Civil war and male infertility in Lebanon

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Objective: To investigate the long-term impacts of the 15-year Lebanese civil war on male infertility.
Design: Clinic-based, case–control study, using reproductive history and risk factor interview data and laboratory-based semen analysis.
Setting: Two IVF clinics in Beirut, Lebanon, during an 8-month period (January–August 2003).
Patient(s): One hundred twenty infertile male cases and 100 fertile male controls, distinguished by semen analysis and reproductive history.
Intervention(s): None.
Main Outcome Measure(s): Standard clinical semen analysis.
Result(s): Infertile male cases were more likely than fertile controls to have lived through the Lebanese civil war and to have experienced war-related trauma (residence in bombing areas, participation in combat, injuries, kidnapping, and displacement from home). Cases had a 57% increase in their odds of exposure to civil war–related trauma.
Conclusion(s): This case–control study demonstrates an association between the Lebanese civil war and male infertility. Wartime and postwar exposure to a number of potential reproductive risk factors—including toxins, injuries, and stress—is believed to be the main factor leading to this finding. (Fertil Steril® 2008;90:340–5. ©2008 by American Society for Reproductive Medicine.)

Key Words: Male infertility, war, reproductive toxins, stress, Lebanon

The effect of war on reproductive health in general and male infertility in particular has been investigated in few studies (1–5). An increased risk of infertility and a longer time to conception were discovered among United Kingdom male veterans of the first Gulf War when compared with the case of non-deployed veterans (1). The same trend was observed among Australian veterans deployed in the first Gulf War (2). Along the same lines, Zorn et al. (3) demonstrated a significant decrease in total progressive motility and rapid progressive sperm motility after the 1991 war in Slovenia. In their retrospective comparative study on the effect of war on semen parameters during and after the Lebanese civil war, Abu-Musa et al. (4) reported a significant drop in sperm concentration during the war period as compared with the 5-year postwar period. However, Ishoy et al. (5) found no differences between Danish veterans of the Gulf War and controls with respect to reproductive hormones and fertility. The way in which war affects male fertility is poorly understood. Many war-related exposures and traumas may put men at risk of infertility during or after a war period. In addition to multifarious reproductive toxins, other risk factors may include psychological stress and injury to the reproductive tract.

The civil war in Lebanon, which lasted for 15 years (1975–1990), could be described as intersectarian in that it involved major fighting between multiple ethnic-religious groups. The war had severe impacts on the sociodemographic, economic and health conditions in the country. At the sociodemographic level, the war resulted in the death of 7% of the Lebanese population, the serious injuries of 10%, the displacement of 25% and the emigration of nearly 30% of the population (6–8). At the economic level, the war resulted in severe deterioration of Lebanon's physical infrastructure, environmental sanitation, social services, health care, and schools. Improper disposal of waste, including toxic waste imported from Europe, was highly prevalent during the war period (9).

In this study, we report the potential impact on male fertility of a variety of war-related exposures during the Lebanese civil war.

MATERIALS AND METHODS

Study Design and Population

Two hundred twenty men who were seeking IVF treatment at two major IVF centers in Beirut, the American University of Beirut Medical Center and FIRST IVF, were included in the study. All patients had been unable to conceive a child for ≥12 months before the study. The patients were divided into two groups according to their fertility status, based

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their semen analyses. The cas
considered infertile because
analyses (10). The control group included 100 men with normal semen analyses but who were seeking fertility treatment because of female-factor infertility, including tubal, polycystic ovary syndrome, unexplained, or endometriosis-related infertility. Subjects underwent semen analysis at the time of the study, generally on the day of study recruitment at the IVF center, to confirm the results of previous analyses.

After obtaining the informed consent of subjects, interviews involving detailed reproductive histories and risk factor assessment were conducted. The study was institutional review board approved, and patients were not entitled to any financial reimbursement.

Data Collection

Data were collected through a semistructured interview schedule, which included baseline information on demographics (age, religion, place of residence, education, income) and reproductive history (age at first sexual intercourse, number of sexual partners, age at marriage, number of marriages, endogamy). War exposures were assessed through men's self-report of participation in fighting; injury (as a soldier or civilian); close residential proximity to bombing; and experiences of kidnapping, imprisonment, torture, and forced displacement. A war index was created to summarize men's often-multiple war exposures, with higher scores reflecting higher numbers of exposures.

In addition to war exposures, other reproductive risk factors were assessed, including various reproductive illnesses, presence of chronic diseases, lifestyle factors (especially tobacco and caffeine consumption), and occupational exposures. This data collection strategy was coupled with laboratory-based semen analysis, which generally was performed at the time of the reproductive interview in the clinic-based IVF laboratories. Semen analysis was reliable and standardized to reflect current World Health Organization guidelines (10).

Data Management and Analysis

After data collection, data were coded and entered by using FoxPro software (version 2.6). Data were analyzed by using the Statistical Package for Social Sciences (version 12; SPSS, Chicago, IL). Univariate analysis consisted of frequency and percentage distributions for the different categorical variables in the study. Means, SDs, and ranges were computed for the different continuous variables, with checking for normality and outliers.

TABLE 1

Patient sociodemographic characteristics.

Characteristic	Cases (n = 120)	Controls (n = 100)
Age, y[a]	38.6 ± 6.7	39.3 ± 5.9
Education, y[a]	13.5 ± 4.2	14.2 ± 5.5
Salary (US $)[a]	1,721 ± 2,435	1,885 ± 2,230
Current residence[b]		
Beirut	42 (35.3)	46 (46.0)
South	25 (21.0)	8 (8.0)
Mount Lebanon	14 (11.8)	10 (10.0)
Elsewhere in Lebanon	13 (10.9)	8 (8.0)
Outside Lebanon	25 (21.0)	28 (28.0)
Religion[b]		
Christian	30 (25)	29 (29.0)
Muslim	86 (71.0)	66 (66.0)
Druze	4 (3.3)	5 (5.2)
Profession[b]		
Blue-collar	16 (13.3)	6 (6.3)
Secretarial related	19 (15.8)	21 (21.2)
Business or teaching	42 (35)	37 (37.4)
Doctor, lawyer, diplomat, or professor	29 (24.2)	28 (28.3)
Government employee	14 (11.7)	6 (6.1)

Note: Data are presented as either mean ± SD or as n (%). Means ± SD were compared by using the *t*-test. Percentages were compared by using the χ^2 test. *P* values comparing cases and controls were not significant for any characteristic.

[a] Data presented as mean ± SD.

[b] Data presented as n (%).

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Bivariate analysis mainly used χ^2 and Fisher's exact test to test the association between the main outcome variable (male infertility) and the various exposure and confounding variables. The purpose of this analysis was to examine crude associations and to check for potential confounders and effect modification.

Multivariate analysis involved a backward logistic regression model, in which analysis included the different exposure and confounding variables that yielded significant results during bivariate analysis. Odds ratios, *P* values, and confidence intervals were computed at a type I error alpha value of 5%. The final model incorporated the exposure and confounding variables that displayed the most significant odds ratios.

RESULTS

As shown in Table 1, there were no significant differences between cases and controls in terms of sociodemographic background. The average age in both groups was 39 years, and most subjects had completed high school. The average monthly income in both groups was around US $1,800. The majority of cases and controls resided in Beirut (46% vs. 35%). The religious backgrounds of cases and controls were similarly heterogeneous. Controls were slightly more likely to be white-collar professionals; however, the professional background of both groups was relatively similar. Reflecting Lebanon's comparatively high educational levels, around 60% of cases and controls held professional-sector jobs, including as physicians, engineers, professors, and businessmen.

When questioned about their experiences of the Lebanese civil war, cases tended to report more exposures to war-related events than did controls. Cases were more likely than controls to have participated in the war as fighters, either in militias or in the Lebanese armed services (11% vs. 2%). They also were more likely to report war-related injuries, some of which were obtained as civilians (12% vs. 8%). Injuries included being struck by bullets in the lower and upper extremities, being hit by shrapnel, and being beaten and tortured. A significant percentage of cases resided in areas of heavy bombing during the war period, exceeding the controls by 11 percentage points (60% vs. 49%). A small number of cases also were kidnapped or were forced to flee from their homes. As shown in Table 2, 60% of cases reported exposure

TABLE 2

Distribution of war exposures among cases and controls.

Characteristic	Cases (n = 120)	Controls (n = 100)	*P* values
Residence near bombing			.118
Yes	68 (59.6)	49 (49)	
No	46 (40.4)	51 (51)	
Injury			.392
Yes	13 (11.5)	8 (8.0)	
No	100 (88.5)	92 (92.0)	
Injury of family members			.969
Yes	10 (8.8)	9 (9.0)	
No	103 (91.2)	91 (91.0)	
Participation in fighting			.011
Yes	12 (10.6)	2 (2)	
No	101 (89.4)	98 (98)	
Being kidnapped			.379
Yes	3 (2.6)	1 (1)	
No	111 (97.4)	99 (99)	
Displacement from home			.028
Yes	8 (7.1)	1 (1)	
No	105 (92.9)	99 (99)	
War exposures index[a]			.236
No event	45 (39.5)	51 (51.0)	
One event	44 (38.6)	32 (32.0)	
Two or more exposures	25 (21.9)	17 (17.0)	

Note: Data are expressed as n (%). Percentages were compared by using the χ^2 test.

[a] A nonweighted index of the summation of the presence or absence of one of these self-reported events: residence near areas of heavy bombing, injury, injury to other family members, participation as a fighter, displacement from home, and being kidnapped or tortured.

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one or more war-related events, vs. 49% of controls. It ›uld be noted that the majority of the cases who reported .ng exposed were oligospermic, with sperm counts of !0 million/mL. In addition, 75% of cases who resided ar areas of heavy bombing were oligospermic, as were % of the cases who were injured, 80% of cases who re-rted injuries to other family members, 92% of the cases ıo reported taking part in the war as combatants, 87% of e cases who reported being displaced from their homes, ıd 67% of the cases who reported being kidnapped or rtured.

Although bivariate analysis showed no significant differ-ıces between cases and controls, upon controlling for other ofactors and potential confounders during the multivariate nalysis phase, cases had a 57% increased odds of exposure ɔ one or more war-related events when compared with con-rols. As shown in Table 3, the odds ratio of exposure to war .vents was 1.57, with borderline significance.

)ISCUSSION

This case–control study demonstrates that exposure to war nay be an independent risk factor for male infertility, when ›ther potential confounders and covariates are taken into con-ıideration. In this study, the odds of exposure to the Lebanese :ivil war were 1.57 times higher among cases than controls, a finding with borderline statistical significance. Cases were more likely than controls to report multiple exposures to war-related traumas, and the majority of these cases were found to be oligospermic. Furthermore, cases were significantly more likely than controls to have been exposed to the worst traumas of war, including participation in fighting, kidnapping and torture, and displacement from home.

This study supports the findings of other investigators (1–4) who reported that war may lead to male-infertility outcomes. A study of male Australian veterans of the Gulf War showed that they had a 40% increased risk of having fertility problems (3). In addition, Maconochie et al. (2) reported an increased risk of infertility and a longer time to conception among United Kingdom male veterans of the Gulf War. Fertility problems among these veterans were mainly associated with teratozoospermia and oligospermia, suggesting apoptosis in the testicular germ cells, Sertoli cells, and/or Leydig cells after exposure to war-related chemicals (2). Along the same lines, Abu-Musa et al. (4) found evidence of decreased sperm concentration during the Lebanese civil war and altered sperm morphology after the war, and this was attributed to the likelihood of increased war-related psychological stress. Only one study to date, of male Danish veterans of the Gulf War, has found no evidence of an effect of war on markers of male fertility (5).

The way in which war affects male fertility is not clear. Psychological stress has been shown to correlate negatively with various parameters associated with semen quality, including sperm concentration, motility, and morphology (4, 5, 11, 12). The increased stress levels may be related to the direct impact of the war experience as well as to the deterioration in the physical infrastructure and socioeconomic conditions. The effects of stress may be via the hormonal component of spermatogenesis. There is evidence that such a phenomenon may be related to hormonal changes observed in men during stressful events. Testicular biopsies obtained from prisoners awaiting sentencing, who are obviously under extreme stress, showed complete spermatogenetic arrest in all cases (13). Milder forms of stress, such as that induced as a result of combat or surgery, have been shown to result in depressed levels of T and LH in affected males (14). These effects are thought to be mediated by the release of endogenous opioids and increased cortisol levels along the hypothalamic-pituitary-adrenal axis (14).

TABLE 3

Multivariate logistic regression analysis.

Characteristic	Adjusted odds ratios	*P* value (95% confidence interval)
Infertility problems in immediate family (yes/no)	2.58	.057 (0.971–6.8)
Kinship between parents and/or grandparents (yes/no)	0.865	.756 (0.34–2.17)
Reproductive health index[a] (no. of events)	1.98	.009 (1.18–3.1)
Intake of coffee (cups/d)	1.05	.288 (0.96–1.14)
Intake of soft drinks (bottles/d)	1.07	.677 (0.77–1.47)
Cigarette smoking (cigarettes × y)	0.999	.183 (0.998–1)
Occupational exposures (yes/no)	1.32	.556 (0.527–3.29)
War exposures index (no. of events)[b]	1.57	.056 (0.989–2.49)

[a] A nonweighted index of the summation of the presence of one of these self-reported conditions: adult-onset mumps, varicoceles, testicular injuries, sexually transmitted diseases, spinal cord injuries, impotence, or premature ejaculation.

[b] A nonweighted index of the summation of the presence or absence of one of these self-reported events: residence near areas of heavy bombing, injury, injury to other family members, participation as a fighter, displacement from home, and being kidnapped or tortured.

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Impaired male reproductive function also may be due to the use of reproductive toxicants during war. In Lebanon, periods of heavy bombing, importation of toxic waste from Europe, improper disposal of toxic waste in poorly designed landfills, open-air incineration of toxic waste, and haphazard dumping of solid waste in inadequate sanitary landfills were part and parcel of the civil war and contributed heavily to the environmental degradation of the country (9). These environmental challenges are of significant concern, given that they pose ongoing risks to air and water quality in the country (15). Heavy metals in particular, including lead, are well-known reproductive toxicants. Whether heavy metals and other forms of long-term reproductive toxicity are impinging upon male fertility in Lebanon remains to be studied. However, reproductive toxicity, along with ongoing postwar stress, may be implicated in the findings of the current study.

Further detailed research to determine the extent, intensity, and types of war-related exposures, as well as their reproductive health impacts, clearly are needed for Lebanon and elsewhere. Research on war and male infertility has just begun but is especially important for the Middle East. This geographical region has suffered through many long-term wars during the past 25 years, including the 8-year Iran–Iraq war; the 15-year Lebanese civil war; and the second Gulf War, now in its 4th year. Furthermore, Lebanon has reentered a period of war and political violence, beginning with the assassination of its prime minister on February 14, 2005 and then the 1-month Israel–Hezbollah clash in July 2006. This 1-month war resulted in a huge unexploded ordinance problem (an estimated 8,500 unexploded ordinances) and had tremendous impacts on the physical environment in Lebanon. Thousands of hectares of agricultural land and greenhouses were destroyed, combined with a 15-ton oil spill into the Mediterranean Sea. These types of environmental and ecosystem disruptions have severe long-term impacts on water and air quality, resulting in impairments to human health (16–18).

Assessment clearly is needed of how different types of warfare, including aerial warfare and on-the-ground combat, affect the reproductive health of both soldiers and male civilians, in the Middle East region as a whole and in Lebanon. Such types of war-related exposure cannot be taken lightly; various chemical toxicants with long half-lives may affect fertility not only of current generations but also of their offspring (19).

One limitation of this study is its reliance on self-report of war exposures. However, such exposures are unlikely to be easily forgotten. Indeed, Lebanese men in this study often talked at great length about their war experiences, detailing their wounds, imprisonment, and evenings spent in bomb shelters, among other things.

Another limitation of the study is its external validity, because a clinic-based convenience sample was used instead of a population-based random sample. However, the study population was selected from two major infertility clinics in Beirut, both drawing patients from the different communities around the country. A larger sample size would have increased the power of the study; however, limitations of time (8 mo) and the stigma of male infertility in Lebanon compromised the recruiting of a larger study sample. These problems of power were not substantial, because the total sample size (220) did not differ markedly from that based on computed power calculations.

In conclusion, this case–control study shows a possible association between male infertility and men's various exposures to the civil war in Lebanon. Such findings must be further assessed through prospective cohort studies among men—both civilians and soldiers—who are facing war in other parts of the Middle Eastern region. Specific and intensive focus on chemical measures is advisable, to determine possible causal mechanisms for male reproductive impairments. We postulate that the observed associations in this study may be due to both increased stress levels and increased chemical exposures, leading to poor sperm counts among vulnerable men who endured the hardships and atrocities of the Lebanese civil war.

REFERENCES

1. Maconochie N, Doyle P, Carson C. Infertility among male UK veterans of the 1990-1 Gulf war: reproductive cohort study. BMJ 2004;329: 196–201.
2. Sim M, Abramson M, Forbes A, Glass D, Ikin J, Ittak P, et al. Australian Gulf Veterans' Health Study 2003. Vol 2. Commonwealth Department of Veterans' Affairs, 2003. Available at: http://www.dva.gov.au/media/publicat/2003/gulfwarhs. Accessed May 10, 2004.
3. Zorn B, Sucur V, Stare J, Meden-Vrtovec H. Decline in sex ratio at birth after 10-day war in Slovenia. Hum Reprod 2002;17:3173–7.
4. Abu-Musa A, Nassar AH, Hannoun AB, Usta IM. Effect of Lebanese Civil War on sperm parameters. Fertil Steril. In press.
5. Ishoy T, Andersson AM, Suadicani P, Guldager B, Appleyard M. Major reproductive health characteristics in male Gulf veterans. Dan Med Bull 2001;48:29–32.
6. Saxena C, Kulczyck A, Jurdi R. Nuptiality transition and marriage squeeze in Lebanon: consequences of sixteen years of civil war. J Comp Fam Stud 2004;35:241–58.
7. Jabbra N. Family change in Lebanon's Biqa Valley: what are the results of the civil war? J Comp Fam Stud 2004;35:259–70.
8. Joseph S. Problematizing gender and relational rights: experiences from Lebanon. Social Politics 1994;1:270–85.
9. Hamdan F. The ecological crisis in Lebanon. In: Ellis K, ed. Lebanon's second republic: prospects for the twenty-first century. Gainesville, FL: University Press of Florida, 2002:175–87.
10. World Health Organization. WHO laboratory manual for the examination of human semen and sperm-cervical mucus interaction. 4th ed. New York: Cambridge University Press, 1993.
11. Giblin PT, Poland ML, Moghissi KS, Ager JW, Olson JM. Effects of stress and characteristic adaptability on semen quality in healthy men. Fertil Steril 1988;4:127–32.
12. Bigelow PL, Jarrell J, Young MR, Keefe TJ, Love EJ. Association of semen quality and occupational factors: comparison of case control analysis and analysis of continuous variables. Fertil Steril 1998;69:11–8.
13. Steve H. Der ein Fluss de nerven System auf ban und Fatigkeit des Geschlechtorgane des Menschen. Stuttgart, Germany: Theim, 1952.
14. Cui K. The effect of stress on semen production in the marmoset monkey (Callithrix jacchus). Hum Reprod 1996;11:568–73.
15. Ministry of the Environment (MOE), Lebanon. State of the Environment Report. p. 41. Available at: http://www.moe.gov.lb/NR/rdonlyres/C694D7C7-C46A-4D9B-9AFB1459B95EF33A/0/Chap3Industry.pdf. Accessed July 19, 2005.

16. United Nations Office for the Coordination of Humanitarian Affairs (OCHA). Revised Lebanon Crisis Flash Appeal 2006. Available at: http://www.reliefweb.int. Accessed September 18, 2006.
17. Government of Lebanon. Setting the stage for long-term reconstruction: the national early recovery process. Presented at the Stockholm Conference for Lebanon's Early Recovery, August 31, 2006. Available at: http://www.lebanonundersiege.gov.lb. Accessed September 18, 2007.
18. United Nations Development Programme document: Lebanon. Quick delivery-high impact. Projects for the Immediate Post-Ceasefire Period. 2006. Available at: http://www.undp.org.lb. Accessed September 18, 2006.
19. Fahey D. The emergence and decline of the debate over depleted uranium munitions, 1991-2004. Available at: http://www.danfahey.com. Accessed April 14, 2006.

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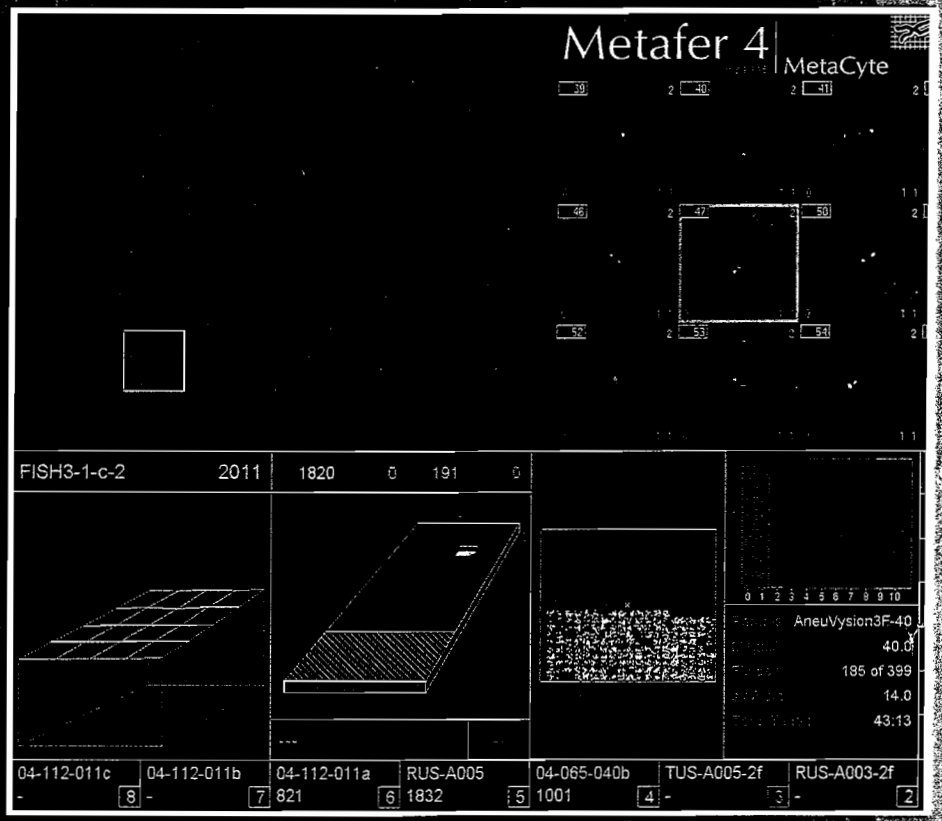

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