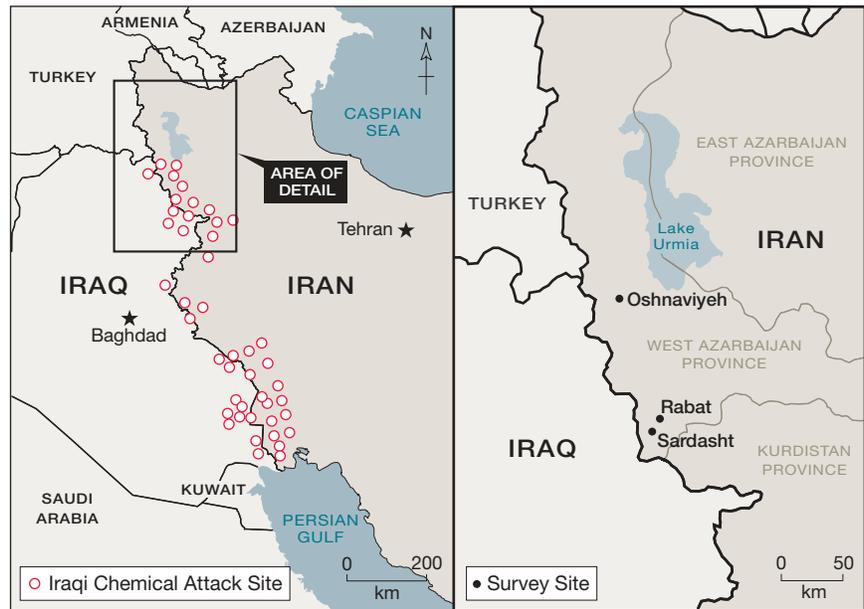
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ducted in Japan 5 years after the 1995 sarin terrorist attack found that 17% of 34 participants met criteria for current PTSD.⁷ Studies among US soldiers who participated in secret military tests of mustard gas during World War II found that 50% experienced partial or full lifetime PTSD⁸ and nearly one third met criteria for full current PTSD 50 years after the exposure.⁹

This study was designed to assess the long-term psychological impact of chemical warfare on a civilian population. It was conducted in 3 Iranian towns with different types of war exposure. The first, Sardasht, was exposed to both high-intensity conventional warfare and chemical weapons. In June 1987, Sardasht, a small Kurdish town in northwestern Iran, was bombarded with four 250-kg sulfur mustard warheads that exploded in the center of town and exposed approximately 4500 residents. Serious skin burns, ocular damage, and respiratory symptoms were among the most common acute and persistent consequences of this chemical weapons exposure.^{10,11} Rabat, the second town, was exposed to high-intensity conventional warfare but not to chemical weapons; and Oshnaviyeh, the third town, was exposed to low-intensity conventional warfare. All 3 towns in the border regions of West Azarbaijan province and have predominantly Kurdish populations. These towns have had similar levels of other stressors, including natural disasters, political unrest, and unemployment.

Based on the experience of World War II veterans exposed to mustard gas, we hypothesized that Iranian civilians exposed to both high-intensity warfare and chemical weapons would be at higher risk of having trauma-related mental health problems (ie, PTSD, anxiety, and depression) than the 2 comparison groups more than 17 years after the Iran-Iraq War. With recent worldwide threats and deliberate acts of terrorism, it is more important to understand the acute and chronic physical and psychological effects of chemical warfare.

Figure 1. Iraqi Chemical Attack Sites During the Iran-Iraq War (1980-1988) and Survey Sites



Source for the location of the chemical attacks is Holt World History.³

METHODS

Study Design and Sample

In July 2004, we conducted a cross-sectional, randomized survey of 153 civilians from 3 towns in West Azarbaijan province in northwestern Iran. In each town, participants were selected using a stratified, systematic random sampling scheme (FIGURE 2). First, the town's official map was divided into 4 sectors. Then, within each sector, we began at a prespecified starting point and attempted to conduct an interview at every third house until 13 surveys were completed. One available adult who was eligible to respond was selected from each participating household. In rare instances in which more than 1 person in the household was eligible, the head of the household or the oldest person was selected to participate in the study. If no eligible participants were available in a household or if the eligible individuals refused to participate, the next household was chosen.

Eligibility criteria included being 18 years or older, living in West Azarbaijan province during the Iran-Iraq War, and not being in field combat. Fur-

ther, in Sardasht, only those who reported having an official chemical attack exposure-related disability score (which was later verified in the medical records of the Janbazan Organization) were eligible for inclusion in the study. The disability score, with a range of 0 to 100 and defined by a standard diagnostic protocol of the Janbazan Organization, is assigned based on clinical severity (none, mild, moderate, or severe) of 3 key symptoms: cutaneous, ocular, and respiratory.¹⁰ Following the completion of interviews in Sardasht, participants from the 2 comparison towns were frequency matched by age range and sex distribution. Assuming a type I error of .05, power of 80%, a 2:1 ratio of unexposed to exposed, and a disease prevalence of at least 25% among the unexposed, a sample size of 150 would be needed to detect an odds ratio of 3 or more.

All interviews were conducted in Farsi by 2 of the authors (F.H. and F.F.) who had received formal training in each of the psychiatric instruments (noted in the Measurement of Outcomes section). The face-to-face inter-

views lasted approximately 90 minutes and were conducted in a private area of the participant's home after voluntary, informed oral consent was obtained. This study was approved by the institutional review boards of the Yale University School of Medicine and the Iranian Janbazan Organization.

Measurement of Exposure

During the Iran-Iraq War, many Iranian towns were targeted by bomb raids causing loss of human life and massive damage to buildings. Although the exact number of bomb raids on each town is not known, according to key West Azarbaijan province officials, Oshnaviyeh, with a 25-km distance from the Iran-Turkey border, was bombed fewer than 10 times, which we define as low-intensity conventional warfare. In contrast, it is estimated that Rabat, with a 20-km distance from the Iran-Iraq border, was bombed more than 75 times and Sardasht, with a 10-km distance from the Iran-Iraq border, was bombed approximately 60 times, both of which we define as high-intensity conven-

tional warfare. In addition, as noted previously, Sardasht was exposed to 1 chemical weapons attack.

Measurement of Outcomes

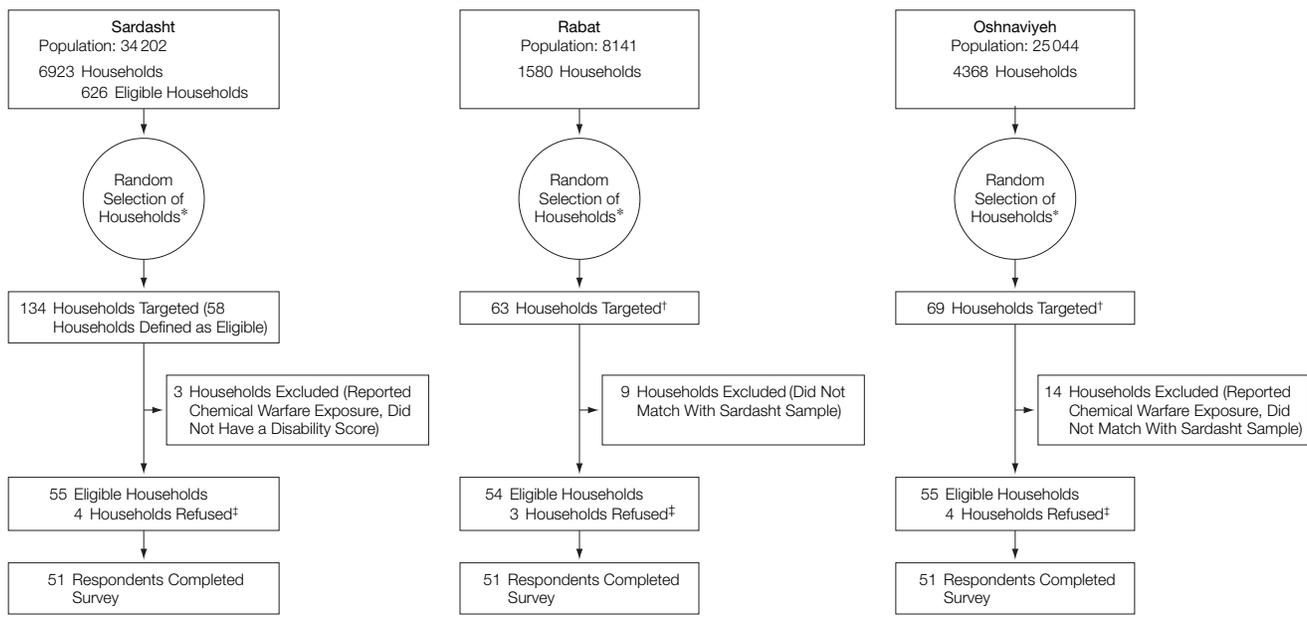
Demographic variables assessed included age, sex, educational level, marital status, employment status, and self-reported ethnic background. The ethnic background question aimed to convey the diversity of the groups living in the West Azarbaijan province, which is composed of Azeris, Kurds, and a small minority of Assyrians, Armenians, and Jews. Those designated as "Unemployed Outside the Home" were homemakers, students, and retirees. In addition to demographic characteristics, the survey instrument included the Persian version of the Beck Depression Inventory (BDI),¹² the Hamilton Anxiety Scale (HAM-A),¹³ and the Clinician-Administered PTSD Scale (CAPS).¹⁴ The BDI-Persian has high internal consistency (Cronbach $\alpha = .87$) and acceptable test-retest reliability ($r = 0.74$).¹⁵ Studies also show high internal consistency for the CAPS-1 Farsi version.¹⁶

Furthermore, the HAM-A is a well-recognized instrument in Iran and has been shown to be valid and reliable.¹⁷

Using CAPS, diagnosis of PTSD was coded as absent, partial, or full for both current (ie, last month) and lifetime PTSD. Trauma exposure was assessed by first reviewing lifetime trauma history. Participants who reported exposure to more than 1 traumatic event were asked to select the worst event. The "A" Stressor criterion specifies that an individual has been exposed to a catastrophic event involving actual or threatened physical harm to self or others, as well as a requirement that the survivor's subjective response was marked by intense fear, helplessness, or horror. If the trauma met criterion A, the rest of the CAPS instrument was administered to evaluate frequency and intensity of current and lifetime PTSD symptoms.

Current and/or lifetime full PTSD diagnostic criteria were met if the participant had 1 or more reexperiencing symptom, 3 or more avoidance symptoms, and 2 or more hyperarousal

Figure 2. Sample Selection



*Towns were divided into 4 sectors. Within each sector, every third household was randomly selected.

†Participants were frequency matched by age range and sex distribution to participants in Sardasht.

‡Reasons for refusal included not having time or interest in participating in the study.

symptoms within the relevant time-frame. We included 2 definitions of current and/or lifetime partial PTSD: either meeting the reexperiencing criterion and having 1 or more avoidance symptom and 1 or more hyperarousal symptom, or meeting both the reexperiencing and the hyperarousal criteria but not the avoidance criterion within the relevant timeframe. These criteria are consistent with criteria for partial PTSD used by other investigators.¹⁸

Statistical Analysis

The data were analyzed using SAS Version 9 (SAS Institute Inc, Cary, NC). We began by describing the demographic characteristics of the sample by town (ie, type of war exposure). Next, we examined the bivariate associations between type of war exposure and each of the outcomes—PTSD (both lifetime and current), anxiety, and depression—using the Mantel-Haenszel χ^2 test for trend and the Fisher exact test by Mehta, as appropriate. Finally, multivariate analyses, controlling for demographic characteristics, were performed using proportional odds logistic regression modeling.^{19,20} This technique, also called ordinal or cumulative logistic regression, was used because each of our outcome measures was ordinal. Specifically, depressive symptoms were categorized as none (0-4), mild (5-7), moderate (8-15), or severe (≥ 16); anxiety symptoms were categorized as none (0-5), minor (6-14), or major (≥ 15); and lifetime and current PTSD diagnoses were categorized as absent, partial, or full (as described previously). For each outcome, cumulative logits were modeled based on increasing severity of psychiatric illness; therefore, the odds ratios (ORs) (and 95% confidence intervals [CIs]) presented are estimates of the likelihood of reporting worse vs better mental health. In this study, a Bonferroni-type correction for multiple comparisons was not used, since the associations examined between type of warfare exposure and psychiatric illness were considered a priori. The α level for statistical significance was set at .05.

RESULTS

Description of the Sample

The participation rate was 93% for Sardasht and Oshanaviyeh and 94% for Rabat. Overall, the mean age of participants was 45 years (SD, 13.7). All participants were of Kurdish background. Demographic characteristics of the sample by type of war exposure are presented in TABLE 1. The 3 exposure groups did not significantly differ with respect to any of the demographic characteristics.

Among individuals exposed to chemical weapons (ie, the Sardasht sample), the median disability score was 30 (range, 5-70). At the time of the study, 56% of the Sardasht sample experienced mild respiratory, ocular, and cutaneous symptoms (the 3 principal components of the disability score), 22% had at least 1 moderate symptom, and 11% had at least 1 severe symptom, 17 years after exposure.

Prevalence of Psychiatric Illness

As shown in TABLE 2, participants exposed to both high-intensity warfare and chemical weapons reported the highest levels of mental health prob-

lems, with prevalence rates for lifetime (full or partial) PTSD, current (full or partial) PTSD, major anxiety symptoms, and severe depressive symptoms of 59%, 33%, 65%, and 41%, respectively. Among the low-intensity warfare group, the corresponding rates were 8%, 2%, 18%, and 6%, respectively, while intermediate rates were found among individuals exposed to high-intensity warfare but not to chemical weapons (31%, 8%, 26%, and 12%, respectively). All tests for trend (or Fisher exact test) were significant at $P < .001$ (Table 2). In a subgroup analysis of the Sardasht sample, we found no significant associations between the chemical exposure-related disability score and level of psychiatric illness. Specifically, participants with severe (≥ 50) and nonsevere (< 50) disability scores had generally similar rates of lifetime partial or full PTSD (67% vs 57%), current partial or full PTSD (50% vs 30%), major anxiety symptoms (67% vs 64%), and severe depressive symptoms (50% vs 41%) ($P > .05$ for all comparisons); however, these post hoc analyses were underpowered.

Table 1. Description of the Sample by Type of War Exposure*

Characteristic	No. (%) of Participants		
	Low-Intensity Warfare (n = 51)	High-Intensity Warfare (n = 51)	High-Intensity Warfare and Chemical Weapons (n = 51)
Age, y			
18-30	10 (19.6)	7 (13.7)	6 (12.2)
31-45	19 (37.3)	22 (43.1)	20 (40.8)
46-60	15 (29.4)	15 (29.4)	17 (34.7)
>61	7 (13.7)	7 (13.7)	6 (12.2)
Sex			
Men	28 (54.9)	29 (56.9)	30 (58.8)
Women	23 (45.1)	22 (43.1)	21 (41.2)
Educational level			
>12th grade	13 (25.5)	7 (13.7)	19 (37.3)
1st-11th grade	19 (37.3)	22 (43.2)	21 (41.2)
None	19 (37.3)	22 (43.2)	11 (21.6)
Marital status			
Not married	8 (15.7)	6 (12.8)	8 (15.7)
Married	43 (84.3)	45 (88.2)	43 (84.3)
Employment status†			
Employed	25 (49.0)	28 (54.9)	20 (39.2)
Unemployed	26 (51.0)	23 (45.1)	31 (60.8)

*None of the group comparisons were significant at the $P < .05$ level. Total number of participants and percentages may not sum due to missing data and rounding.
 †Employment status outside the home.

Ordinal Logistic Regression

Results of the unadjusted and adjusted ordinal logistic regression models are presented in TABLE 3. In the multivariate analysis, compared with individuals exposed to low-intensity warfare, those exposed to both high-intensity warfare and chemical weapons were at substantially elevated risk for lifetime PTSD (OR, 18.6;

95% CI, 5.8-59.4), current PTSD (OR, 27.4; 95% CI, 3.4-218.2), increased anxiety symptoms (OR, 14.6; 95% CI, 6.0-35.6), and increased depressive symptoms (OR, 7.2; 95% CI, 3.3-15.9). In addition, exposure to high-intensity warfare but not to chemical weapons was also significantly associated with lifetime PTSD (OR, 5.4; 95% CI, 1.7-17.6),

compared with individuals in the low-intensity warfare group. Although elevated, none of the other high-intensity vs low-intensity ORs reached statistical significance at the .05 level.

To specifically examine the added contribution of exposure to chemical weapons, we also compared the Sardasht and Rabat samples and found that, compared with individuals exposed to high-intensity warfare alone, those exposed to both high-intensity warfare and chemical weapons were at substantially elevated risk for lifetime PTSD (OR, 3.4; 95% CI, 1.5-7.4), current PTSD (OR, 6.2; 95% CI, 2.0-20.1), increased anxiety symptoms (OR, 5.6; 95% CI, 2.5-12.6), and increased depressive symptoms (OR, 3.7; 95% CI, 1.8-7.2).

Psychiatric Comorbidity

As shown in TABLE 4, there were high levels of comorbidity between PTSD and symptoms of depression and anxiety. Overall, among those with full, partial, or no lifetime PTSD diagnosis, prevalence rates for severe depressive symptoms were 53%, 29%, and 12%, respectively ($P < .001$ for trend); and for major anxiety symptoms, 87%, 51%, and 23%, respectively ($P < .001$ for trend). Similar associations were found with current PTSD diagnosis.

COMMENT

Exposure to chemical weapons may cause serious morbidity and long-term illnesses among survivors. Further, exposure to chemical weapons is an extreme traumatic event that can result in acute helplessness and anxiety, loss of perceived safety, and chronic physical disabilities. To our knowledge, this is the first epidemiologic study to document the long-term negative mental health sequelae of exposure to war and chemical attacks among civilians.

In the present study, 8% of participants exposed to high-intensity conventional warfare met criteria for current partial or full PTSD 17 years after the Iran-Iraq War. This prevalence was higher among individuals exposed to both high-intensity conventional warfare and chemical weapons. Partial or full

Table 2. Type of War Exposure Associated With Mental Health Outcomes*

Outcomes	No. (%) of Participants			P for Trend†
	Low-Intensity Warfare (n = 51)	High-Intensity Warfare (n = 51)	High-Intensity Warfare and Chemical Weapons (n = 51)	
Lifetime PTSD				
Absent	47 (92.2)	35 (68.6)	21 (41.2)	<.001
Partial	4 (7.8)	13 (25.5)	18 (35.3)	
Full	0	3 (5.9)	12 (23.5)	
Current PTSD				
Absent	50 (98.0)	47 (92.2)	34 (66.7)	<.001‡
Partial	1 (2.0)	4 (7.8)	11 (21.6)	
Full	0	0	6 (11.8)	
Anxiety symptoms				
None	24 (47.1)	15 (29.4)	3 (5.9)	<.001
Minor	18 (35.3)	23 (45.1)	15 (29.4)	
Major	9 (17.7)	13 (25.5)	33 (64.7)	
Depressive symptoms				
None	21 (41.2)	16 (31.4)	7 (13.7)	<.001
Mild	8 (15.7)	10 (19.6)	6 (11.8)	
Moderate	19 (37.3)	19 (37.3)	17 (33.3)	
Severe	3 (5.9)	6 (11.8)	21 (41.2)	

Abbreviation: PTSD, posttraumatic stress disorder.
 *Percentages may not sum to 100 due to rounding.
 †Mantel-Haenszel χ^2 test for trend, unless otherwise specified.
 ‡Fisher exact test.

Table 3. Adjusted and Unadjusted Effect of Exposure on Mental Health Outcomes*

Outcomes	Odds Ratio (95% Confidence Interval)		
	Low-Intensity Warfare	High-Intensity Warfare	High-Intensity Warfare and Chemical Weapons
Lifetime PTSD diagnosis			
Unadjusted	1.00	5.3 (1.6-17.5)†	18.4 (5.8-58.6)‡
Adjusted	1.00	5.4 (1.7-17.6)†	18.6 (5.8-59.4)‡
Current PTSD diagnosis			
Unadjusted	1.00	4.2 (0.5-39.2)	26.0 (3.3-204.8)‡
Adjusted	1.00	4.3 (0.5-40.0)	27.4 (3.4-218.2)‡
Depressive symptoms			
Unadjusted	1.00	1.4 (0.7-3.0)	5.6 (2.6-12.0)†
Adjusted	1.00	1.5 (0.7-3.0)	7.2 (3.3-15.9)‡
Anxiety symptoms			
Unadjusted	1.00	2.0 (1.0-4.1)	10.4 (4.6-23.5)‡
Adjusted	1.00	2.1 (1.0-4.6)	14.6 (6.0-35.6)‡

Abbreviation: PTSD, posttraumatic stress disorder.
 *Adjusted for demographic variables that were statistically significant or that had a greater than 10% influence on the parameter estimate.
 † $P < .01$.
 ‡ $P < .001$.

Table 4. PTSD and Comorbid Depressive and Anxiety Symptoms in the Total Sample

Symptom	Lifetime PTSD, No. (%)			P for Trend*	Current PTSD, No. (%)			P for Trend*
	Full (n = 15)	Partial (n = 35)	Absent (n = 103)		Full (n = 6)	Partial (n = 16)	Absent (n = 131)	
Severe depression	8 (53)	10 (29)	12 (12)	<.001	4 (67)	6 (38)	20 (15)	<.001
Major anxiety	13 (87)	18 (51)	24 (23)	<.001	6 (100)	13 (81)	36 (28)	<.001

Abbreviation: PTSD, posttraumatic stress disorder.
 *Mantel-Haenszel χ^2 test for trend.

lifetime PTSD prevalence in such individuals was even higher (59%), compared with 31% of individuals who were exposed to high-intensity warfare and 8% of those exposed to low-intensity warfare. The prevalence of partial or full PTSD in the group exposed to high-intensity warfare alone is consistent with findings from other mental health surveys in postwar settings (Algeria, Afghanistan, and Cambodia).^{5,6} However, the rates of partial or full PTSD are considerably higher for survivors of chemical attacks compared with other conflict-affected populations.

PTSD is not the only psychological disorder associated with extreme traumatic stress. Elevated prevalence rates of depression, anxiety, and substance abuse also have been reported in trauma survivors.²¹ Similarly, in the present study, current prevalence rates of major anxiety and severe depressive symptoms were greater for the survivors of high-intensity warfare and chemical weapons compared with the group exposed to high-intensity warfare alone.

Exposure to high-intensity warfare and chemical weapons was associated with lifetime and current PTSD in this sample. Survivors who were exposed to both high-intensity warfare and chemical weapons were more likely than those who were exposed to high-intensity or low-intensity warfare but not chemical weapons to meet lifetime diagnostic criteria for full or partial PTSD. Survivors of high-intensity warfare and chemical weapons were also more likely to meet diagnostic criteria for current partial or full PTSD than those exposed to low-intensity warfare alone.

It is not known why risk of developing PTSD is significantly higher in the group exposed to high-intensity warfare and chemical weapons compared

with that exposed to high-intensity warfare alone. It is possible that chemical exposure, like exposure to war, causes PTSD in its own right and that the high prevalence rates of PTSD in the group exposed to warfare and chemical weapons represent an additive effect. It is also possible that high prevalence rates in this group may be related to the adverse physical health consequences of chemical exposure.⁹ For example, exposure to mustard gas can cause chronic pulmonary distress, which then serves as a repetitive reminder of the original trauma. The result might be an increase in reexperiencing and hyperarousal symptoms. Furthermore, many participants in this study described being afraid and on guard about the future health consequences of their exposure to toxic agents.

The impact of war and chemical weapons are apparent in symptoms of depression and anxiety as the odds for experiencing these disorders are 7.2 and 14.6 times higher for chemical weapons survivors than for individuals with low-intensity warfare exposure.

In our study, high rates of PTSD comorbidity in survivors of high-intensity warfare and chemical weapons are consistent with previous research in other trauma populations.²²⁻²⁵ There are a number of possible explanations for the high rates of comorbidity in the present study. It is possible that preexisting disorders constitute a vulnerability to PTSD or that comorbid disorders are subsequent complications of PTSD.^{25,26} Other possible reasons could be shared risk factors between PTSD and other *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* axis I disorders or the significant overlap between symptoms of PTSD and symptoms of depression and anxiety.²⁷ Further research is needed to investigate these issues.

Our study has a number of limitations. First, the small sample size and observed small frequencies in subgroups have resulted in large confidence intervals. Second, some of our data are based on retrospective self-report, which is less reliable than data collected prospectively. Respondents may have had difficulty recalling traumatic events and psychological symptoms that were experienced nearly 2 decades ago. Of note, however, self-reported chemical exposure was verified with medical records and chemical exposure-related disability scores. Third, it is possible that prevalence of lifetime and current PTSD are underestimated among all 3 groups in this study, since previous research has shown that severely traumatized individuals from non-Western societies often endorse symptoms of reexperiencing and hyperarousal but do not meet PTSD diagnostic criteria because they do not endorse avoidance/numbing symptoms.²⁸ Consistent with this possibility, only 12% of participants in the total sample endorsed the lifetime avoidance criterion, compared with 63% and 48% who met the lifetime reexperiencing and hyperarousal criterion, respectively. Fourth, because we did not assess prewar anxiety or depression, it is not known to what degree the high levels of current depression and anxiety observed in study participants were directly related to traumatic exposure (ie, bombing and chemical exposure) during the Iran-Iraq War. However, the significantly higher levels of current depression and anxiety in the groups exposed to high-intensity warfare alone and to both high-intensity warfare and chemical weapons, compared with the low-intensity warfare group, suggest that traumas

experienced during the Iran-Iraq War contributed to current symptoms of anxiety and depression.

CONCLUSION

The use of chemical weaponry is now an issue of international security. A terrorist event with chemical weapons has the potential to cause mass casualties, to overwhelm local medical and emergency response resources, and to generate pandemonium and confusion.

The findings of this study suggest that exposure to chemical warfare has severe and long-lasting adverse effects on mental health and that these effects cannot be fully accounted for by exposure to conventional warfare alone.

Despite the lower number of conventional bomb raids in Sardasht (high-intensity warfare and chemical weapons) compared with Rabat (high-intensity warfare alone), residents of Sardasht had significantly higher risks for meeting criteria for lifetime and current PTSD as well as symptoms of depression and anxiety.

Kessler et al²⁹ have previously reported on the enormity of the burden associated with PTSD and found that marital instability, unemployment, and increased use of outpatient care contribute substantially to the cost to society and the individual. Kessler et al also reported that the prevalence and adverse psychological consequences of PTSD are greater in less developed countries that have been exposed to prolonged traumatic experiences associated with political or ethnic violence.

Our findings highlight the importance of examining the long-term course of trauma-related mental health problems, particularly in individuals who have been exposed to chemical warfare. Survivors of Sardasht are a distinct population for such examination, since their traumatic exposures are well documented, relatively uniform, and severe.

In many war-torn regions of the world, because there is a paucity of trained mental health professionals, physicians and other health care professionals must be informed about the psychological consequences of traditional and

chemical warfare (eg, anxiety, depression, and PTSD), as well as evidence-based approaches to mental health care. Survivors of chemical warfare need access to medical, psychological, and social resources. Integrated primary and mental health care that addresses individual as well as community and family needs is crucial for the effective treatment and promotion of mental health in survivors of chemical warfare.

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Study concept and design: Hashemian, Khoshnood, Kasl, Southwick.

Acquisition of data: Hashemian, Falahati.

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Obtained funding: Hashemian, Khoshnood.

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Study supervision: Hashemian, Khoshnood, Kasl, Southwick.

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REFERENCES

1. Taheri Shemirani S. The war of the cities. In: Rajae F, ed. *The Iran-Iraq War: The Politics of Aggression*. Gainesville: University Press of Florida; 1993.
2. News chronology: November 1994 through February 1995. *Chemical Weapons Convention Bulletin: Quarterly Journal of the Harvard Sussex Program on CBW Armament and Arms*. 1995;28: 20.
3. *Holt World History: The Human Journey*. Pupil's Edition Full Volume. http://go.hrw.com/hrw.nd/gohrw_rls1/pKeywordResults?keyword=st%20iran%201988. Accessibility verified July 11, 2006.
4. Fazel M, Wheeler J, Danesh J. Prevalence of serious mental disorder in 7000 refugees resettled in western countries. *Lancet*. 2005;365:1309-1314.
5. Cardozo BL, Bilukha OO, Crawford CA, et al. Mental health, social functioning, and disability in postwar Afghanistan. *JAMA*. 2004;292:575-584.
6. de Jong JT, Komproe IH, Van Ommeren M, et al.

Lifetime events and posttraumatic stress disorder in 4 postconflict settings. *JAMA*. 2001;286:555-562.

7. Ohtani T, Iwanami A, Kasai K, et al. Post-traumatic stress disorder symptoms in victims of Tokyo subway attack. *Psychiatry Clin Neurosci*. 2004;58:624-629.

8. Schnurr PP, Friedman MJ, Green BL. Posttraumatic stress disorder among World War II mustard gas test participants. *Mil Med*. 1996;161:131-136.

9. Schnurr PP, Ford JD, Friedman MJ, Green BL, Dain BJ, Sengupta A. Predictors and outcomes of posttraumatic stress disorder in World War II veterans exposed to mustard gas. *J Consult Clin Psychol*. 2000;68:258-268.

10. Khateri S, Ghanei M, Keshavarz S, Soroush M, Haines D. Incidence of lung, eye, and skin lesions as late complications in 34,000 Iranians with wartime exposure to mustard agent. *J Occup Environ Med*. 2003;45:1136-1143.

11. Ghanei M, Aslani J, Khateri S, Hamadanizadeh K. Public health status of the civil population of Sardasht 15 years following large-scale wartime exposure to sulfur mustard. *J Burns Surg Wound Care*. 2003;2:1-9. http://www.journalofburnsandwounds.com/volume02/volume02_article07.pdf. Accessed June 30, 2006.

12. Beck AT, Beck RW. Screening depressed patients in family practice. *Postgrad Med*. 1972;52:81-85.

13. Hamilton A. Diagnosis and rating of anxiety. *Br J Psychiatry*. 1969;3(special publication):76-79.

14. Blake DD, Weathers FW, Nagy LM, et al. The development of a Clinician-Administered PTSD Scale. *J Trauma Stress*. 1995;8:75-90.

15. Ghassemzadeh H, Mojtabai R, Karamghadiri N, Ebrahimkhani N. Psychometric properties of a Persian-language version of the Beck Depression Inventory—Second Edition: BDI-II-PERSIAN. *Depress Anxiety*. 2005; 21:185-192.

16. Malekzai AS, Niazi JM, Paige SR, et al. Modification of CAPS-1 for diagnosis of PTSD in Afghan refugees. *J Trauma Stress*. 1996;9:891-898.

17. Kavyani H, Mossavi AS, Mohit A. *Psychological Scales and Interviews (Farsi)*. Tehran, Iran: Sana Publications; 2001:179-205.

18. Schnurr PP, Friedman MJ, Rosenberg SD. Premilitary MMPI scores as predictors of combat-related PTSD symptoms. *Am J Psychiatry*. 1993;150:479-483.

19. Strokes ME, Davis CS, Koch GG. *Categorical Data Analysis Using the SAS System*. 2nd ed. Cary, NC: SAS Institute Inc; 2000.

20. Scott SC, Goldberg MS, Mayo NE. Statistical assessment of ordinal outcomes in comparative studies. *J Clin Epidemiol*. 1997;50:45-55.

21. Norris FH, Friedman MJ, Watson PJ, Byrne CM, Diaz E, Kaniasty K. 60,000 disaster victims speak. *Psychiatry*. 2002;65:207-239.

22. Scholte WF, Olf M, Ventevogel P, et al. Mental health symptoms following war and repression in eastern Afghanistan. *JAMA*. 2004;292:585-593.

23. Kulka RA, Schlenger WE, Fairbank JA, et al. *Trauma and the Vietnam War Generation*. New York, NY: Brunner/Mazel; 1990.

24. Kessler RC, Sonnega A, Bromet E, Hughes M, Nelson CB. Posttraumatic stress disorder in the National Comorbidity Survey. *Arch Gen Psychiatry*. 1995;52:1048-1060.

25. Deering CG, Glover SG, Ready D, Eddleman HC, Alarcon RD. Unique patterns of comorbidity in posttraumatic stress disorder from different sources of trauma. *Compr Psychiatry*. 1996;37:336-346.

26. Davidson JR, Kudler HS, Saunders WB, Smith RD. Symptom and comorbidity patterns in World War II and Vietnam veterans with posttraumatic stress disorder. *Compr Psychiatry*. 1990;31:162-170.

27. Green BL, Lindy JD, Grace MC. Posttraumatic stress disorder. *J Nerv Ment Dis*. 1985;173:406-411.

28. McCall GJ, Resick PA. A pilot study of PTSD symptoms among Kalahari Bushmen. *J Trauma Stress*. 2003; 16:445-450.

29. Kessler RC. Posttraumatic stress disorder. *J Clin Psychiatry*. 2000;61(suppl 5):4-12.