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Pregnancy Outcome Among Iraqi Soldiers & Civilians in Iraq and Gulf War 1991

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Abstract

Context: Although Iraqis were exposed to very severe conditions during the 1991 Gulf War, we have very little information on the effect of distance from the war zone on the outcomes of pregnancy and congenital anomalies in children.

Aim: To determine if pregnancy outcomes vary by distance from the 1991Gulf War battle zone.

Methods: The study sample consisted of men between the ages 18-45 years and residents within 360 kilometres in Iraqi providences of Basra & Messan at time of 1991 Gulf War. During 2002, 720 out of 1150 participant were enrolled in the study because they were married and had at least one child. We divided the population study into two main groups: battle and non-battle zone and studied the effects of war on pregnancy outcomes.

Results: Congenital anomalies in the non-battle zones appear to be significantly higher, which implies that the impact of war was not restricted to the war zone.

Conclusion: There is no relationship between geographical closeness to Kuwait and adverse pregnancy outcome.

Keywords: Birth defects; Chemicals exposure; Gulf war; Pregnancy outcome; Stressors exposure

Introduction

War stress can cause all kinds of diseases, in addition to decreased birth rate, increases in ectopic pregnancy rates and a sharp increase in inborn defects [1]. Prenatal stress is associated with pregnancy complications and complications later in life [2,3]. There is a significant rise in abortion, low birth weight, multiple pregnancies and major congenital anomalies in the post war period [4], Previous studies reveal that children born to Gulf War Veterans (GWV) have increased rates of birth defects in connection with their parents war time survival [5-7].

Other studies indicate that birth defects may occur at higher rates in children of deployed GWV than in children of non-deployed GWV [8]. Araneta reported that Goldenhar syndrome was more common among deployed veterans more than non-deployed GWV [9]. Children born to GWV after the war had certain kidney defects that were not found in GWV children born before it [10]. Also, congenital heart defects are the commonest birth defects in the children of GWV [11]. In Kuwait there was an increased incidence of congenital heart defects following the end of the Gulf War (GW) period [12]. The Research Advisory Committee ([8] report discussed the abnormally high rate of birth defects found by several researchers [13-15]. Later studies did find that a limited number of adverse outcomes occurred more commonly in GWV than non-deployed veterans [16]. However, Kang [17] showed that higher rate of miscarriages found in GWV whether male or female compared with their controls [17].

Adverse reproductive outcomes have also been reported among American and Canadian GWV including miscarriages, birth defects, and sexual dysfunction. The United States Accounting Office identified 21 potential reproductive toxicant and teratogens that present in the environment of GW with female veteran exposure to teratogens associated with reduced levels of reproductive hormones among air force personnel [17-20].

Mustard gas exposure in Iran affected parents' fertility and impacted children health and development in the long term [21]. The Kristic study reported that there is an increased percentage of abortions after 12 week gestation after the bombing of Yugoslavia [22] while, in Bosnia and Herzogovenina, there was a decrease in the number of deliveries and increased rate of prenatal and maternal mortality and preterm deliveries [23], while Kang revealed a significant association among index children with mothers' military service in Vietnam [24] and the percentage of miscarriage was higher in Vietnam veteran than controls [25]. High frequency of birth defects and miscarriages was also observed in Fallujah, Iraq after 2003 [26].

Conversely, several studies found that the risk of birth defects in those who served in the GW or who never served in it approximate the risk in general civilian population, suggesting no relationship between service in the GW and severe birth defects (birth defect study of veterans' children showed no linkage to service in the war of 1991 [27]. In one study done in Hawaii the prevalence of birth defects was similar for GWV and non-deployed veterans' children who were conceived both before and after the war [27]. The prevalence of major birth defects sponsored by the Department of Défense was 3-4% with the most commonly diagnosed birth defects being patent ductus arteriosus, hypospadious and epispadious, ASD and VSD. This is consistent with civilian birth defects surveillance data [28].

Wells states that there is no association present between service in the 1991 GW and adverse reproductive outcomes after the war [29], also Penman revealed that there is no evidence of an increase in birth defects and health problems among children born to Persian GWV [13]. David also discovered that there is no association between the risk of severe birth defects and service in the Gulf War for either men or women [30], Doyle concluded that there is no evidence to date for an effect of service in the first GW on the risk of major birth defects in offspring conceived after deployment whilst for infertility and miscarriage, there is some evidence of a small increased risk associated with service in GW [31].

A study by Verret revealed no evidence for association between paternal exposure during the GW and increased risk of birth defects among French Persian GWV children [32], also there is no evidence that war time conditions impedes perinatal survival in Norway after World War II, whether directly or indirectly [33]. There was no significant post war increase in the prevalence of congenital malformations despite pollution in the same region of former Yugoslavia [34]. Also in United Kingdom veterans, there was no evidence of a link between parental deployment to GW and increased risk of still births, chromosomal malformations or congenital syndromes [35], while for male Australian veterans of the 1991 GW, one study done by Kelsall did not reveal an increased risk of adverse reproductive outcome in the Australian male of GWV[36]. Erickson revealed that there was no association between greater opportunity for exposure to agent Orange in the Vietnam War and overall risk of fathering a baby with all types of birth defects combined [37]. There are different factors when comparing deployed and non-deployed solders, besides GW exposure and environmental exposure, e.g. most deployed soldier was not accustomed to the geographic characteristics and climate of the region [38]. Another major limitation is when other previous studied soldiers had left the Gulf region to their original countries for some time [39].

Pregnancy outcomes vary by geographical distance from GW 1991 battle zone. Two objectives will be tested:

The aim of the study is to determine if

1. If the impact of the war environment on birth defect outcomes in pregnancy is different according to war zone; and
2. If the prevalence of birth defects in GW 1991 is different according to war zones.

Methods

The study sample consisted of men only who were soldiers or civilians between the ages of 18-45 years and a resident in the Iraqi provinces of Basra and Messan at time of the 1991 Gulf War. They had to live within 360 kilometres of the war zone (Kuwait) border to be eligible for the study. Out of 1150 eligible participant enrolled during 2002, only 720 were included in the study because they were married and had at least one child. Resident physicians from Basra University were trained to participate in data collection through a constructive interview. Individuals who accompany patients to three outpatient government clinics in Basra and Messan provinces in Iraq were the target population. The three clinics were run by the Iraqi Health Ministry and available to all Iraqis.

The resident physicians followed a standard algorithm to identify and interview the participants. Potential participants were asked about their interest in participating in a health study of GW. Participation was voluntary and respondents were able to withdraw from the study at any time. A verbal consent was obtained. To ensure confidentiality, interviews were done in a physician's office. The questionnaire used was based on a survey used in several studies of American GWV [40-41]. This original questionnaire was translated into Arabic and then re-translated into English to ensure the validity of the questions. The questionnaire included questions regarding demographic characteristics, smoking history and medical conditions (illnesses; symptoms). The distance from the Kuwait border (stationed or residential) was inquired from the participants and was classified into two zones: Battle Zone which included those who lived within 100 kilometres from Kuwaiti border and by that Non-Battle Zone. included those who lived within 100-300 kilometres from the Kuwaiti border. Participants recorded their city or villages in which they resided during the 1991 GW. We assigned the zones based on the distance from Kuwait. Included individuals in the study were asked about their wives' previous conception status and any abnormality or history of death in their born children, those reported abnormal or stillborn children. They were asked more detailed questions about the abnormal or stillborn child by the research team (resident physician) to identify the nature of the abnormality.

Chemical and Non-Chemical (psychological) environmental war exposures were assessed by asking the respondents a series of questions, e.g. for chemical exposure: "During the GW did you have direct contact with the following exposure? smoke from oil fires, exhaust from heaters or generators, diesel fumes, petrochemical fuel on your skin, exposed to pesticides or your cloth contaminated with pesticide, food contaminated with chemicals, burning trash or faeces, water contaminated with chemicals and bathe or swim in a local pond, river, or the Gulf sea. For non-chemical exposure questions included e.g. hearing chemical alarms sounding, scud missiles exploding within one mile, artillery fire within one mile, coming under small arms fire, seeing dead bodies and seeing people emotionally stressful. The chemical and non-chemical environmental exposure score was calculated by aggregating the respondent's answer to 12 chemical and 8 non-chemical environmental exposure questions. The score was then converted into a percentage with 0% representing the lowest exposure and 100% representing the highest level of exposure. This calculation was applied for each question of the 20-questionnaire based on duration of exposure and severity of exposure. The Cronbach's alpha for the chemical exposure scale was 0.87, while the Cronbach's alpha for the nonchemical exposure scales was >0.75 [14,43]. All the analysis was done with SPSS Version 19 and the statistical significance was set at $P < 0.05$, two sided.

Results

Of the total study group (n=720), 604 were in non-battle zones, whilst 116 were within the battle zone. Table 1 shows mean and SD of some variable while Table 2 shows the number and percentage of participants in each zone by demographic variables. Significant differences between the two groups was found in the subcategory of most of the demographic variables e.g. age, education, occupation, all exposure [Chemical exposure and non-chemical], also when comparing birth defects to normal pregnancy or when the frequency of birth was tested between the two groups. Table 3 displays the outcome of pregnancy in the study population in which most of the population reported no birth defects; chromosomal abnormalities and congenital heart disease being the most common birth defect in the two zones. While Table 4 shows that age, education and environmental exposure [Chemical and Non-chemical] and the predict risk factors for birth defects among participants who were present in GW 1991.

Variable	Non-Battle Zone (n=604)		Battle Zone (n=116)		Total (n=720)	
	Mean	SD	Mean	SD	Mean	SD
Age ***	28.9	4.92	30.4	3.0	29.1	4.71
All Chemical & Non-chemical Environmental Exposure ***	3.0	8.83	6.8	7.79	3.7	8.78
Only Chemical Environmental Exposure ***	1.3	4.12	6.3	7.52	2.1	5.16
Only Non-chemical Environmental Exposure* **	5.0	15.00	7.5	11.59	5.4	14.53

*** $P < 0.001$

Note: The total numbers of participants depend on the numbers of respond to each variable

Table 1: Test of significance between study groups and different variables (part 1).

Variable	Non-Battle Zone		Battle Zone		Total Population	
	No.	%	No.	%	No.	%
Education *						
H.S. or less	484	81.5	84	73.7	568	80.2
> High School	110	18.5	30	16.3	140	19.8
Occupation at time of survey ***						
Other Occupation	368	63.1	84	78.5	452	65.5
Health Profession/	143	24.5	13	12.1	156	22.6
Smoking status *						
Smokers	330	55.4	76	65.5	406	57
Never smoke	266	44.6	40	34.5	306	43
Birth Defect **						
Normal birth	556	92.1	113	97.4	669	92.9
Defect	48	7.9	3	2.6	51	7.1
Frequency of Birth ***						
One child	79	13.1	6	5.2	85	11.8
Two children	126	20.9	13	11.2	139	19.3
Three Children	117	19.4	22	19	139	19.3
Four Children	97	16.1	23	19.8	120	16.7
Five Children	74	12.3	17	14.7	91	12.6
Six Children	53	8.8	8	6.9	61	8.5
7-13 Children [Range]	58	9.4	27	23.2	85	11.8
*P < 0.05; ** P < 0.01; *** P < 0.001						

Table 2: Test of significance between study groups and different variables (part 2).

Grouping Birth Defect	Type of defect	Zone of participants				
		Non-Battle Zone		Battle Zone	All Zone	
Chromosomal anomalies	**Down's Syndrome**	10	4.52	1.81	11	3.98
Congenital heart disease	**Cong. Heart dis.**	10	4.52	1.81	11	3.98
Neural tube defect	**Meningocele**	2	0.9	1.81	2	0.72
	Skull Defect	2	0.9		2	0.72
	Spine Bifida	1	0.45		1	0.36
	Hydrocephaly	2	0.9		3	1.09

Miscellaneous	**Neonatal Asphyxia**	3	1.36		3	1.09
	Epilepsy	3	1.36		3	1.09
	Slow physical growth	2	0.9		2	0.72
	Jaundice /Child Dead	2	0.9		2	0.72
	Cleft Lip	2	0.9		2	0.72
	Cerebral Palsy	2	0.9		2	0.72
	Birth Trauma	2	0.9		2	0.72
	Imperforated Anus	2	0.9		2	0.72
	Still birth	2	0.9		2	0.72
	Club Foot	2	0.9		2	0.72
	Poor Vision	2	0.9		2	0.72
	Abnormal baby	2	0.9		2	0.72
	Low birth Weight	1	0.45		1	0.36
	Polydactyly	1	0.45		1	0.36
	Splenomegaly	1	0.45		1	0.36
Total birth defect		56	25.3	5.44	59	21.37
Total birth without defect		2160			2708	979
Total birth		2210			2761	1000
Total Population		604			720	

Table 3: Number & Prevalence of birth defect and [type and group] per 1000 birth by Battle Zone.

Likelihood birth defect	Sig.	Odds Ratio	95% C.I. for OR	
			Lower	Upper
Participants in Battle zone were Reference	.003	6.467	1.859	22.504
Chemical &Non-chemical Exposure [Continuous]	.000	4.200	2.131	8.281
Age [Continuous]	.007	1.091	1.024	1.163
High School & above were Reference	.061	2.785	.956	8.117
Occupation	.471	1.371	.582	3.229
Smoking	.223	1.460	.795	2.684
Constant	.000	.000		

Table 4: Logistic regression analysis to predict risk factors to birth defect among participants who were present in GW 1991.

Discussion

To the best of our knowledge, this is one of the first epidemiological studies of adverse pregnancy outcomes in soldiers and civilians in Iraq involved in Gulf War operations in 1991. Moreover, we have assessed Iraqis and applied a theoretical dose response model, based on priori assumptions [24,39]. Those in battle zone were hypothesized to have been more exposed to chemical environmental agents, including chemical warfare agents and oil fire smoke. Individuals battle zone were hypothesized to exhibit higher cumulative harmful war related effect of exposure as compared to those further away from Kuwait. The highest war related exposure was predicted to be in south west of Iraq where the largest chemical weapon storage and destruction took place including aerial bombing by the Allied forces.

This is also one of the first studies to collect detailed environmental exposure data and relate it to adverse birth outcomes in culturally and ethnically identical populations in two zones from the centre of the war. A major concern in studies based on retrospective exposure and outcome data is possible recall bias and preferentially recall. We therefore grouped the adverse pregnancy outcomes into four main groups according to the ICD-9CM nationally recognized coding system that identify birth defects in 45 major malformation categories [c] and studied their prevalence in the two study zones according to their closeness to the war central Kuwait, by this we believe, we have been able to control possible reporting bias.

Another study concern is that maternal age was not part of the questionnaire, paternal age was taken instead and the questionnaire used was based on a survey used in several studies of US GWV [40,41], but as per Doyle [31] al, no link was found between paternal deployment to the Gulf War and increased risk of stillbirth, chromosomal malformations, or congenital syndromes. Associations were found however between fathers' service in the Gulf War and increased risk of miscarriage and less well-defined malformations, and there was no evidence of an association between risk of miscarriage and mothers' service in the Gulf.

We were able to reject the hypothesis that says the Iraqi veterans are more prone to adverse pregnancy outcomes because of higher exposure to a war environment and this comes in agreement with Verret [32]; Kelsall [30]; Wells [29]; Doyle [31]; Sumanovic [34]; Doyle [35]; Araneta [27]; David [30]; Penman [13]. However, we are in disagreement with other researchers [1,4,6,7,8,18]. Of special concern is that congenital anomalies, for example, congenital heart disease and chromosomal anomalies are mostly prevalent in the Non-battle zone (>=100 km). We have no children with Goldenhar syndrome or kidney defect which does not fit with Araneta and Gamboa studies [9,10]. In the Verret [32] study, the percentage of birth defect was 2.7%, and the main defects were musculoskeletal abnormalities (0.5%) and urinary abnormalities (0.3%) [32], the main defects were chromosomal anomalies (3.98/1000) and heart defects (3.98/1000), which is close to the Sumanovic [34], study as the musculoskeletal defect factor also was the highest (2.82/1000) in 1995 and 2.26/1000 in 2000 [34]. Of the 604 persons inhabiting the non-battle zone, only 10 civilians came with children that have chromosomal anomalies with the prevalence of 4.52/1000 which is much more than 1.81/1000 in battle zone. This is may be because they were not taking any protective measures against environmental exposure to war agents, while in the Sumanuvic [34] study the prevalence of chromosomal anomalies in civilians was 2.16/1000 and in Sumanuvic (1995) was 2.05 /1000 [34].

The prevalence of congenital heart disease in our study was 4.52/1000 in non-battle zones and 1.81/1000 in battle zones. This in agreement with several prior studies [12,18,26,34]. While the neural tube defect prevalence in non-battle zone was 3.15/1000 compared to battle zone 1.81/1000. In Sumanovic-Glamuzina it was 2.73/1000. Gastrointestinal Tract (GIT) defects like imperforate anus prevalence in non-battle zone was 0.90/1000 while in the Sumanovic-Glamuzina study was 3.42/1000 and was 6.4/1000 in deployed soldiers in Araneta (2003) study [18]. Spina bifida was found only in one patient in the non-battle zone with prevalence of 0.54/1000 while the prevalence of spina bifida in Araneta (2003) study was 4.3/1000 in deployed and 4.5 /1000 in non-deployed [18]. Reasons for magnified results of birth defects in non-battle zones in our study may be due to reporting issues or maybe due to associated increased exposures during the war to air bombardment and no protected against environmental exposures.

Having resident physicians deliver the survey questions may decrease reporting errors; conversely, looking further into respondents reported exposure indices may shed light on reason for the increased prevalence found in our study. Other reasons for more birth defect in the non-war zone could be secondary to foliate deficiency in both areas secondary to the war effect as M. Al-Sabbak, et al. [44] showed 17-fold increase in birth defects in the Iraqi cities of Al Basrah (in south of Iraq) and Fallujah (in Central Iraq) are mainly foliate dependent defects. In our study, this data set was not originally used for the purpose of analysing pregnancy outcomes and this may have limited the recall bias present within respondents. There was inclusion of individuals with reportedly high level of exposures. We were able to control reasonably well for confounding factors such as smoking status and occupation. This held true even after adjusting the confounders. There were no differences in smoking habits between deployed soldiers and civilians as revealed by having the mean value. Although the study sample is considered as a convenience sample, the participants were blindly selected as they were accompanying patients who attend three general governmental outpatients' clinics for different reasons in two the provinces. Also studying the impact of the chemical and non-chemical environmental exposures on the outcome pregnancy especially the study data were collected from people still living in the Gulf area for more than 10 years after the GW 1991.

In this study we concluded that there is no relationship between geographical closeness to Kuwait and adverse pregnancy outcome and we reported that person who lived close to the war zone have less prevalence adverse pregnancy outcome than those live far from the war centre which could indicate the whole Iraq was expose to different chemical and non-chemical environmental exposure because of the GW 1991.

Conclusions

For future studies on war and pregnancy outcome, this study demonstrates the importance of including specific factors of exposure as well as duration of exposure, using more than location or deployment as factors of exposure and to consider the war zone effect on other outcomes as prematurity, and long term childhood developmental war effects between the war zones. This study also decreases the disparity that exists in the reproductive health of Iraqi civilians and soldiers exposed to the 1991 GW and therefore sheds light on the importance of not only studying the implications of war on veterans but also on the civilians who are exposed to the war.

Author Contributions

H. Jamil had full access to all of the data in the study and takes responsibility for statistical analysis.

T. Hamdanm supervised the data collection in the field.

S. Yaso wrote the draft of the article.

S. Shukri checked the accuracy of the data and interpreted the results.

S. Aljoboori, S. Rawaf, E. Dubois, and B. Arnetz integrated the data and improved the draft of the writing. All authors contributed to the final writing of the manuscript.

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Competing Financial Interests:

There are no competing financial interests.

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